

Section 10 Clinical and Counseling Procedures

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Section 10 Clinical and Counseling Procedures

This section presents information related to the clinical assessments and counseling sessions performed for HPTN 058. The clinical assessments include obtaining medical histories and performing physical examinations on participants. The counseling procedures include pre- and post-test HIV counseling, and drug- and risk-reduction counseling. A thorough description of the drug- and risk-reduction counseling principles and procedures is provided in the BDRC Counseling Manual. Detailed information on performing laboratory procedures to complement clinical assessments is presented in Section 11 of this study-specific procedures (SSP) manual. Detailed information on completing data collection forms associated with these activities and on safety monitoring and adverse event (AE) reporting is provided in SSP Section 7 and Section 12 respectively.

10.1 Screening Procedures

A focused baseline medical history and physical examination are obtained from potential study participants at screening. Medications used by the participant also are ascertained and documented at this time. This information is used to:

- Assess and document participant eligibility for the study,
- Assess use of concomitant medications that may interact with BUP/NX (including those taken previous to initial administration of BUP/NX as the medication may not have been fully excreted),
- Assess and document the participants' baseline medical conditions for comparison with signs, symptoms, and conditions that may be reported during follow-up.

10.2 Initial Screening Visit

No protocol-specified procedures or assessments can be undertaken until written informed consent is obtained, which begins the actual study screening process. Activities undertaken prior to this are considered 'pre-screening' activities. For most participants, the study screening process will take place over two or more visits. Regardless of the number of screening visits required, eligible participants must be randomized within 28 days of the initial blood draw for HIV testing.

Documentation to address all of the eligibility criteria, including but not limited to, the clinical eligibility criteria above must be present in the participant's record. Acceptable and appropriate documentation would be:

“Participant does not have any serious medical or psychiatric condition that would make participation unsafe or would otherwise interfere with study objectives or interpretation.”

A blanket statement regarding inclusion is not acceptable. An example of *inadequate* documentation is:

“The participant meets all inclusion criteria outlined in the protocol.”

The Eligibility Checklist is not to be utilized for source documentation of any eligibility criteria.

10.2.1 Pre- and Post-test HIV counseling

All sites will perform two rapid HIV tests and confirm all positive or discordant results with a WB or IFA. Each site is required to develop a local standard operating procedure (SOP) for HIV pre- and post-test counseling. Although these SOPs will be site-specific, they should all contain the following elements:

Informed decision and informed consent

- Each individual should be provided with enough information to make an informed decision about whether or not to be tested for HIV.

Confidentiality

- The HIV testing and counseling procedures should be conducted in a place and manner to ensure privacy and confidentiality.
- Participants should be assured that their HIV status will not be revealed to others without consent.

Appropriate counseling

- Testing should be linked with information and recommendations regarding HIV, specifically: risk avoidance, risk reduction and treatment options.
- Adequate pre- and post-test counseling should be provided to all individuals being tested.
- Disclosing HIV status to others should be discussed with all participants.

Referrals

- Appropriate referrals will be made as available at each site. Referral lists will be updated at least every six months (see Appendix IV of protocol).

Resources for HIV voluntary counseling and testing (VCT) procedures are listed below:

“Revised Guidelines for HIV Counseling, Testing, and Referral,” set forth by the CDC in 2001. This document can be downloaded at <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5019a1.htm>.

“Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings,” the CDC updated some of the above guidelines in 2006.

This document can be downloaded at <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5514a1.htm>

“HIV Voluntary Counseling and Testing (VCT): A Reference Guide for Counselors and Trainers,” which was revised by the Institute for HIV/AIDS at Family Health International in January 2004. A copy of this document can be requested from the CORE protocol specialists.

10.2.2 Assessing Opioid Dependence

The diagnosis of opioid dependence is based on criteria set forth in the Diagnostic and Statistical Manual, 4th Edition (DSM-IV). The diagnosis is made after a clinical interview using the DSM-IV Worksheet (see SSP Appendix F) and is based on a cluster of behaviors and physiological effects occurring within a specific time frame. While this assessment may be performed by a

staff member such as an interviewer or counselor, the study physician must approve the diagnosis during the clinical portion of the screening. The diagnosis of opioid dependence rather than opioid abuse is required for inclusion in this study.

10.2.3 Screening Laboratory Assessments

Detailed information on specimen preparation is available in Section 11 of this SSP manual. Stored sera drawn at the Screening Visit will be tested for HIV in the case that a participant tests HIV-positive later in the study. For participants who do not consent to long-term specimen storage and possible future research testing, archived serum will be discarded after all protocol-required and quality assurance testing has been completed.

Blood and urine specimens will be prepared for laboratory assessments listed below.

- Hematology (CBC and platelet count)
- Blood chemistry (creatinine)
- Liver function tests (ALT, bilirubin)
- Hepatitis B surface antigen and hepatitis C antibody testing
- Urine test for opiates and other drugs
- Urine test for pregnancy

It is expected that the results from the hematology, chemistry, and liver function will be available approximately one week following the screening visit. Study physicians must review the results of the tests to determine final eligibility or if further testing is required. Each site will determine the procedures for informing participants of their laboratory results, scheduling the enrollment visit (if eligible), and making referrals for conditions identified by laboratory assessments. Enrollment and randomization must occur within 28 days of the initial screening blood draw for HIV testing.

10.2.4 Screening Medical History

If participants are HIV negative and meet other initial screening criteria, a targeted medical history will be taken to further assess eligibility and baseline health. The sites may use their own medical history form or the non-DataFax Medical History form supplied by SCHARP (Appendix F of this SSP). This will be the source document for collecting pertinent medical history data. For enrolled participants, all ongoing baseline conditions identified prior to randomization also are documented on the DataFax Pre-existing Conditions form (PRE-1). Recurring and/or chronic conditions are considered ongoing whether or not they are present or active at baseline.

When obtaining a targeted medical history for HPTN 058, it is not necessary to document the participant's lifetime medical history. Rather, focus on conditions that have occurred since the participant became a drug user, and probe for the most accurate information available on the participant's current health status. Several additional guidelines are presented below:

- Record symptoms, illnesses, allergies, and surgeries
- Record both chronic and acute conditions, including psychological and cognitive conditions, as well as both ongoing and resolved conditions

- Pregnant or currently breast-feeding; current use of birth control
- Record suspected *acute* hepatitis
- Record any current use of medication, including methadone, and why (see SSP section 10.2.6)

10.2.5. Pre-existing conditions

All ongoing conditions identified in the baseline history should be documented on the DataFax Pre-Existing Conditions form (SSP Appendix F) and graded in the source documentation. Recurring or chronic conditions are considered ongoing whether or not they are active at baseline. For example, oral Herpes Simplex Virus could be listed as a pre-existing condition if the participant has a history of recurrent oral herpetic lesions. Other examples of pre-existing conditions that a participant reports but are not apparent during screening, such as asthma, TB, and skin conditions, will also be reported as a pre-existing condition.

10.2.6 Concomitant Medications

The HPTN 058 protocol requires documentation of all medications taken by all participants beginning at screening and continuing throughout Week 52. For purposes of this study, medications include prescription and “over-the-counter” medications and preparations, regardless of route of administration. Vitamins and other nutritional supplements should be included, as well as herbal and naturopathic preparations. Starting with the screening visit, the DataFax Concomitant Medications Log form (CM-1) is used to collect information on participant’s use of medications. Concomitant medications should be documented for all participants whether or not they are being treated with BUP/NX.

Each month, preferably at the same visit when participants have the urine drug screen, the staff will actively assess use of concomitant medications and follow-up on previously listed medications. At any time during the first 52 weeks of treatment, participants may report use of other medications, herbs, or nutritional supplements. Staff will update the concomitant medication log whenever they become aware of changes. Medications taken and stopped during the 28-day screening period must still be reported on the Concomitant Medications Log form (CM-1).

10.2.7 Screening Physical Exam

During screening, a physical exam will be performed to determine eligibility and baseline health status. The site may use their own form or chart notes to document the physical exam or the non-DataFax Physical Exam supplied by SCHARP (Appendix F). Unless otherwise indicated, height, weight, and temperature are reported in metric terms. The exam will be performed according to standard procedures at the site but at a minimum is recommended to include assessment and documentation of:

- General status: mood, orientation, pain, hygiene
- Vital signs:
 - Weight and height
 - Respiratory rate
 - Pulse

- Blood pressure, diastolic and systolic
- Temperature, oral or infrared ear thermometry
- Skin: rashes, scars, bruising, needle tracks, jaundice
- Mouth: presence of lesions or exudates; oral hygiene
- Heart: rhythm, murmurs, endocarditis
- Lungs: observation of character of respirations, auscultation
- Abdomen: palpable spleen, liver
- Lymph: palpable cervical, axillary and/or inguinal lymph nodes
- Assess any psychological disturbance or cognitive impairment interfering with the participant's ability to comply with the study visit schedule and procedures
- Assess any other medical or psychiatric condition that would make participation in the study unsafe or interfere with interpreting the study data or achieving the study objectives.

All pertinent exam findings may be recorded on the Physical Exam non-DataFax form or on a site specific form; all abnormal or ongoing findings should also be recorded on the Pre-Existing Conditions DataFax form.

10.3 Drug- and Risk-Reduction Counseling

All enrolled participants will receive drug- and risk-reduction counseling throughout the first year of enrollment. The counseling will be conducted in individual sessions, based on a model of relapse prevention and skills building. These counseling services will be delivered weekly during the first 12 weeks followed by monthly sessions every four weeks through week 52. Weekly individual counseling visits will last about 45 minutes and will start no later than one week following randomization. Supervising staff will conduct periodic reviews of counseling content and administration to assure quality of the counseling intervention. A detailed counseling manual is supplied in Appendix H.

The monthly counseling sessions, beginning at approximately Week 16 and continuing through Week 52, will also follow a standard manual. These sessions will re-emphasize key strategies conveyed and practiced during the first 12 weeks of counseling and focus on strategies for handling challenges faced by participants.

The counseling sessions will start as soon as possible, and no later than a week, following randomization. Ideally, the same counselor will be assigned for each session throughout the year of treatment so that a therapeutic relationship can be sustained. Counseling sessions may be scheduled the same day as dosing visits and, when feasible, follow-up visits at Weeks 26 and 52 to reduce the visit burden on the participant. Whenever a participant is scheduled to receive a dose of BUP/NX and counseling the same day, it is up to the site staff to determine which is scheduled first. Typically, counseling should take place immediately following completion of dosing in order to minimize participant's anxiety about potential withdrawal symptoms if medication dosing is delayed.

10.4 Follow-up Visits

Follow-up visits at Weeks 26 and 52 require an interim medical history and symptom-directed physical exam, as well as associated laboratory tests. Follow-up visits at Weeks 78, 104, 130, and 156 do not include a physical exam or medical history, but do include HIV testing and urine test for opiates.

10.4.1 Assessments during Safety Phase

The first 50 participants enrolled at each site will undergo the following examinations and laboratory tests **each week** during the **first four weeks** of study participation:

- Interim medical history
- Symptom-directed physical exam
- Hematology (CBC and platelet count)
- Blood chemistry (creatinine)
- Liver function tests (ALT, bilirubin)
- Urine tests for opiates and other drugs
- Assessment of social harms
- Acceptability assessment at Week 4 only
- Pregnancy test at Week 4 only for all females

After the first four weeks, the follow-up schedule of procedures will be the same as for all participants.

10.4.2 Interim Medical History

An interim history will be performed each week during Weeks 1-4 for those enrolled during the Safety Phase. Otherwise, an interim history and symptom-directed exam is done at Weeks 26 and 52 on all participants. These follow-up examinations will be driven by signs and symptoms reported by the participant at this or the last visit. All signs, symptoms, and diagnoses should be recorded and graded in the source documentation and followed until resolution. Detailed instructions for reporting and follow-up of adverse events are in SSP Section 12.

At a minimum, the interim medical history is recommended to include:

- Review of medications being taken at the last visit and enquiries about any new medications begun since then.

Note: All medications, including traditional medicines, vitamins, etc., should be recorded on Concomitant Medications Log.

- Follow up on any problems identified at the previous visit.
- An open-ended question, such as “Have you had any health problems since your last exam?”

10.4.3 Follow-Up Concomitant Medications

During follow-up at Weeks 26 and 52, retrieve the participant’s previously completed DataFax Concomitant Medications Log (CM-1), record any new medications provided to the participant by study staff, and **actively** inquire as to whether the participant is still taking medications listed previously, at the same dose and frequency. Also **actively** inquire as to whether the participant

has begun taking any new medications since the last study visit when concomitant medication information was collected. To further probe for updates, if the participant reports any illnesses or symptoms, inquire as to whether any medications were taken in response to these conditions. Add all new information to the DataFax Concomitant Medication Log (CM-1), using additional pages as needed. Concomitant medications are not collected during the second and third year of follow-up.

10.4.4 Symptom-directed Physical Exam

A symptom-directed physical exam will be performed each week during Weeks 1-4 during Safety Phase and at Weeks 26 and 52. These follow-up exams will be driven by problems or issues identified during the interim medical history, as well as at the last follow-up visit. For example, the clinician could ask: “Have you noted any change in your appetite or energy? Have you had any episodes of coughing, diarrhea, or fever?” or similar questions to ascertain change since baseline.

At a minimum the symptom-directed physical exam will include assessment and documentation of:

- General status: mood, orientation, pain, hygiene
- Vital signs: weight, respiratory rate, blood pressure, pulse and temperature
- Skin: rashes, scars, bruising, jaundice, needle tracks
- Heart: rhythm, murmurs
- Lung: observation of character of respirations, auscultation

Information obtained from the physical exam should be recorded on the non-DataFax Physical Exam form or in participant chart notes. All signs, symptoms, and diagnoses should be graded in the source documentation and followed until resolution. For all illnesses/AEs reported, sufficient detail must be obtained to allow for severity grading according to the *DAIDS Table for Grading the Severity of Adult and Pediatric Adverse Events* (Appendix D) of this SSP Manual, as well as details such as onset, duration, current status, etc.

10.4.5 Follow-Up Laboratory assessments

Specific instructions for collecting and processing laboratory specimens are included in Section 11. Clinicians are expected to review, assess, and provide clinical management for all laboratory tests. When lab results are received, staff will:

- Sign and date the result report to document appropriate clinical review
- Provide appropriate clinical follow-up and management of abnormal results
- Transcribe results onto case report forms

All participants will have ALT and total bilirubin tests at approximately Weeks 12 and 40 in addition to those done at Weeks 26 and 52.

At weeks 26 and 52 (+/- 28 days), the following tests are conducted:

- Rapid HIV testing

- Hematology (CBC and platelet count)
- Blood chemistry (creatinine)
- Liver function tests (ALT, bilirubin)
- Urine test for opiates and other drugs
- Urine test for pregnancy (Pregnancy tests are done at Week 4 for all female participants enrolled during Safety Phase, every four weeks for all female participants in the substitution treatment arm, prior to any repeat induction for women in the substitution arm, and for any female participant in the detoxification arm who undergoes a second detoxification at Week 26.)

Testing for Hepatitis B and C may be performed at any time during the first year if clinically indicated.

The following laboratory assessments are done at Weeks 78, 104, 130, and 156:

- Rapid HIV testing
- Urine test for opiates and other drugs

See the Protocol Appendix I-A: Schedule of Procedures and Evaluations for the chart of follow up assessments.

10.5 Access to HIV-Related Care

All HIV-infected participants identified during the study, whether at screening, follow-up or interim visits, should be actively referred to medical and psychosocial care and treatment. Sites should establish formal referral mechanisms or agreements with appropriate programs and be familiar with their requirements or criteria for accepting new patients. Each site will determine a mechanism of following up with participants to determine if the referral was used and the results which they will detail in their SOP on Post-test counseling for HIV positive participants. **Sites will maintain a list of referral sources and update it as needed as noted in Appendix IV of the protocol.**