

Section 4. Index and Partner Accrual

4.1 Overview of Section 4

This section provides an overview of requirements and procedures for recruiting, screening, and enrolling participants in HPTN 074 and the study extension.

4.2 Target Enrollment

The target population will include at least 500 network units (one index participant and at least one network injection partner) at three sites. Each site will aim to enroll 167 index participants.

Table 4-1 Summarizes target enrollment for the study and at each site.

Table 4-1		
	Total, All sites	Total, Per Site
HIV-infected Index Participants	500	167
HIV-uninfected Network Injection Partners	~750	~250
Late-entry HIV-uninfected Network Injection Partners (replacements)	~ 75	~ 25

Following the main study, indexes will be invited to re-enroll in the 9-12 month study extension. No partners will be enrolled. Each site will aim to re-enroll as many of the indexes at their site as possible.

4.2.1 Index participants

Index participants* will:

- Be HIV-infected PWID (men and women who report injecting drugs at least 12 times in the past three months and at least 6 times in the past month and report sharing needles, syringes or drug solutions) and,
- Have an HIV viral load $\geq 1,000$ copies/mL at Screening.
- Have a CD4 >50 cells/mm³ at Screening.
- This may include individuals who report that they are:
 - (a) ART-naïve (expected to be about half of participants at each site),
 - (b) ART-exposed but currently off therapy, or
 - (c) on ART.

See Protocol Sections 3.1, 3.2 and 3.3 for more information. Sites should create a system for tracking ART history of enrolled index participants per target for ART-naïve participants, as noted above.

*There are no re-enrollment eligibility criteria for indexes to re-enroll in the study extension, except for previously being an index in the main study and undergoing HIV testing at re-enrollment.

4.2.2 Network injection partners

In order for the index to enroll they must enroll at least one (but may enroll up to 5 at a time) HIV-uninfected active injection partners. It is estimated that each site will enroll approximately 250 HIV-uninfected injection network partners of index participants. This is based on an estimated average of 1.5 partners per index. Referred network injection partners who have one or more reactive/positive HIV tests at study entry will be eligible for enrollment as a partner. However, as specified in LoA 1, this person may enroll as an Index if the original referring Index does not enroll.

Due to the dynamic nature of injection drug partnerships, provision is made for replacement of network injection partners (late-entry HIV-uninfected network injection partners) during the study. If partners withdraw from the study, additional partners may be enrolled, as long as no more than 5 concurrent partners are being followed at the same time per index participant. Although the number of replacement partners is not limited, the team expects each site may enroll approximately 25 replacement partners. New partners cannot be recruited after the index's penultimate or termination visits. All replacement (or late enrolling) partners will have a Week 4 visit before assuming the visit schedule of the corresponding index.

4.3 Screening and Enrollment Logs

The DAIDS Policy for Requirements for Essential Documents at Clinical Research Sites Conducting DAIDS Funded and/or Sponsored Clinical Trials, <http://www.niaid.nih.gov/LabsAndResources/resources/DAIDSClinRsrch/Documents/essentialdocpolicy.pdf>, requires study sites to document screening and enrollment activity on screening and enrollment logs. Screening and enrollment logs may be maintained separately or combined into one document.

The DAIDS Policy for Requirements for Essential Documents at Clinical Research Sites Conducting DAIDS Funded and/or Sponsored Clinical Trials specifies that participant initials be recorded on screening and enrollment logs, in addition to PTID numbers. However, per HPTN policy and in agreement with DAIDS, participant initials need not be recorded on 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. This link log (and all participant identifying information) should be stored in a secure, locked location to prevent a breach of confidentiality.

The SDMC will report to the team the number of participants screened and enrolled based on data received and entered into the DataFax study database. This information, including screen failure information, will be available on the SCHARP atlas portal (<https://atlas.scharp.org>).

As the study accrual period comes to an end at each site, care must be taken to manage the recruitment, screening, and enrollment process in order not to exceed the protocol-specified sample size of 167 index participants enrolled at each site. Particularly in the last month of accrual, enrollment must be monitored closely, and potential participants must be informed

that although they may screen for the study, they may not be enrolled if the target sample size is reached before they are able to complete the screening and enrollment process. 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.

Screening and enrollment logs should include the following information:

- PTID
- Date of confirmation of HIV status of index
- Date of enrollment/randomization or screen fail
- Reason for screen fail based on the codes on the applicable CRF

4.4 Site Specific 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 (including ARV history quotas)
- Recruitment methods and venues
- Methods for identifying the recruitment method or venue for index participants
- Methods for ensuring the validity of network/index connection
- Methods for discussing HIV status disclosure issues with index participants
- Methods for timely evaluation of the utility of recruitment methods and venues
- Pre-screening procedures
- Ethical and human subjects considerations (including any plans for working with local law enforcement)
- Staff responsibilities for all of the above (direct and supervisory)
- Staff training requirements
- QC/QA procedures related to the above (if not specified elsewhere)
- Copies of recruitment worksheets, scripts, eligibility screening surveys, and other operational tools

These plans should be reviewed by community representatives.

4.5 Recruitment Plans and Targets

Recruitment of index participants will take around 15 months. We have estimated a screening ratio of more than 4:1 will likely be needed to consent and enroll 167 HIV-infected index participants at each site. Follow up of all index participants will be for a minimum of 12 months and a maximum of 24 months, regardless of study arm. All participants will end study participation when 27 months have passed since the first enrolled participant at the site. Network injection partners (including replacement partners) will be followed until the corresponding index participant reaches his/her Exit visit.

For the study extension period, sites will aim to re-enroll as many indexes as possible.

Index participants may be recruited using a variety of methods, including:

- Referral from HIV-testing sites
- Community outreach
- Personal referrals
- Identification of substance treatment program failures

Each index participant will recruit one to five HIV-uninfected network injection partners using referral identification cards. These should be individuals with whom they:

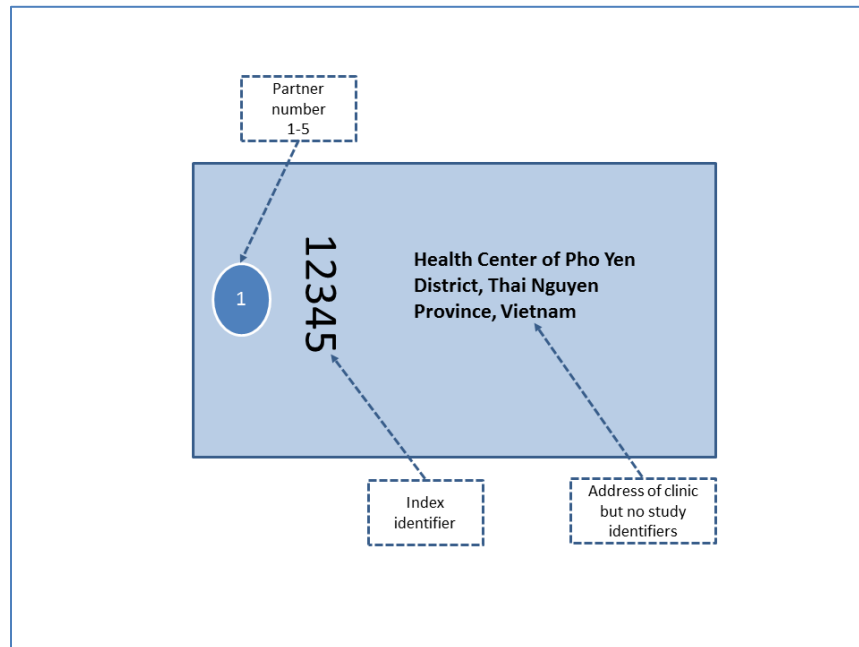
- Engage in HIV-risk related injection activities
- Interact with at least once a week, and
- Have known for at least one month.

The index participants will be asked to prioritize recruitment of the network injection partners **with whom they have the most HIV-risk-related exposures**, as assessed by sharing needles, syringes, or injection solution. Index cases should receive compensation (amount to be determined locally) for successful enrollment of network injection partners. Although other means of identification of network injection partners will be accepted from the index, each partner referral should be evaluated to minimize the probability that a referral is being made for economic benefit only without actual injection exposure to the index case.

The first network injection partner enrollment must occur within 60 days after the screening blood draw for the index participant (per SSP Section 8). If the first network injection partner presents to be screened more than 60 days after the index participant's screening blood draw, the index participant may be asked to return for another Screening visit prior to randomization and the initial partner may be asked to return for an Enrollment visit. (It will not be necessary to repeat HIV testing for any participant whose HIV positive infection status was previously confirmed. In any case, HIV status must be confirmed using two separate samples collected on different days.)

During screening, Index participants will be provided with referral identification cards marked with their study identification number to facilitate the recruitment of their network members. They will be asked to describe the injection drug partners they intend to recruit (for verification of identity). There will be no identifying information on the cards to indicate participation in an HIV or substance use study. Eligible index participants will be asked to give the cards to injection drug use partners and will encourage the partner(s) to bring the cards to the local study site to serve as their identification for participation in screening.

Figure 4.1



When a network injection partnership ends, the partner will continue to be followed. The index participant will be asked to recruit a new partner to replace the ending partnership, if an alternative partner is available and willing to enroll. The index participant may also recruit a new partner at any point during the course of the study prior to the termination visit of the index if the index participant develops a new relationship and has fewer than five partners enrolled in the study. Follow-up of all partners will end when the corresponding index participant completes his/her last study visit.

4.6 Screening

Participants who fail screening may re-screen only once. This includes those who do not enroll during the 60 day window previously identified.

4.6.1 Index

Outreach workers should be trained to not pre-select individuals who fit their description of “drug users”; instead, they will provide information to a range of individuals and encourage those individuals to pass information about the study to others in the community. Outreach workers will be selected from the community and must be knowledgeable about the community’s dynamics and trained on basic methods of rapid assessment procedures in order to target areas of high drug use. They will also be trained, as part of the study, in methods of approaching and communicating with potential participants, personal safety, and confidentiality.

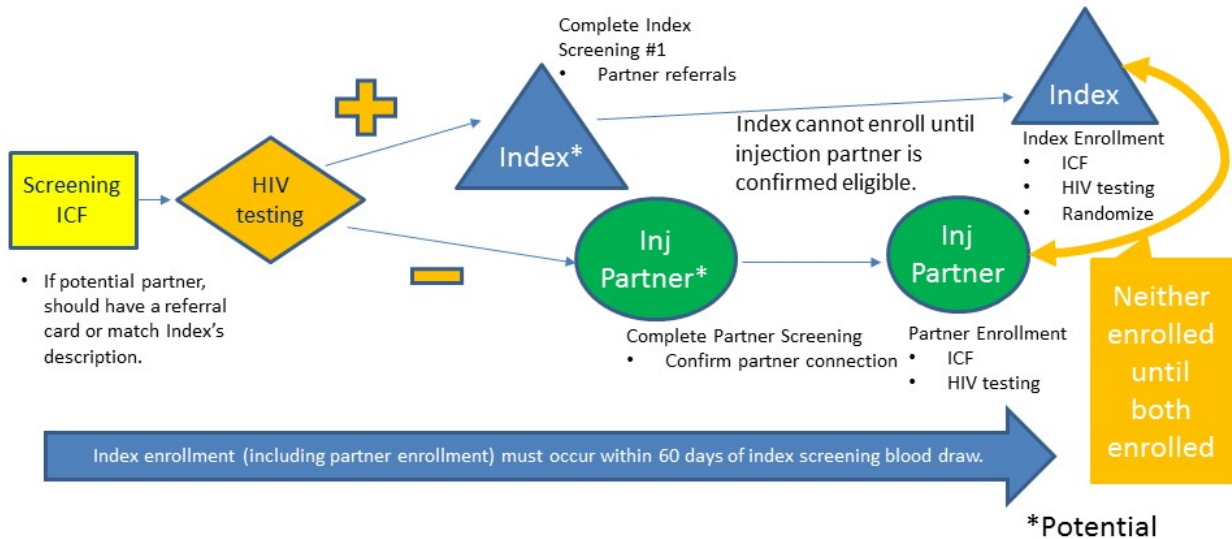
Potential index participants may be recruited outside of the clinic, or seen for the first time in the clinic. In either case, site staff may administer a pre-screening form (Table 4.1) to assess potential eligibility prior to consenting. They will be asked to

provide informed consent for Screening (see Section 4.11). Potential index participants who present at the study site will be offered HIV counseling and testing (after consent) and receive a brief introduction to the study. Please note that potential participants do not need to be literate to participate. A sample of the consent forms can be found in Appendix IV of the Protocol which should be altered according to site specific requirements and translated into the local language. All site specific informed consents should be reviewed by the HPTN LOC and approved by local IRB/ECs prior to site activation. Potential participants will be informed that they should pass the information on to other individuals if the study does not apply to them.

After providing informed consent for screening, volunteers will undergo an eligibility screening survey. If at any time during screening, they are found to be ineligible, screening will be discontinued; however, HIV counseling and testing will be offered to all persons who present for screening.

Index participants who are confirmed to be HIV-infected (see SSP Section 8) will not be randomized to a study arm until their first HIV-uninfected network injection partner is enrolled. After confirmation of eligibility of their first HIV-uninfected network injection partner, the index participant will return to the study site for randomization. The effective point of enrollment is randomization of the index participant. See Figure 1 below for suggested order of recruitment of index and their network injection partners. Study site staff members are responsible for developing and implementing local SOPs to help ensure index participants return for randomization. These procedures will be similar to the participant retention procedures (as described in Protocol Section 3.6).

Figure 4.2



HIV testing

- HIV test results from both the Screening and Enrollment visits will be used to determine study eligibility.
- At least one HIV test (e.g. HIV rapid test) must be positive/reactive at the Enrollment visit for the index participant to be considered eligible for the study.
- Referred network injection partners who have one or more reactive/positive HIV tests at study entry (Screening and/or Enrollment) may enroll as an Index participant.

Partners

- Each index participant will recruit one to five concurrent HIV-uninfected network injection partners; at least one partner must be enrolled before the index and his/her partner(s) are randomized.
- For HIV-uninfected injection partners to participate in the screening process, they must either present at a local study site with a card bearing their index participant's identification (ID) number, or match the description provided by the index during his or her screening survey in terms of name, age, gender, frequency of contact with the index, and duration of relationship with the index.
- The first network injection partner **enrollment must occur within 60 days** after the screening blood draw of the index participant.

4.6.2 Injection drug partners

For HIV-uninfected injection partners to participate in the screening process, they must either present at a local study site with a card bearing their index participant's identification (ID) number, or match the description provided by the index during his or her screening survey in terms of name, age, gender, frequency of contact with the index, and duration of relationship with the index. Site staff may administer a pre-screening form (Table 4.2) to assess potential eligibility prior to consenting. HIV-uninfected injection partners will then be asked to provide study informed consent for enrollment. Individuals who provide study consent will complete the social network interview, the baseline sexual and drug behavior data collection, and will participate in HIV risk reduction counseling and testing.

Injection partners who are confirmed to be HIV-infected at Screening may elect to be enrolled as an index participant, given the original referring index does not enroll. Once an HIV-uninfected injection partner is enrolled in the study as a network injection partner, he/she will be unable to enroll as an index participant (i.e., if he/she acquires HIV infection during the study), or as another index

participant's network injection partner (each network injection partner should be associated with a single index participant throughout the study). The frequency with which HIV-uninfected partners are referred by more than one index participant will be documented and assessed as part of the network structure.

4.7 Age Verification Procedures

In order to be eligible for enrollment, participants must be between 18-60. Age should be verified by local procedures including appropriate identification.

4.8 HIV Disclosure of Index Participants

The index participant should be informed that his/her HIV status will need to be disclosed to any network injection partners who are referred for study screening. The index participant must be counseled at the time of consent to disclose his/her HIV status prior to referring the partner for the study. Brief counseling by study staff should be provided to support this disclosure (see the Intervention Manual for suggestions). If the index participant prefers, he/she may opt to bring the partner to the study site for screening and undergo a joint disclosure session with the study staff. Finally, the index participant may opt not to have his/her HIV status directly disclosed to the injection partner. In this case, the network injection partner will be able to deduce the HIV status of the index through the screening consent process. The informed consent procedures for the index must clearly address the need for disclosure and the options for disclosure. Social impacts (positive and negative) of study participation will be elicited from all participants after screening. Care must be taken to prevent inadvertent HIV disclosure in individual networks. Site staff should take care not to divulge the HIV status of network partners who present for enrollment, but cannot enroll with the index who referred them because they are HIV infected.

4.9 Compensation

Index participants will receive compensation for successful enrollment of partners. Partners also will be compensated for their time and participation. The amount and form of compensation will vary by site. Each site/country will be encouraged to include fair and ethical compensation in their site specific Informed Consent Forms which will be reviewed and approved at the local level. Sites will review partner referrals for validity to ensure that partner referrals are not based solely for economic benefit.

4.10 Eligibility Determination

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:
 - Screening eligibility assessment procedures
 - Procedures for establishing if a potential participant is an active drug user

(defined as self-report of: a) injecting drugs at least 12 times in the past three months and at least 6 times in the past month; and b) a PWID in the opinion of site staff

- Procedures for documenting and tracking ART history
- Procedures for documenting, tracking and verifying index/partner link
- Post-screening visit eligibility assessment, confirmation procedures and timelines
- Final confirmation and sign-off procedures prior to enrollment
- 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)

The effective point of enrollment is randomization of the index participant. While all participants are required to meet the inclusion/exclusion criteria described in Section 3 of the protocol, study staff should also assess whether a participant is a good candidate for enrollment in the study. This assessment can be a bit subjective, however the goal is to make sure that sites are enrolling participants who will return for their follow-up visits and continue to participate in study procedures. For example, if an index participant identifies that they usually inject drugs alone (has no injection partners), they may not be a good candidate for this study.

If there is ever any uncertainty about whether to enroll a participant or how to classify a participant, sites should contact the LOC and the protocol team before proceeding. Section 3 (Documentation Requirements) includes a sample table that sites may use to identify the source documents that will be used to demonstrate participant eligibility.

4.11 Informed Consent

Informed consent is a process by which an individual voluntarily expresses his/her willingness to participate in research, after having been informed of all aspects of the research that are relevant to his/her 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 — each of which is described below. 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.

During screening, participants will be administered a screening informed consent. If a participant meets the eligibility criteria for the study and the study staff agree that they can fulfill the study requirements, they will be asked to enroll and complete an enrollment informed consent. For all enrolled participants, informed consent should be considered as an ongoing process that continues throughout the duration of the study. Participants from the main study who are interested in continuing in the study extension will be re-consented with

a new informed consent form, specific for the study extension.

Because of the constantly evolving nature of HIV prevention research, new information may be released in the form of a letter during the course of the trial. This letter is to be approved by the Protocol Team and DAIDS prior to distribution to the sites. At the time of distribution, HPTN LOC will instruct the site teams on whether currently enrolled participants should be provided the letter at their next scheduled visit or if an extra visit should be scheduled as soon as feasible. Sites should follow their local regulatory requirements for having this letter promptly reviewed and/or approved by their IRB/ECs.

U.S. regulations specify the elements of informed consent that must be conveyed to research participants through the informed consent process (45 CFR 46 and 21 CFR 50). It is the responsibility of the IoR, and his/her delegated staff, to deliver all required information to potential research participants. Staff who can conduct informed consent discussions should be identified in the Study Staff Roster.

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 LOC 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 these sections.

4.11.1 Deliver All Required Information in a Manner that is Understandable to Potential Participants

Give the participant a copy of the informed consent form to read during both 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. As a starting point at the screening visit, assess participant literacy in one of the languages of the approved site-specific informed consent forms. The process for determining literacy should be detailed in the site-specific SOP on informed consent.

If the participant is literate, give him/her a copy of the informed consent form to read. Also provide the participant with any other IRB/EC-approved informational materials developed to complement the informed consent form (the responsible IRBs/ECs must approve such materials prior to use). Allow the participant to take as much time as they need to review the consents and other materials. Because many of the research concepts and terms may be unfamiliar even to literate people, the consent form must be reviewed very carefully with each potential volunteer. After the participant has read the written material, verbally review the information provided. It is suggested that each paragraph be reviewed by the study staff member conducting the consent discussion and that the key points of each be emphasized, pausing often to allow for questions and to probe for understanding.

If the participant is not literate, read the materials verbatim – pausing after each paragraph to emphasize key points and to allow for questions. A checklist highlighting key points may serve as a useful guide for reviewing the consent with the potential participant. 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 and/or concerns expressed by the participant, and discuss these thoroughly. Take as much time as needed to address each question and concern.

Note: If the participant is not literate in one of the languages of an approved informed consent form, a witness literate in one of the languages of the site-specific informed consents must be present during the entire informed consent discussion. As part of the documentation step described here, 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. 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 (in terms of staff of volunteers) may serve as the witness to the informed consent process. It is recommended that each site seek IRB/EC review and approval of these procedures.

4.11.2 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 medical care and other services routinely available from the clinic or hospital associated with the site will not be affected by their decision whether or not to take part in the study. Encourage the participant to take as much time as he/she needs — and to talk about his/her potential participation with others, if he/she chooses — before making a decision.

Note: If the participant is not literate, 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.

4.11.3 Confirm That the Participant Comprehends the Information

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

One approach to assessing comprehension is to use a “quiz” (either oral or written) or other assessment tool that participants must complete prior to signing or making their mark on the informed consent form. 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. Table 4.4 includes a sample informed consent assessment tool which sites may choose to adapt for their local use. For sites that choose to adopt tools such as those included in 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/her to sign the informed consent form or screen for the study. Similarly, if the participant has concerns about possible adverse impacts on him/her if he/she were to take part in the study, or indicates that he/she may have difficulty adhering to the study requirements, do not ask him/her to sign the informed consent form to screen for the study.

4.11.4 Document the Process

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 DAIDS 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 initials or nickname); the policy 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. Some sites find it helpful to use a cover sheet attached to the Informed Consent Forms to document all items in this process. See Table 4.3 for a sample coversheet that sites may wish to adapt and use. 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.

Note: If the participant is not literate, the witness who was 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. If the participant cannot write his/her name or the date, this should be documented in the research record, in a chart note and/or on a face sheet or other documentation tool. In addition, the participant printed name, signature, and signature date blocks on the informed consent form should be completed as follows:

- *The “participant’s printed name” block should be left blank and the name should be recorded below the line by the person conducting the consent discussion, and initialed and dated.*
- *The participant chart should include documentation that the participant could not sign for him/herself.*
- *The participant should make his/her mark in the “participant’s signature” block.*
- *The “participant signature date” block should be left blank and date should be recorded below the line by the person conducting the consent discussion, and initialed and dated.*

4.11.5 Continue the Informed Consent Process throughout the Study

The previous sections describe aspects of obtaining informed consent from study participants prior to initiating screening/their involvement in the study. Given the ongoing nature of informed consent, key elements of informed consent should also 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, participants should be encouraged to ask questions as they arise and recognize that poor adherence to ART or substance abuse treatment (for example) will not affect their continued participation in the trial.

4.11.6 ICF Requirements for Protocol Amendments

According to DAIDS policy (Protocol Registration Policy and Procedure Manual), the site’s IRB/EC is/are ultimately responsible for determining whether study participants need to be re-consented for a protocol amendment. If re-consent is required, the process and details for re-consenting participants should be determined based on discussions with the Medical Officer, OCSO, the protocol team and the site PI. Version 2.0 of the HPTN 074 protocol requires participants to be re-consented, due to the nature of the change in the protocol (i.e., the study extension).

4.11.7 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 informed consent
- Procedures for ascertaining participant identity and age

- Procedures for ascertaining participant literacy
- Considerations and requirements for illiterate participants, including specification of who may serve as a witness to the informed consent process
- Procedures for providing all information required for informed consent to the participant
- HIV status of index disclosure to referred partners (or refer to another SOP where this is described)
- 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
- 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, coversheets, worksheets, or checklists to be used during the informed consent process

4.12 Screening procedures

See Protocol Section 3.3 for important screening information and Protocol Section 5.4.1 for the complete list of screening visit procedures.

- Screening may be discontinued at any time if a participant is found to be ineligible.
- Participants who fail screening for any reason may rescreen one additional time.
- It is the responsibility of the local site to determine the best approach to screening which will be documented in a site specific SOP.
- For each participant, independent written informed consent for Screening will be obtained before any Screening procedures are initiated.
- For each index participant, Enrollment must occur on a separate date within 60 days of screening blood draw.
- Note that all Screening procedures (including completion of the HIV testing algorithm – see SSP Section 8 for this algorithm- for the Screening visit) must be completed before a participant is enrolled.

4.13 Enrollment/Randomization Visit

- Written informed consent will be obtained from each study participant again at enrollment (prior to completing any enrollment study procedures). See SSP Section 4.11 for more information on obtaining informed consent.
- Index participants who are confirmed to be HIV-infected will not be randomized to a study arm until their first HIV-uninfected network injection partner is enrolled. See SSP Figure 4.2 for a sample timeline for index-partner enrollment.
- The effective point of enrollment is randomization. See SSP Section 10 (Randomization) for randomization procedures.

- After confirmation of eligibility of their first HIV-uninfected network injection partner, the index participant will return to the study site for randomization and will initiate study activities, as appropriate.
- If an eligible HIV-uninfected network injection partner identified by the Index does not enroll within 60 days of the date of blood collection of the Index's Screening Visit, an Index partner will not be considered enrolled and must re-screen.
- HIV test results from both the Screening and Enrollment visit will be used to determine study eligibility for all participants and these visits must be on different days. See Lab section 8 for more information.
- Baseline risk assessments (Baseline sexual behavior, injection risk behaviors, substance use, substance use treatment and ART use and adherence interviews) should be completed prior to risk reduction counseling (HIV pre-test risk reduction and post-test counseling, brief standardized injection and sexual transmission risk reduction counseling session).
- As described in the Index Network Status CRF, index participants will complete a Social Network Interview at each visit from enrollment through the end of the study, focused on current injection partners, including terminated and new relationships, and (2) social network measures, including turnover of all injection network members, network density, network support for adherence to ART and/or substance use treatment, and (3) frequency of injection and sexual risk behaviors with each identified injection network member (including both persons enrolled and not enrolled in the study). Network injection partners will also complete the Social Network Interview at each visit from enrollment through the end of the study.
- After randomization, a referral for ART (if clinically indicated according to national guidelines and/or participant is randomized to the intervention group) should be provided. ART will be provided through the local authorities. The participants should be provided with a letter describing participation in the study and stating approval from the appropriate regulatory agencies. The letters should be personalized and appropriately authorized to minimize the potential for forgery.
- As noted in Protocol Section 4.0, all participants will receive a comprehensive set of integrated harm reduction services aimed at reducing HIV risk behavior. Index participants in the intervention arm will also be offered systems navigation and psychosocial counseling as described in the Intervention Manual. Counselors can also offer a dyad session with the index participant and their identified support person (who may be an enrolled network partner), at the request of the index participant.
- The re-enrollment visit for indexes enrolling in the study extension will essentially be the same as another follow-up visit (FUV), with re-enrollment included. See Appendix IV of the protocol for further details (Appendix IV - Schedule of Procedures and Evaluations – Index participants during the 12 month extension period beyond original Exit).

Table 4.1 Sample Pre-Screening Questionnaire for potential Index participants

Age 18-60	<input type="checkbox"/> Yes (continue)
	<input type="checkbox"/> No (stop)
Injects drugs at least 12 times in the past three months and six times in the past month	<input type="checkbox"/> Yes (continue)
	<input type="checkbox"/> No (stop)
Shared needles/ syringes or drug solutions one time in last month	<input type="checkbox"/> Yes (continue)
	<input type="checkbox"/> No (stop)
Reports that she or he is HIV positive	<input type="checkbox"/> Yes or Don't Know (continue)
	<input type="checkbox"/> No: Recently tested negative (stop)
Believes that someone who injects drugs with them (HIV injection risk behaviors) would be willing to enroll and be followed	<input type="checkbox"/> Yes (continue)
	<input type="checkbox"/> No (stop)
No plans to relocate in the next few years	<input type="checkbox"/> Yes (continue)
	<input type="checkbox"/> No (stop)

Table 4.2 Sample Pre-Screening Questionnaire for potential Partners

Age 18-60	<input type="checkbox"/> Yes (continue)
	<input type="checkbox"/> No (stop)
Injects drugs at least 12 times in the past three months and six times in the past month	<input type="checkbox"/> Yes (continue)
	<input type="checkbox"/> No (stop)
Shared needles/ syringes or drug solutions one time in last month with an Index participant (referral identification card of index participant should be shown or should match other identifiers given by Index participant)	<input type="checkbox"/> Yes (continue)
	<input type="checkbox"/> No (stop)
Reports that she or he is HIV negative	<input type="checkbox"/> Yes (continue)
	<input type="checkbox"/> No (stop)
No plans to relocate in the next few years	<input type="checkbox"/> Yes (continue)
	<input type="checkbox"/> No (stop)
Currently a partner of another Index participant	<input type="checkbox"/> Yes (STOP)
	<input type="checkbox"/> No (continue)

Table 4.3 Sample Screening Informed Consent Coversheet for HPTN 074

Participant name:	
Date of informed consent discussion:	
Time of informed consent discussion (Completed):	
Name of study staff person completing informed consent discussion (and this coversheet):	
Is the participant literate in one of the languages of the approved available informed consent forms? (circle one option)?	Yes No
How was literacy determined and documented for this participant?	
If the participant was not literate, please note the name of the witness here:	
In what language was informed consent obtained?	
Was this a re-consent of a participant who had previously consented?	
Did the participant accept a copy of the informed consent form (circle one option)?	Yes No
Notes/Comments (not documented elsewhere):	

Table 4.4_S HPTN 074 Sample Screening Informed Consent Assessment Tool

	Date: Participant ID:			Staff name/initials
		Participant's Response	Correct Answer	Notes
1	Participation in this research study is voluntary	<input type="checkbox"/> True <input type="checkbox"/> False	<input checked="" type="checkbox"/> True <input type="checkbox"/> False	
2	The purpose of this research study is to help us develop a new and better way to prevent the spread of HIV from HIV-infected people who inject drugs to HIV uninfected people with whom they share needles/syringes or drug solutions	<input type="checkbox"/> True <input type="checkbox"/> False	<input checked="" type="checkbox"/> True <input type="checkbox"/> False	
3	This research study is part of the regular medical care offered here at [clinic name].	<input type="checkbox"/> True <input type="checkbox"/> False	<input type="checkbox"/> True <input checked="" type="checkbox"/> False	
4	After these screening tests, you will automatically be enrolled in the study.	<input type="checkbox"/> True <input type="checkbox"/> False	<input type="checkbox"/> True <input checked="" type="checkbox"/> False	
5	You will be told the results of all of your screening tests as soon as they are available.	<input type="checkbox"/> True <input type="checkbox"/> False	<input checked="" type="checkbox"/> True <input type="checkbox"/> False	
6	If you agree to be screened for the study you may have up to two visits over the course of several weeks, and each visit will last about [one to two hours]	<input type="checkbox"/> True <input type="checkbox"/> False	<input checked="" type="checkbox"/> True <input type="checkbox"/> False	
7	In order to participate in the study, we will ask you to identify at least one person with whom you regularly share needles/syringes or drug solutions who you believe does not have HIV and who is willing and eligible to participate.	<input type="checkbox"/> True <input type="checkbox"/> False	<input checked="" type="checkbox"/> True <input type="checkbox"/> False	
8	Your blood tests must be HIV negative to be part of this study.	<input type="checkbox"/> True <input type="checkbox"/> False	<input type="checkbox"/> True <input checked="" type="checkbox"/> False	

Table 4.4_E HPTN 074 Sample Enrollment Informed Consent Assessment Tool

	Date: Participant ID:			Staff name/initials
		Participant's Response	Correct Answer	Notes
1	You must stay in this study until clinic staff tell you that you can stop.	<input type="checkbox"/> True <input type="checkbox"/> False	<input type="checkbox"/> True <input checked="" type="checkbox"/> False	
2	The purpose of this research study is to help us develop a new and better way to prevent the spread of HIV from HIV-infected people who inject drugs to HIV uninfected people with whom they share needles/syringes or drug solutions	<input type="checkbox"/> True <input type="checkbox"/> False	<input checked="" type="checkbox"/> True <input type="checkbox"/> False	
3	You can choose which group (intervention or control) you will be in.	<input type="checkbox"/> True <input type="checkbox"/> False	<input type="checkbox"/> True <input checked="" type="checkbox"/> False	
4	Regardless of which group you are in, if you have HIV we will recommend that you start anti-HIV drugs before your T-cell count gets so low that it would make you very sick.	<input type="checkbox"/> True <input type="checkbox"/> False	<input checked="" type="checkbox"/> True <input type="checkbox"/> False	
5	Each person will be in this study for two years at the most.	<input type="checkbox"/> True <input type="checkbox"/> False	<input checked="" type="checkbox"/> True <input type="checkbox"/> False	
6	After this study ends, you will have on-going access to care for substance use and to treat your HIV infection.	<input type="checkbox"/> True <input type="checkbox"/> False	<input checked="" type="checkbox"/> True <input type="checkbox"/> False	
7	There is no risk that someone may learn that you are in this study.	<input type="checkbox"/> True <input type="checkbox"/> False	<input type="checkbox"/> True <input checked="" type="checkbox"/> False	
8	Index participants and their enrolled partners have to make sure they come back to the clinic for every visit at the same time.	<input type="checkbox"/> True <input type="checkbox"/> False	<input type="checkbox"/> True <input checked="" type="checkbox"/> False	
9 INDEX	Although participation in this study may also prevent you from spreading the HIV virus to others, no guarantee	<input type="checkbox"/> True <input type="checkbox"/> False	<input checked="" type="checkbox"/> True <input type="checkbox"/> False	

	can be made, you should not share drugs, needles or works with anyone.			
9 PARTNER	Even if the person you share drugs with is getting treatment for their HIV, you should not share drugs, needles or works with your partner or anyone else in order to protect yourself from getting HIV.	<input type="checkbox"/> True <input type="checkbox"/> False	<input checked="" type="checkbox"/> True <input type="checkbox"/> False	