Section 3: Accrual and Retention

3.1 Overview of Section 3

This section provides an overview of requirements and procedures for recruiting and retaining participants in the study.

Once a participant enrolls in HPTN 091, the study site will make every effort to retain them for their full follow-up in order to minimize possible bias associated with loss-to-follow-up. Successful retention begins with the recruitment of participants who fully understand what study participation involves and collection of exhaustive locator information from each study participant. It also relies on development and implementation of a comprehensive retention plan.

The term "retention" refers, in general, to the completion of study follow-up visits and procedures as specified in the study protocol. Participants who do not complete a particular scheduled visit, but do complete the next scheduled visit, will not be considered retained for the visit that they missed, but will be considered retained for the next scheduled visit. Thus, during the study retention rates can fluctuate over time and across visits. Importantly, retention can be improved by ensuring that participants return for their next scheduled visit after missing a visit.

3.2 Target Enrollment and Retention

Enrollment Targets

Approximately 310 HIV-uninfected transgender women (TGW), ages 18 and older, at risk for acquiring HIV infection will be enrolled in to the HPTN 091 study. Participants will be selected for the study according to the criteria in Sections 4.1 and 4.2 of the HPTN 091 Protocol. Due to staggered timelines of study activation, each site-specific accrual period may vary as this period is considered to begin on the first day of participant enrollment at each individual site.

A subset of up to ~12 enrolled TGW per site (maximum 60 total), will participate in serial qualitative assessments of: decision making around PrEP, experiences with PrEP use, experiences with co-located services, and acceptability of co-located services.

Further details on the qualitative interviews will be included in the Qualitative Manual (Appendix I of the SSP manual)

A subset of up to ~50 enrolled TGW will participate in the Drug-Hormone Interaction Sub-study and will be asked to participate in additional study procedures. Further details on the Drug-Hormone Interaction Sub-study can be found in Sections 6.7 and 8.7 of the HPTN 091 protocol.

Enrollment will be monitored closely. Enrollment slots may be shifted amongst sites in order to ensure that the overall study is enrolled as expeditiously as possible. For each site, accrual will begin after all applicable approvals are obtained and a Site-Specific Study Activation Notice is issued by the LOC.

Retention Targets

Ideally, each site should strive for 100% retention. However, recognizing that this ideal may not always be attainable, per the protocol, each study site will target an average annual retention rate of at least 90%, measured from enrollment.

Screening, enrollment and retention data will be captured on electronic case report forms (e-CRFs) within the electronic data capture system. The SDMC will provide screening, enrollment, and routine retention reports available on the Atlas portal. The SDMC will also generate a final end-of-study retention rate for each site after the study is completed. See SSP Section 12 for more information about Retention Reports.

3.3 Eligibility Determination

It is the responsibility of the site IoR 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. It is recommended that this SOP contain the following elements:

- Eligibility determination procedures, including:
    - pre-screening procedures
    - Post-screening visit eligibility assessment, confirming 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)

Sites may choose to conduct pre-screening activities, as determined by relevant local IRB/EC policies, SOPs and standard of care practices.

Section 2 (Documentation Requirements) includes a table that sites may wish to use as a

template to adapt to a site-specific format for source documents that can be used to demonstrate participant eligibility. Sites may choose to develop their own site-specific documentation to specify the source for each eligibility criteria.

3.4 Recruitment and Retention Plans

Each site is responsible for establishing a community engagement work plan and/or a recruitment and retention plan/SOP for this study, and for updating the plan if needed to meet the targeted enrollment and retention goals.

Because elements of the plan will affect study participants, it is recommended that the site seek input from the relevant Institutional Review Board (IRB)/Ethics Committee (EC), as well as the Community Advisory Board (CAB) before implementing the plan. However, IRB/EC approval is not required for the plan. The plan should be re-evaluated and modified in response to lower than anticipated enrollment and retention rates, or at any other time when strategies are modified.

The work plan/SOP should contain the following elements as necessary and as applicable to the study:

- Site-specific accrual and retention goals
- Methods for tracking actual accrual and retention versus accrual and retention goals
- Recruitment methods and venues
- Methods for timely evaluation of the utility of recruitment and retention methods
- Acknowledgement that retention begins with screening and enrolling "good candidates" (as described in Section 4.4 of the SSP manual). During screening, a particular emphasis should be placed on the requirement that participants must be willing to attend all visits and do not plan to relocate out of the study area for the duration of the study. In addition, a thorough explanation of the procedural requirements and the importance of the two arms to the overall success of the study should take place during the informed consent process and be re-emphasized at each study visit.
- Methods for ensuring participants are not co-enrolled in another HIV prevention study
- Pre-screening activities
- Recruitment timelines
- Methods for identifying the recruitment source of participants who present to the site for screening
- Procedures for collecting detailed locator information (see sample locator information sheet in Table 4-1) at the study Screening Visit, and active review and update of this information during subsequent visits.
- Use of appropriate and timely visit reminder strategies, such as personalized calendars or post cards, electronic reminders, and phone calls.

- Plans for mobilization of trained outreach staff to complete in-person contact with participants at their homes or other community locations to remind them of study visits or to deliver important study-related information. No study specific assessments or evaluations can be conducted off-site.
- Methods and timeframes for identifying when a visit has been missed.
- Procedures for immediate and multifaceted follow-up on missed visits including what outreach/locator efforts, such as phone calls and home visits, are taken within 24 hours, 1-3 days, 1 week, 2 weeks, and 3-4 weeks after a missed visit.
- Plans for regular communication with the community at large to increase awareness about HIV/AIDS and explain the purpose of HIV prevention research and the importance of retention in order to produce valid results.
- Ethical and human subjects' considerations
- Staff responsibilities for all of the above (direct and supervisory)
- Staff training requirements
- QA/QC procedures related to the above (if not specified elsewhere)

3.5 Obtaining and Updating Locator Information

Successful retention begins with collection of exhaustive locator information from each study participant. All study participants will be asked to provide locator information at their Screening Visit and to continually review/update this information at each subsequent visit. Each study site is encouraged to develop an exhaustive locator form to maximize contact effectiveness and participant retention (see sample form in Section Table 4-1). Potential locator items include:

- Participant's full name, alias, and/or nickname; government-issued identification number; home address; home phone number; mobile phone number(s); work address; work phone number; e-mail address; daytime and night-time hangouts.
- Walking/driving/public transport directions and/or pictorial map to the participant's home, workplace, etc.
- Electronic/social media contact information (e.g., Facebook, Twitter, Instagram, Tumblr, WhatsApp).
- Name, address, telephone number, and/or other contact information for stable community contacts (i.e., participant's family members and friends) who typically know the whereabouts of the participant.

  Note: Although contact information for a participant's current primary partner will likely be useful, contact information for other contacts also should be collected, since the participant's relationship with this partner could change during the course of the study.
- Name, address, telephone number, and/or other contact information for the participant's health care provider, school or training program, or case workers.
- Name, address, and/or other contact information for other locations frequented by the participant, such as bars, sports venues, or coffee shops.

During the informed consent process and when collecting locator information, study participants must be informed that their locator sources will be contacted if study staff are unable to locate the participant directly. Study staff will discuss with the participant how they will identify themselves when locator sources are contacted. These arrangements, agreed upon with the participant, should be documented on the locator form and reviewed before each participant contact.

Study staff should view every participant contact as an opportunity to update the participant's locator information. When updating locator information, site staff should actively review each item on the locator form to determine whether the information is still current (i.e., rather than simply asking "Has any of your information changed since your last visit?"). In addition, site staff should probe for additional locator information that the participant was not able or willing to provide at previous visits.

Study staff should document in their source documentation (e.g. chart notes, visit checklist) that they reviewed the locator information with the participant at every visit. Any updates to the locator form should use standard GCP corrections with initials and date of the staff member making the changes.

3.6 Participant Tracking Database

Due to the potential complexities that may be encountered when scheduling and completing follow-up visits, it is recommended that sites use a participant visit tracking sheet or database. Any participant tracking database that is developed is to be used for tracking purposes only. The database may not be used to record source data or to generate source documents unless specified in the site SOP for Source Documentation. All information entered into the database must be based on other source documents contained in participants' study charts.

3.7 Tips and Reminders

Recruitment and retention can be more challenging than expected. Therefore, it is important to plan ahead, closely monitor recruitment and retention data throughout the accrual period and study and make adjustments as needed.

- Dedicate adequate staff time and effort to enrollment and retention efforts.
- At screening, it is important that the staff assess the likelihood that a participant will be able to meet the visit schedule for the full length of the study.
- Be judicious about participant enrollment. Do not enroll participants who seem ambivalent about study participation. Be sure that volunteers fully understand what is involved in study participation before they are enrolled.
- Treat every participant with respect. Keep their information confidential.
- Make the visits as pleasant and short as possible for participants. Do not keep participants waiting unnecessarily.
- Emphasize the value of the participant’s involvement in the study during the study informed consent process and subsequently at follow-up visits. When participants complete scheduled visits, acknowledge and compliment their commitment, time, and effort devoted to the study.

- Whenever possible, make appointments to fit participants' needs, such as offering clinic hours during the evening, weekend, or early in the morning.
- Work with community advisory board members and key stakeholders to identify the most applicable accrual and retention strategies for the local study population, including the type and amount of participant incentives.
- Keep participants, community advisory board members, and key stakeholders up-to-date on study progress to foster a sense of partnership and ownership of the study (through the use of study newsletters, or quarterly meetings, for example).
- Inform local service providers who interact with the study population about the study and address any questions or concerns they have related to the study. Encourage them to express their support for the study and inform potential participants and key stakeholders about the study.

Recruitment Tips

Recruitment methods and venues should be assessed on an ongoing basis. The usefulness or "yield" of various recruitment sources should be tracked over time. Sites should identify recruitment sources of participants who screen and enroll and track methods for timely evaluation of the usefulness of recruitment methods and venues. The following point should be considered:

- Of all participants contacted through a particular method or at a particular venue, how many eventually enroll in the study?
    - If this number (percentage) is high, keep using that method or venue.
    - If not, try different recruitment methods or identify new venues.
- Designate a Recruitment Coordinator who is responsible for tracking accrual rates and managing recruitment efforts over time.
- Engage community representatives on accrual issues and strategies throughout the accrual period.

Retention Tips

- Use a Tracking Database to easily identify when participants' scheduled visits are due. Establish routine mechanisms to remind both study staff and participants of upcoming scheduled visits.
- Always schedule the participants' next visit before they complete the prior contact or visit. During clinic visits give the participant an appointment card with the next scheduled visit date and time noted.
- Prepare a calendar of scheduled visits or input scheduled visit dates on participant's cell phone for each enrolled participant, based on the enrollment date (or offer a planner/calendar as an incentive and note all study appointments). Note the dates of all scheduled visits in the participant's file for easy reference.
- Follow-up on missed appointments with an attempt to contact and reschedule as soon as possible (preferably on the same day). Continue these efforts per the local retention plan until contact is made.

- Keep locator information up-to-date and maintain thorough documentation of all efforts to contact the participant. Keep all this information in an organized manner, so that different staff members can easily review the information and contribute to contact efforts when necessary.
- Use all information collected on the participant's locator form while being careful to protect the participant's privacy. Even if a locator source is not useful/ successful on one occasion, try it again later unless it is proven to be incorrect.
- Use all available contact methods the participant agreed to (e.g., phone, mail, home visits, street outreach, cell phone texts, e-mail, and social media). Also make use of other available locator information sources, such as phone and post office directories and other public registries.
- Post outreach staff at other local service organizations used by the study population, such as health care clinics. Be sure to maintain participant confidentiality in these public situations.
- Attempt contact with the participant at different times during the day and the week, including evenings and weekends.
- Assist participants in making transportation arrangements if necessary. This may be done with mass transit vouchers, site-owned vehicles, or assistance with other modes of transportation.
- If a participant dies during the study (even if that participant is lost to follow up), every effort should be made to locate copies of official paperwork if it exists (e.g., a death certificate) to verify this information and ascertain the cause of death.

3.8 Participant Withdrawal

Regardless of the participant retention methods described above, participants may voluntarily withdraw from the study for any reason at any time. The IoR or designee also may withdraw participants from the study in order to protect their safety and/or if they are unwilling or unable to comply with required study procedures after consultation with the Protocol Chair, Division of AIDS (DAIDS) Medical Officer, Statistical and Data Management Center (SDMC) Protocol Statistician, and the HPTN Leadership and Operations Center (LOC) Clinical Research Managers (CRMs).

In general, participants should not be withdrawn from the study except in the case of a) withdrawal of consent; b) death; c) extreme/unusual circumstances to protect participant safety; d) they are unwilling or unable to comply with required study procedures, determined in consultation with the CMC; or e) become HIV positive and are not interested in continuing participation (otherwise, the visit schedule and procedures for *Participants with Suspected or Confirmed HIV Infection* outline in the study protocol, Section 6.4.3 should be followed).. Any such safety-related participant terminations should only be implemented after consultation with the Protocol Chair, Division of AIDS (DAIDS) Medical Officer, Statistical and Data Management Center (SDMC) Protocol Statistician, representatives from the Laboratory Center (LC), the Leadership and Operations Center (LOC) Clinical Research Manager (CRM), and others. Participants may be withdrawn if the study sponsor, government or regulatory authorities (including

Office for Human Research Protections [OHRP] and the FDA), or site IRBs/Ethics Committees (ECs) terminate the study prior to its planned end date.

Every reasonable effort will be made to complete a final evaluation of participants who terminate from the study early, and study staff will record the reason(s) for all withdrawals from the study in participants' study records.

In general, for participants who withdraw consent from the study prematurely during a study visit, the requirements for that visit should be completed to the extent possible except for provision of study product and will be considered their final visit. When possible, a plan should be made to give final laboratory results to the participant.

Table 4-1

PARTICIPANT LOCATOR INFORMATION SHEET--SAMPLE

(Additional information from the participant may be written on the reverse of this form)

1. Personal Details

Full legal name: _____

Name commonly used in the community: _____

Pronouns: _____

ID number:_____

Home Address: _____

_____

Address Change #1: (date and initial)

_____

_____

Address Change #2: (date and initial)

_____

_____

Please describe the route to get to your home from the Clinic: (draw map on back if needed)

_____

_____

_____

_____

_____

Home Phone Number: _____

Phone Change #1: (date and initial) _____

Phone Change #2: (date and initial) _____

Cell Number: _____

Cell Change #1: (date and initial) _____

Cell Change #2: (date and initial) _____

Email: _____

Email Change #1: (date and initial) _____

Email Change #2: (date and initial) _____

Can we VISIT you at home? ☐ Yes ☐ No

Can we PHONE you at home? ☐ Yes ☐ No

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2. Contact Information

Please tell us names of two people who will always know how to find you even if you move. We will contact these people if needed, but we will not tell them why we are looking for you.

Contact #1: _____

What is your relationship to this person? _____

What is the phone number for this person? _____

What is the address of this person? _____

_____

Contact #2: _____

What is your relationship to this person? _____

What is the phone number for this person? _____

What is the address of this person? _____

_____

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3. Workplace or School Details

Workplace or School Name _____

Workplace or School Address _____

Work or School Phone Number: _____

When are you usually at work or school? _____

_____

Can we VISIT you at work or school? ☐ Yes ☐ No

Can we PHONE you at work? ☐ Yes ☐ No

Workplace Change #1 (date and initial):

Workplace Name: _____

Workplace Address:_____

Workplace Phone: _____

Workplace Change #2 (date and initial):

Workplace Name: _____

Workplace Address:_____

Workplace Phone: _____

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4. Places frequently visited in the community

Please tell us the names and addresses of other places that you like to visit or where you often can be found such as bars, coffee shops, or sports venues.

_____

_____

_____

_____

_____

_____

5. Electronic/social media contact information (e.g. Facebook, Twitter, Instagram, Tumblr, WhatsApp)

_____

_____

_____

_____

_____

6. Other details regarding how to contact you

Document how staff should identify themselves and why they are looking for you when trying to locate you for study purposes.

_____
_____
_____
_____