MATRIX-003 Study-Specific Procedures (SSP) Manual
Section 3 – Accrual and Retention

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3 Introduction

This section provides information on requirements and procedures for recruiting and retaining participants in MATRIX-003. This section also presents information related to definitions, requirements, and procedures for participant retention.

3.1 Pre-screening Procedures

Sites are encouraged to implement pre-screening procedures for MATRIX-003 as part of their outreach and recruitment strategy. Like all outreach and recruitment approaches, materials used during the pre-screening process must be submitted and approved by local Institutional Review Boards (IRBs)/Independent Ethics Committees (IECs).

During pre-screening, staff may explain MATRIX-003 to potential study participants and ascertain elements of presumptive eligibility, which should be confirmed at an on-site screening visit. The information obtained during pre-screening activities cannot be considered for study eligibility determination.

Participants found to be presumptively eligible may also be provided the study informed consent form or other IRB/IEC-approved informed consent materials for review prior to their screening visit as part of the pre-screening procedures. Participant identifiers (PTIDs) should not be assigned until after participants provide written informed consent at the screening visit. No information collected from participants during

pre-screening activities may be used for publication purposes unless written informed consent is provided from potential participants.

3.2 Participant Accrual

Enough participants will be recruited to have approximately 100 evaluable participants (approximately 20 per site) across five US and sub-Saharan African research sites. To meet the accrual target within the designated accrual period outlined in the protocol, each site should aim to enroll at a rate of 4 – 7 participants per month. Up to 30 participants will be selected and invited to participate in the In-depth Interview (IDI) Subset (approximately 6 per site). A subset of up to 30 sexual partners of evaluable MATRIX-003 participants will be selected and invited to participate in the Sexual Partner – IDI Subset (approximately 6 per site).

Screening and enrollment data will be captured on electronic Case Report Forms (CRFs)/Instruments in the University of Pittsburgh Research Electronic Data Capture (REDCap) system. The MATRIX Clinical Trials Hub (CTH) Data Management & Statistical Support team will provide information on a regular basis about the number of participants screened and enrolled based on data entered in the study data system. Please see SSP Section 14 (Reporting Plan) for more details on MATRIX CTH Data Management & Statistical Support Screening and Enrollment Reports.

3.2.1 Accrual Tips and Reminders

Sites should develop methods for tracking actual versus targeted accrual, including monitoring the expected screening-to-enrollment ratios and how they change over time. Recruitment methods and venues should be assessed on an ongoing basis. The usefulness, or "yield", of various recruitment sources should also be tracked over time.

Routine team meetings should be held to identify recruitment sources of participants who are screened and enrolled and methods for timely evaluation of the usefulness of recruitment methods and venues. Discussion points should include items such as the following:

- Of all participants contacted through a method or at a venue, how many eventually enroll in the study?
- If this number (percentage) is high, keep using that method or venue
- If not, move on to different methods or venues

Staff responsibilities may include the following:

- Designate a Recruitment Coordinator who is responsible for tracking accrual rates and managing recruitment efforts over time
- Hold weekly or biweekly meetings among staff involved in accrual activities – community educators, recruiters, outreach workers, others – to discuss current and ongoing strategies
- Engage community representatives on accrual issues and strategies throughout the accrual period

Site should continue to discuss as a team, over time, the following characteristics of "good candidates" for study participation and the recruitment methods and venues that are most effective in yielding potential participants with these characteristics:

- Likely to be retained for the duration of the study
- Likely to be willing to administer the study product at applicable visits
- Likely to attend all study visits and adhere to protocol requirements, including those pertaining to abstinence from vaginal products/practices

3.2.2 Participant Accrual Standard Operating Procedures (SOP)

Site staff are responsible for establishing a study-specific participant accrual plan in the form of an SOP; the SOP and recruitment efforts undertaken to meet site-specific accrual goals should be updated if needed. The accrual SOP should contain, at minimum, the following elements:

- Site-specific accrual targets
- Pre-screening procedures (if applicable)
- Recruitment methods/venues and approaches for timely evaluation of the utility of recruitment methods/venues
- Methods for identifying the recruitment source of participants who present to the site for screening
- Methods for tracking actual accrual versus accrual targets
- Ethical and human subjects' considerations
- Staff responsibilities for all of the above (direct and supervisory)
- Quality control (QC)/quality assurance (QA) procedures related to the above (if not specified elsewhere)

3.3 Participant Retention

The term "retention" generally refers to completion of follow-up visits and procedures as specified in a study protocol. This definition must be operationalized for any study, and operational definitions usually reflect the primary objectives and endpoints of a study.

For MATRIX-003, two retention measures are planned to be used. Additional retention measures may be defined and used during the study if desired by the Protocol Chair(s) and/or Protocol Statistician.

- Retention per Study Visit: Calculated as the percentage of the total number of participants who complete a visit (within the visit window) divided by the total number of participants expected to complete that visit. Participants who complete a regularly scheduled visit within the visit window will be considered 'retained' for that visit.
- Overall Study Retention: Calculated as the percentage of the total number of visits completed by all participants (within their allowable visit window) divided by the total number of visits expected for all participants. A visit is considered expected for a participant once the allowable window closes, regardless of whether a participant is lost to follow-up or terminated early from the study.

As indicated above, participants who do not complete a scheduled visit within the allowable window, but then complete the next scheduled visit (including any required make-up procedures that were missed), will not be considered retained for the missed visit. However, they will be considered retained for the next scheduled visit. Thus, retention rates can fluctuate over time and across visits.

The MATRIX CTH Data Management & Statistical Support team will produce reports presenting retention rates for key study visits designated by the MATRIX Management Team. The MATRIX CTH

Data Management & Statistical Support team also will generate a final end-of-study retention rate after the study is completed.

3.3.1 Retention Requirements

The sites should target a 90% retention rate of enrolled participants over the follow-up period. The purpose of the 90% retention target is to ensure the accuracy of study results by minimizing bias that can be caused by missing data. Active efforts to retain participants, even if they miss visits over time is critical to achieving this retention goal.

Low retention rates can have serious impacts on the accuracy of the study results because it is unknown whether participants who do not return for scheduled study visits liked the product or had adverse effects resulting from using the product. This will result in missing laboratory and safety evaluations at specified study time points. To avoid these problems, and thereby avoid bias in the study results associated with loss-to-follow-up, high participant retention rates must be maintained throughout the study.

Per Protocol Section 10.3, replacement participants will be considered if loss to follow-up is higher than expected.

3.3.2 Participant Retention SOP

Site staff are responsible for establishing an SOP that outlines participant retention to meet the study retention goal. This SOP should be re-evaluated and modified in response to lower than anticipated retention rates, or at any other time when retention strategies are modified.

The SOP should minimally contain the following elements:

- Site-specific retention goals
- Methods for tracking actual retention versus retention goals and for the timely evaluation of the utility of retention methods
- Site-specific definition of "adequate" locator information (for purposes of determining participant eligibility) and procedures for obtaining and updating locator information
- Visit reminder methods and timeframes
- Methods and timeframes for identifying when a visit has been missed and planned retention methods
- Ethical and human subjects' considerations
- Staff responsibilities for all of the above (direct and supervisory)
- QC/QA procedures related to the above (if not specified elsewhere)

3.3.3 Locator Information

Provision of "adequate" contact/locator information during screening is a study eligibility requirement, and each site must specify its definition of adequate locator information in an SOP. This information should be maintained in an organized manner so that different staff members can easily review the information and contribute to re-contacting the participant when necessary. All study participants will be asked to provide contact/locator information during the study screening process. Information provided should be regularly reviewed/updated at enrollment and during follow-up. Each study site is

encouraged to develop an exhaustive locator form to maximize contact effectiveness and participant retention.

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 them directly. Study staff shounegotiate with the participant how they will identify themselves when locator sources are contacted. Arrangements agreed upon with the participant should be documented on the site-specific locator form.

Study staff should view every participant contact as a potential opportunity to update the participant's locator information. Sites should advise participants to report any changes to their contact information as soon as they become aware of those changes. When updating locator information, site staff should actively review each item on the locator form to determine whether the information is still current. Site staff should also probe for additional information that the participant was not able or willing to provide at previous visits.

Study staff should document in chart notes and/or the visit checklist that they reviewed the locator information with the participant at every visit/contact as defined in the protocol. Any updates to the locator form should use standard corrections per Good Clinical Practice (GCP) with initials and date of the staff member making the changes. The locator information form includes participant identifiers and should be filed securely as outlined in site SOP.

3.3.4 Retention Tips

Some additional strategies for maximizing participant retention are as follows:

- Dedicate adequate staff time and effort to retention efforts.
- 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.
- Build a rapport and ensure participants feel welcome and comfortable during their visits.
- Consider comfort of the waiting area and clinic rooms.
- Make use of all available contact methods (i.e., phone, mail, e-mail, etc.) as well as other available locator information sources, such as phone and other public registries.
- Use tracking systems to identify when participants' scheduled visits are due and/or overdue. Establish routine mechanisms to remind both study staff and participants of upcoming scheduled visits.
- Prepare a calendar of scheduled visits to give each enrolled participant at each scheduled clinic visit, based on their enrollment date, or offer a planner/calendar as an incentive and note all study appointments in the planner/calendar. Note the dates of all scheduled visits in the participant's file for easy reference.
- Confirm the scheduling of the next contact/visit at each follow-up visit and give the participant an appointment card with the scheduled visit date and time noted, if applicable.
- Pay close attention to the allowable visit window and prioritize retention efforts for participants nearing the end of the window. Organize daily caseloads and work assignments based on these priorities. For participants who demonstrate a pattern of late or missed appointments, schedule follow-up visits for the beginning of the allowable visit window (if applicable) to allow maximum time for re-contact and re-scheduling if needed.

- Follow-up on missed appointments with an attempt to re-contact/re-schedule within 24 hours (preferably on the same day). Continue these efforts per the site SOP until contact is made.
- Keep participants and community members up to date on study progress to foster a sense of partnership and ownership of the study. For example, sites may choose to use participant newsletters or other IRB/IEC-approved method of communication with participants.
- Inform local service providers who interact with the local study population about the study, so that they also can express their support for the study.