Section 3. Accrual and Retention

This section provides information on requirements and procedures for recruiting participants in MTN-026. 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 MTN-026 as part of their outreach and recruitment strategy. Like all outreach and recruitment approaches, strategies and materials used during the pre-screening process must be submitted and approved by local IRBs/ECs.

During pre-screening, staff may explain MTN-026 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 or other IRB approved informed consent materials for review prior to their screening visit as part of the pre-screening procedures. PTIDs should not be assigned until after participants provide written informed consent at the screening visit.

***Note**: 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

Approximately 27 participants (male and females) will be recruited across three sites: two US sites and one site in Thailand. Each site is to complete their accrual in 6-8 months. Each site-specific accrual period may vary as this period is considered to begin on the first day of participant enrollment at each site. To meet the target accrual time, each site will enroll nine (9) participants at a rate of 1-2 participants per month per site.

A site's total accrual target may change if enrollment slots need to be transferred from one site to another, as authorized by the study leadership.

***Note**: A minimum of six female participants will be enrolled in the study, at sites with capacity (Pittsburgh and Alabama sites only).*

For each site, accrual will begin after all applicable approvals are obtained and a Site-Specific Study Activation Notice is issued by the MTN Leadership and Operations Center (LOC) at FHI 360.

Screening and enrollment data will be captured on case report forms (CRFs) and entered into the Medidata Rave clinical database. Site staff will complete the Eligibility Criteria CRF for each participant enrolled or who screens out of the study.

The SDMC will provide information on the number of participants screened and enrolled based on data entered into the study database. Please see Section 14 of this manual for more details on SCHARP Screen Out 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 screen and enroll and methods for timely evaluation of the usefulness of recruitment methods and venues.

Discussion points should include the following:

- 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, move on to different methods or venues

Staff responsibilities 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, peer educators, others – to discuss current and ongoing strategies
- Engage community representatives on accrual issues and strategies throughout the accrual period

Continue to discuss as a team, over time, the following characteristics of "good candidates" for study participation:

- Likely to be retained for the duration of the study
- Likely to use study product as indicated for the duration of the study

3.2.2 Participant Accrual SOP

Site staff are responsible for establishing a study-specific participant accrual plan in the form of a SOP on Participant Accrual; 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)
- QC/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 MTN-026, 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 and/or Protocol Statisticians.

- During the study, retention for each regularly scheduled follow-up visit will be defined based on whether participants complete the visit within the visit window. Participants who complete a regularly scheduled visit within the visit window will be considered ‘retained’ for that visit.
- Overall study retention is calculated as the percentage of the total number of visits completed by all participants (within their allowable visit window) divided by the number of visits expected for all participants. A visit is considered expected for a participant once the allowable window closes, regardless of whether or not a participant is lost to follow-up or terminated early from the study. For MTN-026, each site should target a 95% retention rate of enrolled participants over the follow-up period.

As indicated above, participants who do not complete a particular 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 MTN SDMC will post reports on their ATLAS portal presenting retention rates for key study visits designated by the Protocol Team. The SDMC 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 95% retention rate of enrolled participants over the follow-up period. The purpose of the 95% retention target is to ensure the accuracy of study results by minimizing bias that can be caused by missing data.

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 used the study product, liked the product or had adverse effects resulting from using the product. This will result in missing laboratory evaluations (PK, PD and safety) 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 10.5, individuals lost to follow-up or to permanent product discontinuation may be replaced. To ensure accurate study results are obtained, participants who do not receive the single dose or any of the 7 daily doses will be replaced (see section 5 for further information).

3.3.2 Participant Retention SOP

Site staff are responsible for establishing a standard operating procedure (SOP) for Participant Retention to meet the study retention goal of 95%. 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" locator information during screening is a study eligibility requirement, and each site must specify its definition of adequate locator information in its Participant Retention 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 locator information during the study screening process. Information provided should be regularly reviewed/updated 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 the participant directly. Study staff will negotiate with the participant how they will identify themselves when locator sources are contacted. Arrangements agreed upon with the participant should be documented on the locator form.

Study staff should view every participant contact as an opportunity to update the participant's locator information. When updating locator information, 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?"). 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. Any updates to the locator form should use standard GCP corrections with initials and date of the staff member making the changes.

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.
- Develop rapport and ensure participants feel welcome and comfortable during their visits.
- Consider comfort of the waiting area and clinic rooms, especially the area where participants will spend long days at the clinic providing PK samples.

- Make use of all available contact methods (e.g. phone, mail, e-mail, etc.). Also, make use of other available locator information sources, such as phone and postal directories 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 for each enrolled participant, based on his/her 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 visit at each follow-up visit and give the participant an appointment card with the scheduled visit date and time noted.
- 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 local retention 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, site may choose to use participant newsletters or other IRB-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.
- Host gatherings, parties and/or other social events for participants. Host social, educational, and/or other events for participants' partners.