

Section 3. Participant Accrual and Retention

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3. Introduction

This section provides information on requirements and procedures for recruiting participants in MTN-034. Information on required screening and enrollment procedures are included in Section 5 of this manual. 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-034 as part of their outreach and recruitment strategy. Like all outreach and recruitment strategies, pre-screening approaches and materials used during the pre-screening process must be IRB approved.

During pre-screening, staff may explain MTN-034 to potential study participants and ascertain elements of presumptive eligibility, to be confirmed at an on-site screening visit. The information obtained during pre-screening activities cannot be considered for eligibility determination. No information collected from participants may be used for publication purposes unless written informed assent/consent is provided from potential participants.

Note: PTID assignment should not occur until after the participant provides written informed assent/consent at the screening visit.

It is recommended that pre-screening cover behavioral and basic demographic eligibility criteria, such as (but not limited to):

- Age
- Willingness to comply with protocol requirements, such as:
 - Able to obtain parental/guardian permission, if required
 - Attend study visits for approximately a year and half
 - Using study products, both the ring and tablets
 - Not participating in other research studies
 - Having a history of sexual intercourse
 - Use an effective contraceptive method

Participants found to be presumptively eligible may also be provided the study informed assent/consent or other IRB approved informed consent (IC) materials for review prior to their screening visit as part of the pre-screening procedures. For participants that will require parental permission to join the study, it may be important to discuss the content of the parental permission form and specify what information will and will not be provided to her parent/guardian. This will help

ensure she is making an informed choice on whether to discuss her potential study interest with her parent/guardian.

3.2 Participant Accrual

3.2.1 Study Accrual Plan and Site-Specific Accrual Targets

Protocol Version 2.0, LoA #03 clarified that a total of 247 participants aged 16-21 (inclusive) have been enrolled across four sites. Each site enrolled approximately 60 participants.

A site's total accrual target and accrual completion timeline may have changed slightly due to COVID-19 impact, or due to enrollment slots needing to be transferred from one site to another, as authorized by the study leadership.

For each site, accrual began after all applicable approvals were obtained and a Site-Specific Study Activation Notice was 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 Medidata Rave as per Study-Specific Procedures (SSP) Manual Section 12. The Eligibility Criteria CRF will be completed for all participants once they are enrolled at the Enrollment Visit or have screened out of the study at the Screening Visit or the Enrollment Visit.

The MTN Statistical Data Management Center (SDMC) provides information on the number of participants screened and enrolled based on data received and entered into the study database. See Section 14 of this manual for more details on study Enrollment Reports.

3.2.2 Accrual Tips and Reminders:

Sites should develop methods for tracking actual versus targeted accrual, including monitoring the expected screening to enrollment ratios and how these change over time.

Recruitment methods and venues should be assessed on an ongoing basis. The usefulness or "yield" of various recruitment sources should be tracked over time. 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.

In addition to tracking accrual and recruitment methods, sites should also monitor early screening and enrollment visits for flow, participant comfort and visit length. Accrual pacing should allow for enough time to adjust techniques as necessary to maximize participant retention and buy-in.

Staff responsibilities include the following:

- Designate a Recruitment Coordinator who is responsible for tracking accrual rates and managing recruitment efforts over time. The Recruitment Coordinator, in collaboration with the Investigator of Record (IoR), should also assist/advise in pacing accrual to ensure that enough time is allowed between participant visits to make any necessary refinements to visit flow in support of participant comfort and efficient visits
- Hold weekly 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

3.2.3 Participant Accrual SOP

Site staff members are responsible for establishing a study-specific participant accrual plan in the form of a Participant Accrual standard operating procedure (SOP); and updating the SOP and recruitment efforts undertaken if needed to meet site-specific accrual goals. The accrual SOP should contain, at minimum, the following elements:

- Site-specific accrual targets
- Methods for tracking actual accrual versus accrual targets
- Recruitment methods and venues
- Methods for identifying the recruitment source of participants who present to the site for screening
- Methods for timely evaluation of the utility of recruitment methods and venues
- Pre-screening procedures
- 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

3.3.1 Retention Definitions

The term “retention” generally refers to completion of follow-up visits and procedures as specified in a study protocol. For MTN-034, two retention measures are planned to be used. Additional retention measures may be defined and used during the study if desired by the Protocol Chairs 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.

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. Importantly, retention shortfalls can be made up by ensuring that participants return for their next scheduled visit after missing a visit.

The MTN SDMC will post reports on their ATLAS portal presenting retention rates for study visits. Monthly cumulative retention reports for sites are included in the Data Summary Report on ATLAS. The SDMC also will generate a final end-of-study retention rate after the study is completed.

3.3.2 Retention Requirements

Each study site will target retention of at least 95% of enrolled study participants for each scheduled follow up visit. 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 use of the product. Low retention is also closely linked with low adherence to the study product. If a participant misses her regularly scheduled visit, she may not have access to the vaginal ring or tablets for the coming month(s). Poor adherence makes it harder to evaluate study objectives. To avoid these problems, and thereby avoid bias in the study results, high participant retention rates must be maintained throughout the study.

3.3.3 Retention SOPs

Site staff members are responsible for establishing a Participant Retention SOP 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
- Procedures for completing and updating participant locator information
- Site-specific definition of "adequate" locator information (for purposes of determining participant eligibility)
- Visit reminder methods and timeframes
- Methods and timeframes for identifying when a visit has been missed
- Planned retention methods (including what outreach/locator efforts are taken within 24 hours, 1-3 days, 1 week, or 2 weeks after a missed visit)
- Methods for timely evaluation of the utility of 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)

3.3.4 Obtaining and Updating Locator Information

Successful retention begins with collection of locator information from each study participant. All study participants will be asked to provide locator information during the study screening process, and to continually review/update this information during follow-up. 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.

Each study site is encouraged to develop an exhaustive locator form to maximize contact effectiveness and participant retention.

Potential locator items include:

- Participant's full name, alias, and/or nickname; government-issued identification number; home address; home phone number; mobile phone number; work address; work phone number; or e-mail address; daytime and nighttime locations, meeting places and hangouts.
- Name, address, telephone number, and/or other contact information for stable community contacts (i.e., participant 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 study. Locator forms that include partner contact information should also include an indication of whether the participant gives permission to contact the partner.

During the informed assent/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 on the visit checklist or chart notes that they reviewed the locator information with the participant at every visit. Any updates to the locator form should use standard good clinical practice (GCP) corrections with initials and date of the staff member making the changes.

3.3.5 Use of a Participant Tracking System

Implementation of a participant tracking system will assist sites in accurately assessing participant retention in the study. This system may be paper-based, or an electronic database. The system chosen must be able to provide the site with a listing of all participants who have missed scheduled study visits.

It is expected that each site will have specific staff members designated to retention efforts and the maintenance of this system to track participant visits from the day that accrual starts.

The participant tracking system should be able to inform the site team of the following:

- Number of participants who are expected in the next week/day (to allow for visit reminders to be made in the timeframe specified in site Retention SOP).
- Participants who have missed their scheduled visit and are still within the visit window (ideally so that participants whose window is about to close can be prioritized for tracing).
- Participants who have missed their scheduled visit and need study product(s) to be replaced.
- Participants who have missed their scheduled visit and the window has closed (and a missed visit CRF is needed).

3.3.6 Retention Tips

Some general strategies for maximizing participant retention are as follows:

- Emphasize the value of the participant's involvement in the study during the study informed assent/consent process and subsequently at follow-up visits. When a participant completes scheduled visits, acknowledge and compliment her commitment, time, and effort devoted to the study.
- Create and maintain a youth friendly clinic space to ensure a comfortable space for participants while attending clinic visits.
- 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 re-contact efforts when necessary. Make use of all information collected on the participant's locator form. Even if a locator source is not useful/successful on one occasion, try it again later.
- Schedule all follow-up visits at the participant's Enrollment Visit. Thereafter, at each follow-up visit, confirm the scheduling of the next visit and give the participant an appointment card with the scheduled visit date and time noted.
- Prepare a calendar of scheduled visits for each enrolled participant, based on 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.
- Strategize ways within the clinic to ensure efficiency of study visits; keeping visits short and at a time that is convenient (after school hours for example). Formal visit flow assessments should be used periodically to identify inefficiencies.
- Provide snacks and activities to keep the participants entertained while waiting for visit procedures.
- Provide childcare for participants when needed.

- For participants who demonstrate a pattern of late or missed appointments, schedule follow-up visits for the beginning of the allowable visit window to allow maximum time for re-contact and re-scheduling if needed.
- 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.
- Make use of all available contact methods (e.g. WhatsApp/text messages, phone, mail, home visits, street outreach, e-mail/internet).
- Dedicate adequate staff time and effort to retention efforts.
- Work with community members to identify the most applicable contact and retention strategies for the local study population, including the type and amount of participant incentives.
- Keep participants and community members up-to-date on study progress to foster a sense of partnership and ownership of the study.
- 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 and/or parents.
- 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, such as SMS messages or phone calls.
- 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 Participant Retention SOP until contact is made.

3.3.7 Participants Who Voluntarily Discontinue Study Participation

If a participant wishes to discontinue participation in the study, her wishes must be respected. The participant should be advised that she is always welcome to come back if she wishes. Refer to SSP Section 5.11 (Voluntary Withdrawal of Study Participation) for procedures to be followed for participants who prematurely discontinue study participation.