

## Section 3. Participant Accrual, Screening and Enrollment

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This section provides information on requirements and procedures for recruiting, screening, and enrolling participants in MTN-024/IPM 031.

### 3.1 Pre-Screening Procedures

Sites are encouraged to implement pre-screening procedures for MTN-024/IPM 031 as part of their outreach and recruitment strategy. Like all outreach and recruitment strategies, pre-screening approaches and materials used during pre-screening must be IRB approved.

During pre-screening, staff may explain the study to potential participants and ascertain elements of presumptive eligibility, to be confirmed at Screening and Enrollment visits. 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 consent is provided from potential participants.

**Note:** Participant IDs (PTIDs) should not be assigned until after participants provide written informed consent. As such, sites may need to assign different prescreening IDs to maintain confidentiality. Process information (e.g., number of potential participants contacted, number presumptively eligible) may be recorded and stored at the study site in the absence of written informed consent from potential participants, provided the information is collected in such a manner that it cannot be linked to participant identifiers. Once accrual is initiated at each site, study staff may be asked to report prescreening and screening information to MTN CORE throughout the accrual period.

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

- Age
- Use of hormonal replacement therapy or contraception
- Willingness to comply with protocol requirements, such as:
  - Attending monthly study visits for three months
  - Using a vaginal ring
  - Not participating in other research studies

Participants found to be presumptively eligible may be provided the informed consent form or other IC materials for review prior to their Screening visit as part of the pre-screening procedures.

### 3.2 Study Accrual Plan and Site-Specific Accrual Targets

MTN-024/IPM 031 will enroll approximately 96 women across three US sites. The study wide accrual period is 12 months. Site staff should make every effort to complete accrual at a rate of about 2-3 participants per month per site.

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

Screening and enrollment data will be captured on a case report form (CRF) and submitted to MTN Statistical and Data Management Center (SDMC). The Eligibility Criteria CRF will be completed and faxed for all participants once they are enrolled or have screened out. Reasons for screen failure will also be recorded on the Eligibility Criteria CRF. If a participant is rescreened, a new Eligibility Criteria CRF should not be completed for the second screening attempt. Instead, the Eligibility Criteria CRF from the first screening attempt should be updated and refaxed to SDMC.

The SDMC will provide information on the number of participants screened and enrolled based on data received and entered into the study database. Please see Section 13 of this manual for more details on SCHARP reports.

Throughout the accrual period, the Protocol Team will review measures of implementation performance from each site to determine whether accrual targets should be adjusted across sites to achieve the study objectives most efficiently and to determine when to discontinue accrual at each site. Throughout the accrual period care must be taken to manage the recruitment, screening, and enrollment process in order not to exceed site-specific accrual targets.

### **3.3 Participant Accrual SOP**

Study staff are responsible for establishing a Participant Accrual Standard Operating Procedure (SOP) and updating this SOP if needed to meet site-specific accrual goals. The Participant Accrual SOP should at a minimum contain the following elements:

- Site-specific monthly accrual targets
- Methods for tracking actual accrual versus accrual targets
- Recruitment methods and venues and methods for timely evaluation of the utility and yield of recruitment methods and venues
- Methods for identifying the recruitment source of participants who present to the site for screening
- Identification of accrual back-up plans should accrual rates be lower than initially expected, as well as operational triggers and implementation plans for each
- Pre-screening procedures
- Ethical and human subjects considerations Staff responsibilities for all of the above (direct and supervisory)
- QC/QA procedures (if not specified elsewhere)

### **3.4 Screening and Enrollment**

#### **3.4.1 Screening and Enrollment Timeframe**

All protocol-specified screening and enrollment procedures must take place within 45 days of when the potential participant provides written informed consent.

If all screening and enrollment procedures are not completed within 45 days of obtaining written informed consent, the participant must repeat the entire screening process, beginning with the informed consent process. A new PTID is not assigned when a participant repeats the screening process. The term “screening attempt” is used to describe each time a participant screens for the study (i.e., each time she provides written informed consent). Participants may only screen twice for MTN-024/IPM 031 (i.e. one rescreening attempt is allowed).

#### **3.4.2 Screening and Enrollment Logs**

The DAIDS policy on *Requirements for Essential Documents at Clinical Research Sites Conducting DAIDS Funded and/or Sponsored Clinical Trials* requires study sites to document screening and enrollment activity on screening and/or enrollment logs. Screening and enrollment logs may be collected from sites periodically to assist in data cleaning, and therefore should be updated in real time and completed once a participant provides informed consent for screening and when enrolled/randomized into the study. Participants who are approached, but do not provide informed consent should not be included on this log.

### 3.4.3 Definition of Screening

The term “screening” refers to all procedures performed to determine whether a potential participant is eligible to take part in the MTN-024/IPM 031 study. The study eligibility criteria are listed in protocol Sections 5.2 and 5.3. Required screening procedures are listed in protocol Section 7.2. All eligibility criteria are initially assessed at Screening, and some are reconfirmed on the day of Enrollment.

Sites will be provided with an Eligibility Checklist (in Word format) which can be used to document participant eligibility for study participation. The Eligibility Checklist provides further operational guidance on the timing of each assessment and source documentation for each eligibility criterion. This document is available on the MTN-024/IPM 031 Study Implementation Materials webpage under Checklists: <http://www.mtnstopshiv.org/node/4924>.

### 3.4.4 Eligibility Determination SOP

It is the responsibility of the site Investigator of Record (IoR) and other designated staff to ensure that only participants who meet the study eligibility criteria are enrolled in the study. Each study site must establish a SOP that describes how study staff will fulfill this responsibility. Minimally the SOP should contain the following elements:

- Eligibility determination procedures, including:
  - During-visit eligibility assessment procedures
  - Post-screening visit eligibility assessment and confirmation procedures (i.e. review of laboratory results)
  - Final confirmation and sign-off procedures prior to enrollment/randomization
  - Documentation of each eligibility criteria (met or not met)
- Ethical and human subjects considerations
- Staff responsibilities for all of the above (direct and supervisory)
- QC/QA procedures (if not specified elsewhere)

Should study staff identify that an ineligible participant has inadvertently been enrolled in the study, the IoR/designee should contact the MTN-024/IPM 031 Management Team.

### 3.4.5 Screening Procedures

Screening procedures are specified in protocol section 7.2 and are reflected in the Screening visit checklist, which is available on the MTN-024/IPM 031 Study Implementation Materials webpage under Checklists: <http://www.mtnstopshiv.org/node/4924>.

- Informed consent must be obtained prior to conducting any study procedures. After consenting, participants will be assigned a PTID and undergo a series of behavioral assessments, clinical evaluations, and laboratory tests. Screening visit procedures are detailed in Protocol Table 4.
- Locator information will be collected initially during the screening visit, and updated at subsequent visits throughout the study. Staff should confirm adequate locator information is provided prior to enrollment/randomization.
- Eligibility criteria which are based on self-report may be evaluated by administration of the Screening Behavioral Eligibility and Enrollment Behavioral Eligibility worksheets. It is suggested that staff administer these questionnaires early in the visit, so that more time-consuming clinical and laboratory evaluations can be avoided if the participant is determined ineligible due to behavioral criteria (unless sites decide to administer clinical and laboratory evaluations regardless of eligibility as a service to the participant). These documents are available on the MTN-024/IPM 031 Study Implementation Materials webpage under Counseling Tools/Worksheets: <http://www.mtnstopshiv.org/node/4924>.

Clinical screening visit procedures are further detailed in Section 7 of this manual. In brief, clinical procedures include:

- Collection of medical, menstrual and menopausal history including assessing concomitant medications, conducting a physical exam and a pelvic exam and specimen collection.  
NOTE: Biopsies are not considered exclusionary procedures under exclusion criteria 6i. More invasive procedures within 90 days of enrollment are considered exclusionary (such as LEEP, tubal ligation, dilation and curettage, or piercings). See SSP Section 7.9 for more information regarding Pap smear follow-up prior to enrollment.
- Evaluation of the use of prohibited medications including the use of non-study vaginal product such lubricants, vaginal moisturizers and/or topical or systemic hormone replacement therapies, assessing STI/RTI/UTIs, genital signs/symptoms, history of genital/gynecologic procedures and overall general health.
- Undergoing HIV testing, urine pregnancy and follicle-stimulating hormone test (FSH) testing.
- Provision of all available test results and treatment or referrals for UTI/RTI/STIs.
- Provision of risk reduction, male condom, and HIV pre-and post-test counseling. Further considerations related to counseling requirements are detailed in Section 9 of this manual.

Details regarding laboratory tests and sample collection at screening are provided in Section 10 of this manual. In summary:

- Participants will undergo testing for STIs (Gonorrhea, Chlamydia, Syphilis, Trichomonas, and HIV), liver and kidney function (serum chemistries: AST, ALT and Creatinine), and a complete blood count with platelets.
- If indicated, participants may be tested for bacterial vaginitis, vaginal candidiasis, or herpes simplex virus (per local standard of care).
- If required for eligibility or clinically-indicated, a Pap smear specimen will also be done.

Note: Hematology tests (CBC with Platelets) and chemistry tests (AST, ALT and Creatinine) results are documented on the Safety Laboratory Results (SLR-1) CRF. HIV test results are documented on the HIV Results (HIV-1) CRF. Vaginal wet prep, GC/CT, Trichomonas rapid test and other if indicated test results are documented on the STI Test Results (STI-1) CRF. Follicle-stimulating hormone test (FSH), urine pregnancy and Syphilis RPR test results are maintained at the site in local testing logs, lab results report and/or chart notes. These results are not documented on a CRF.

Designated staff will document the status of eligibility criteria assessed at screening, as applicable, by checking each set of "yes/no" checkboxes upon assessment and initialing and dating on the "Screening Visit" column of the MTN-024/IPM 031 Eligibility Checklist.

Between Screening and Enrollment, appropriately delegated site staff should review available lab results and other eligibility criteria and update the "Screening Visit" column of the MTN-024/IPM 031 Eligibility Checklist. No screening CRFs should be faxed to SCHARP until a participant is enrolled. Should a participant be ineligible for enrollment, the Eligibility Criteria CRF should be completed and faxed, and the screening file should be retained on site per the site's Data Management SOP. Refer to section 3.4.7 below for further information on the appropriate documentation which should be included in the participant chart for all screened out participants.

If the participant meets eligibility criteria at the end of the Screening visit, she should be scheduled for her Enrollment Visit, making sure the Enrollment visit takes place within the allowable 45-day time frame. Participants should be provided with study informational material, clinic contact information, and instructions to contact the clinic with any questions as needed prior to her scheduled Enrollment visit.

### 3.4.6 Assignment of Participant ID Numbers

The MTN SDMC (SCHARP) will provide each study site with a listing of participant identification numbers (PTIDs) for use in MTN-024/IPM 031. The PTIDs will be provided in the form of a hard-copy MTN-024/IPM 031 PTID-Name Linkage Log (see Figure 3-1). Information regarding the storage and completion of the PTID-Name Link Log can be found in the site's Data Management SOP. Additional information on the structure and use of PTIDs can be found in the Data Collection section of this manual (Section 11). PTIDs will be assigned to all potential participants who provide informed consent, regardless of whether they enroll in the study. Only one PTID will be assigned to each potential participant, even if the participant undergoes two screening attempts.

**Figure 3-1**  
**Sample Site-Specific PTID-Name Linkage Log (PTID List) for MTN-024/IPM 031**

	Participant ID	Name	In-depth Interview?		Date ddMMMy	Initials
1	XXX-00001-Z		yes	no		
2	XXX-00002-Z		yes	no		
3	XXX-00003-Z		yes	no		
4	XXX-00004-Z		yes	no		
5	XXX-00005-Z		yes	no		

### 3.4.7 Participants Found to be Ineligible (Screen Failures)

Screening should be discontinued if the participant is determined to be ineligible. If a participant screens out due to a clinical condition requiring follow-up, appropriate referrals should be provided. Documentation of all referrals should be included in the participant chart. All lab results should be provided and explained to participants within a reasonable timeframe, regardless of eligibility determination. For all screened out participants, the following documentation should be in place:

- Completed informed consent form
- Reason(s) for ineligibility, with date of determination, as per the completed Eligibility Checklist
- Completed Eligibility Criteria CRF, updated with screen failure reason(s) and faxed to SCHARP
- Necessary referrals on file (as appropriate) and documentation that any clinically significant abnormalities (labs, etc.) were communicated to the participant (even if referral is not necessary)
- All source documentation complete up until the time that ineligibility was determined
- Chart notes complete up until the time ineligibility was determined
- Indication of what visit procedures were conducted (on visit checklists)

In addition, the Screening and Enrollment Log should be updated with date of discontinuation of screening and reason for screen failure. Once ineligibility status is determined, the MTN-024/IPM 031 Eligibility Checklist may be stopped and the remaining items may be left blank. Site staff should document in chart notes why items of the checklist were left blank.

## 3.5 Enrollment

### 3.5.1 Definition of Enrollment

Participants will be considered enrolled in MTN-024/IPM 031 once they have been assigned an MTN-024/IPM 031 Randomization Envelope. Further information on methods and materials for random assignment is provided in Section 3.5.3.

### 3.5.2 Enrollment Procedures

Study enrollment procedures are specified in protocol section 7.3 and reflected in the Enrollment visit checklist, which is available on the MTN-024/IPM 031 Study Implementation Materials webpage under checklists: <http://www.mtnstopshiv.org/node/4924>. Additional details regarding enrollment procedures are outlined below.

The following procedures should be completed as part of eligibility confirmation prior to randomization on the day of enrollment. The IoR or designated staff will reconfirm and document the criteria indicated on the "Enrollment Visit" column of the MTN-024/IPM 031 Eligibility Checklist prior to proceeding with randomization/enrollment per site SOPs. Before randomization, the participant should undergo the following procedures:

- Confirm the informed consent form is signed and dated and the participant remains willing and able to participate in the study
- Confirm 45-day screening window has not been exceeded
- Update and re-confirm adequacy of locator information
- Confirm behavioral eligibility criteria through administration of the Enrollment Behavioral Eligibility worksheet or Eligibility Checklist
- Review/update medical/medication history since screening visit. Re-evaluate use of prohibited medications, STI/RTI/UTIs, genital signs/symptoms, history of genital/gynecologic procedures and overall general health
- Collect blood for plasma archive
- Provide protocol adherence and HIV/STI risk reduction counseling and male condoms
- Conduct a physical exam and a pelvic exam
- Provide all available test results and treatment or referrals for UTI/RTI/STIs.
- Administer behavioral assessments: Vaginal Practices CRF and the Baseline CASI questionnaire
- NOTE: Vaginal ring (VR) adherence counseling may be conducted prior to randomization as it could be helpful to provide the participant with more information about the ring prior to her final decision to enroll in the study

Designated staff will document the status of eligibility criteria assessed at Enrollment, as applicable, by checking each set of "yes/no" checkboxes upon assessment and initialing and dating on the "Enrollment Visit" column of the MTN-024/IPM 031 Eligibility Checklist. A staff member and the IoR/designee must review and sign/date the MTN-024/IPM 031 Eligibility Checklist to document the participants eligibility status is confirmed prior to enrollment/randomization. The Eligibility Criteria CRF must also be completed for all screened participants once the participant's eligibility/enrollment status is determined. If the participant is confirmed to be eligible based on procedures listed above, the IoR or designee should complete final sign-off of eligibility on the Eligibility Criteria CRF, have this verified by a second staff member who will also sign-off on the Eligibility Criteria CRF.

After randomization, participants will undergo the following procedures:

- Provision of VR instructions and one VR for self-insertion
- Demonstrated attempt to remove and insert the VR
- Digital (bimanual) exam to check for correct placement
- Reimbursement
- Schedule next visit

To ensure an accurate assessment of baseline conditions is documented and eligibility is confirmed on the day of randomization, the Enrollment visit should not be conducted as a split visit. If for some reason the participant cannot complete the Enrollment visit in a single day, (e.g. participant has to leave early due to an emergency) follow the guidance below:

- If she has not been randomized, reschedule the participant for the Enrollment visit within the 45 day window. No CRFs from an incomplete Enrollment visit should be sent to SCHARP.
- If she has been randomized, the visit is considered her Enrollment visit regardless of whether all procedures post-randomization were completed. Document any procedures not done. If the participant did not receive a study ring at the Enrollment Visit, she should be scheduled to come in as soon as possible after Enrollment to receive her first study ring and associated procedures (first product use, digital (bimanual) exam etc.).

No missed Enrollment visit procedures should be made up prior to the 4-Week visit with the exception of ring provision (described above) and the collection of plasma archive. If blood for plasma archive was missed during the Enrollment visit, the site should make every attempt to bring the participant back as soon as possible to collect and archive this specimen as part of an interim visit. Contact SCHARP with any CRF completion questions if this situation occurs.

### **3.5.3 Random Assignment/Prescription Assignment**

Participants will be randomly assigned 3:1 to one of the two study arms.

The SDMC will generate and maintain the study randomization scheme and associated materials. Randomization Envelopes will be shipped from the SDMC to each study clinic. Envelopes are stored in the clinic and must be assigned in sequential order to each participant who has been confirmed as eligible and willing to take part in the study. Only one envelope may be assigned to each participant; once an envelope is assigned to a participant, it may not be re-assigned to any other participant. All envelopes are sealed with a security tape to ensure envelopes are not tampered with or opened prior to assignment to a participant.

Envelope assignment will be documented on the Randomization Envelope Tracking Record. The act of assigning a Randomization Envelope to a participant is considered the effective act of randomization and enrollment in the study. Once the Randomization Envelope is assigned, the participant is considered 'enrolled' in the study. Once assigned, the prescription should be completed as outlined in Section 6 of this manual and provided to the pharmacy.