Section 4. 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-020.

4.1 Study Accrual Plan and Site-Specific Accrual Targets

MTN-020 will enroll approximately 3476 women. Accrual of all 3476 participants is targeted to be completed within approximately 12 months from the time the first participant is enrolled in the study.

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) at FHI 360.

Screening and enrollment data will be captured on case report forms (CRFs) 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.

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 17 of this manual for more details on SCHARP Enrollment 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. These measures of performance include, but are not limited to:

- Screening and enrollment progress
- Monthly retention rates
- Protocol deviations (team review of number and type)
- PPD monitoring report and FHI 360 assessment visit findings
- Data quality report statistics (QC rate, time to fax)
- Study product adherence metrics

Evaluations of performance will be ongoing throughout the accrual period. Discussions will be held with sites if or when there are any recommendations to changes in accrual targets. Adjustments may be made after MTN Study Monitoring Committee and/or Data Safety Monitoring Board reviews of MTN-020.

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. As total enrollment approaches the protocol-specified target per the SCHARP database, sites will be notified to stop screening.

4.1.1 Accrual SOP

Study staff members are responsible for establishing study-specific participant accrual SOPs and updating these SOPs if needed to meet site-specific accrual goals. Accrual SOPs should minimally contain the following elements:

- Site-specific monthly accrual targets
- Methods for tracking actual accrual versus accrual targets
- Expected screening to enrollment ratios
- 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 and yield of recruitment methods and venues
- 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 (if any)
- Ethical and human subjects considerations (in addition to the ethical approvals necessary for the intended accrual methods, sites are encouraged to seek ethical approvals as needed for any *potential* recruitment activities in the event that recruitment is slower than expected and new methods need to be implemented)
- Staff responsibilities for all of the above (direct and supervisory)
- QC/QA procedures (if not specified elsewhere)

4.2 Screening and Enrollment

4.2.1 Screening and Enrollment Timeframe

All protocol-specified screening and enrollment procedures must take place within 28 days of when the potential participant provides written informed consent for screening.

If all screening and enrollment procedures are not completed within 28 days of obtaining written informed consent for screening, the participant must repeat the entire screening process except for PTID assignment, beginning with the screening informed consent process. A new participant identification number (PTID) is not assigned when a participant repeats the screening process (see Section 4.3.5 below). 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 for screening). Participants may only screen twice for MTN-020 (one rescreening is allowed). Participants may or may not be rescreened per the discretion of the site Investigator of Record (IoR).

4.2.2 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 enrollment logs. These logs may be maintained electronically but must be 21 CFR Part 11 compliant if the log is considered a source document. 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. Participants who are approached, but do not provide informed consent for screening should not be included on this log. A sample screening and enrollment log suitable for use in MTN-020 is shown in Appendix 4-1, and is also available on the ASPIRE website under *Study Implementation Materials*. Study sites are encouraged to reference the eligibility criteria item numbers in protocol Sections 5.2 and 5.3 when recording the reason for screening failure/discontinuation on the screening and enrollment logs; these item numbers are also shown on the Eligibility Checklist (Appendix 4-2). As mentioned above, reasons for screen failure will also be recorded on the Eligibility Criteria CRF and datafaxed to the SDMC. If a participant is rescreened, a new Eligibility Criteria CRF should not be completed for the second screening attempt (see Section 14). Instead, the Eligibility Criteria CRF from the first screening attempt should be updated and refaxed to SCHARP.

4.3 Screening

4.3.1 Definition of Screening

The term "screening" refers to all procedures performed to determine whether a potential participant is eligible to take part in MTN-020. 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 the Screening Visit, and some are reconfirmed on the day of Enrollment. The Eligibility Checklist in Appendix 4-2 provides further operational guidance on the timing of assessment and source documentation for each eligibility criterion.

4.3.2 Pre-Screening Procedures

It is encouraged that sites implement pre-screening procedures for MTN-020 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 MTN-020 to potential study participants and ascertain elements of presumptive eligibility, to be confirmed at an on-site screening visit. No information collected from participants may be used for publication purposes unless written informed consent is provided from potential participants. Note that SCHARP-provided PTIDs should not be assigned until after participants provide informed consent for screening.

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

- Age
- Recent or current pregnancy, current breastfeeding, or pregnancy intentions
- Current contraceptive use, and intention to continue use
- Willingness to comply with other protocol requirements, such as:
  - Monthly study visits for 1-2 years and associated monthly HIV and pregnancy testing
  - Use of a vaginal ring
  - Non-participation in other research studies
- Self-assessment of risk of HIV acquisition as an indicator of motivation to use study product and comply with protocol requirements

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

4.3.3 Eligibility 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 standard operating procedure that describes how study staff will fulfill this responsibility. This SOP minimally 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 or designee should contact the MTN-020 study management team, using the following email address: mtn020mgmt@mtnstopshiv.org.

4.3.4 Screening Procedures

Study screening procedures are specified in the MTN-020 protocol section 7.2 and reflected in the visit checklists contained in Section 7 of this manual. Note also a change to pelvic exam frequency per LoA#1 – pelvic exams and associated sample collection will be required at screening visits, and only if indicated at enrollment visits.

Per protocol, informed consent for screening must be obtained prior to conduct of any screening procedures. After consenting, participants will be assigned a PTID and undergo a series of behavioral assessments, clinical evaluations, and laboratory tests. Locator information will be collected initially during the screening visit, and updated at visits throughout the study. Staff should confirm adequate locator information is provided prior to enrollment as defined in their site-specific SOP for retention.

Eligibility criteria which are based on self-report will be evaluated by administration of non-datafax Screening Behavioral Eligibility CRF provided by SCHARP. It is suggested that staff administer this questionnaire early in the screening 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). To maintain consistency across sites and participants, questions on this form will be translated into local-languages so that they are asked verbatim.

Clinical screening visit procedures are described in detail in Section 10 of this manual, briefly:

- Clinical procedures include collection of medical, menstrual, pregnancy, and contraceptive history, concomitant medications, contraceptive medications, physical exam, and pelvic exam.
    - NOTE: IUCD insertion and biopsy are <u>not</u> considered exclusionary procedures under exclusion criteria 7g. Tissue invasive procedures within 90 days of enrollment are considered exclusionary (such as LEEP, tubal ligation, dilation and curettage, or piercings). See section 10.5 for more information regarding Pap smear follow-up prior to enrollment.
- Participants will be evaluated for use of prohibited medications, STI/RTI/UTIs, genital signs/symptoms, history of genital/gynecologic procedures, drug/alcohol use and overall general health.
- Participants will also receive contraceptive counseling, urine pregnancy testing, and discussion of pregnancy/breastfeeding history and future pregnancy intentions.
- Participants should receive all available test results and treatment or referrals for UTI/RTI/STIs.

Details regarding laboratory tests and sample collection at screening are provided in Section 13 of this manual. In summary:

- Participants receive testing for STIs (Gonorrhea, Chlamydia, Syphilis, Trichomonas and HIV), pregnancy testing, serum chemistries, and CBC with platelets.

    - NOTE: repeat testing of exclusionary laboratory values at screening should only be conducted with specific clinical rationale for retesting. Chart notes should document decisions and rationale behind the retesting of abnormal, exclusionary results.
- Gram stain and endocervical swab samples will be collected. These samples will be destroyed if the participant does not enroll in MTN-020.
- Vaginal pH will be measured.
- If indicated, participants may be tested for Bacterial Vaginitis, vaginal candidiasis, or herpes (if per local standard of care).
- If required for eligibility or clinically-indicated, a Pap smear specimen will be collected.

The HIV testing algorithm for screening and testing consideration can be found in Section 13. Participants will receive HIV pre- and post-test counseling as well as risk reduction counseling, including provision of condoms in conjunction with HIV testing during screening. Counseling considerations are described in detail in SSP Section 12.

Designated staff will document the status of each eligibility criteria prior to randomization (or when a participant screens out of the study) by checking "Yes" or "No" on the MTN-020 Eligibility Checklist (Appendix 4-2). 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 28-day time frame and not during menses. Participants should be provided any study informational material (i.e. informed consent booklet and/or enrollment informed consent for review), clinic contact information, and instructions to contact the clinic with any questions as needed prior to their scheduled enrollment visit.

Between screening and enrollment, appropriately delegated site staff should review lab results and other eligibility criteria as outlined in the site-specific Eligibility SOP. 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 (see also Section 4.3.6).

4.3.5 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-020. The PTIDs will be provided in the form of a hard-copy MTN-020 PTID-Name Linkage Log (see Figure 4-1). 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. PTIDs will be assigned to all potential participants who provide informed consent for screening, regardless of whether they enroll in the study. Only one PTID will be assigned to each potential participant, even if she undergoes 2 screening attempts.

Figure 4-1
Sample Site-Specific PTID-Name Linkage Log (PTID List) for MTN-020

	Participant ID	Participant Name	Date	Staff Initials
1	XXX-00001-Z			
2	XXX-00002-Z			
3	XXX-00003-Z			
4	XXX-00004-Z			
5	XXX-00005-Z			
6	XXX-00006-Z			
7	XXX-00007-Z			
8	XXX-00008-Z			
9	XXX-00009-Z			
10	XXX-00010-Z			

4.3.6 Participants Found to be Ineligible (Screen Failures)

Screening should be discontinued if the woman is determined to be ineligible. If the participant is found to be ineligible at the beginning of the screening visit, sites may choose to continue with clinical and laboratory evaluations as a service to the participant, per their site SOPs. If a participant screens out due to a clinical condition requiring follow-up, appropriate referrals should be provided to ensure well-being of the participant. 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 Screening ICF
- Specific, per protocol, reason(s) for ineligibility, with date of determination, as per the completed Eligibility Checklist. Documentation in chart notes, by designated staff, can be substituted if preferred.
- 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 (list item number as appropriate from the Eligibility Checklist) and the Eligibility Criteria CRF should be completed and faxed.

4.4 Enrollment

4.4.1 Definition of Enrollment

Participants will be considered enrolled in MTN-020 once they have been assigned a MTN-020 Prescription. Further information on methods and materials for random assignment is provided in Section 4.4.3.

4.4.2 Enrollment Procedures

Study enrollment procedures are specified in protocol section 7.3 and reflected in the visit checklists contained in Section 7 of this manual. According to Protocol Section 7.3, if a participant is menstruating on the day of enrollment, her entire visit should be rescheduled for two days after the completion of menses. Genital bleeding on the day of enrollment determined not to be menses (e.g. spotting) does not require rescheduling, as long as the participant is comfortable with continuing. Menstruation on the day of enrollment is not one of the formal exclusion criteria for the study and does not pose a safety concern to participants. Note that per LoA#1 pelvic exams and associated pelvic samples are no longer required at the enrollment visit unless clinically indicated. Additional details regarding enrollment procedures are outlined below.

The following procedures will 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 Eligibility Checklist (Appendix 4-2) prior to proceeding with randomization/enrollment per site SOPs.

Before randomization, the participant will undergo the following procedures:

- Obtain informed consent for enrollment (must be conducted before any other procedures on the day of enrollment).
- Confirm 28-day screening window has not been exceeded
- Update and confirm adequacy of locator information
- Confirm behavioral eligibility criteria through administration of the non-datafax Enrollment Behavioral Eligibility CRF
- Update medical/menstrual history since screening visit. Evaluate use of prohibited medications, STI/RTI/UTIs, genital signs/symptoms, history of genital/gynecologic procedures, drug/alcohol use and overall general health.
- Provide contraceptive counseling and discussion of pregnancy/breastfeeding history and future pregnancy intentions.
- Perform pregnancy testing, HIV testing, and plasma archive (**Note for sites not conducting finger stick HIV rapids:** to reduce participant burden, sites should consider collecting plasma archive and HIV samples as part of a single blood draw, prior to randomization)
- In conjunction with HIV testing, participants will receive HIV pre- and post-test counseling as well as risk reduction counseling, including provision of condoms.
- Conduct a physical exam (see Section 10 for required components)
- If indicated, conduct a pelvic exam
- If indicated, participants should be tested for Trichomonas, Bacterial Vaginitis, vaginal candidiasis, herpes lesions, or vaginal pH
- Participants should receive all available test results and treatment or referrals for UTI/RTI/STIs.

- Complete the following behavioral assessments: Baseline Behavior Assessment and Baseline Vaginal Practices CRFs, and Baseline ACASI
- Protocol adherence and vaginal ring (VR) adherence counseling
    - NOTE: this may also be conducted after randomization, but it could be helpful to provide the participant with more information about the ring prior to her final decision to enroll in the study
- Collection of blood for plasma archive
- Self-collection of swab for vaginal fluid (per LoA#2)

Designated staff will document the status of each eligibility criteria prior to randomization by checking "Yes" or "No" on the MTN-020 Eligibility Checklist (Appendix 4-2). 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, and proceed to randomization. All staff members who are responsible for signing off on the Eligibility Criteria CRF should be clearly delegated per the Delegation of Authorities Log and listed as sub-investigators on the FDA Form 1572. Further details regarding randomization procedures can be found in Section 4.4.3.

<u>After randomization,</u> participants will undergo the following procedures:

- Provision of study VR instructions and one study VR for self-insertion
- Demonstrated attempt to remove and insert the VR
- Digital exam to check for correct placement
- If per site practice, provision of a bottle of water for rinsing ring
- Reimbursement
- Schedule next visit

Detailed instructions on VR use including insertion/removal procedures and first product use, as well as VR adherence counseling is provided in Section 12 of this manual.

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 (e.g. participant has to leave early due to an emergency) follow the guidance below:

- If she <u>has not</u> been randomized, reschedule the participant for the enrollment visit within the 28 day window. All procedures must be repeated with the exception of Enrollment Informed Consent. No CRFs from an incomplete enrollment visit should be sent to SCHARP. Note that the plasma archive sample collected at the incomplete enrollment visit should be destroyed and removed from LDMS. The initial baseline ACASI should be marked as a 'duplicate' in the Data Manager program (see SSP Section 16.11). If the participant enrolls indicate the actual enrollment date in the comments field of the Enrollment CRF that is faxed to SCHARP.
- If she <u>has</u> 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, digit exam etc.). For further guidance on visit

code assignment for interim visits conducted between Enrollment and Month 1, refer to the Data Collection section of this manual.

No missed enrollment visit procedures should be made up prior to the Month 1 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, call the participant back as soon as possible for specimen collection. Note that the baseline ACASI should not be made up if missed at Enrollment.

4.4.3 Random Assignment/Prescription Assignment

At all sites, participants will be randomly assigned in equal numbers to one of the two study arms.

Random assignment to study product will occur through assignment of a MTN-020 Prescription. Study prescriptions will be shipped from the MTN SDMC in a binder to each study clinic. They will be stored in the clinic and assigned by appropriate clinic staff in sequential numeric order based on randomization number. Each prescription will have a unique randomization number pre-printed on it. Prescriptions must be assigned in sequential randomization number in order to maintain the integrity and balance of the randomization design. Only one prescription is assigned to each participant. Once a prescription is assigned to a participant, it may not be re-assigned to any other participant.

Prescription assignment is documented using the hard-copy MTN-020 Randomization/Prescription Tracking Record provided by the MTN SDMC (Figure 4-2). The act of assigning a prescription is considered the effective act of enrollment into the study. Once assigned, the prescription should be completed as outlined in Section 9.2.2 and provided to the pharmacy.

Figure 4-2
Sample MTN-020 Randomization/Prescription Tracking Record

MTN-020 Randomization/Prescription Tracking Record Page 1 of 1

CRS Name:	Sample Site	DAIDS Site ID:	99999
CRS Location:	Sample City, Sample Country		

Instructions: Complete one row each time a MTN-020 prescription is assigned to a study participant (randomized). All entries must be made in blue or black ink. Corrections may be made by drawing a line through incorrect entries, entering correct information, and initialing and dating the correction.

MTN-020 Randomization Number (from Prescription)	Prescription Assigned to Participant ID # (111-22222-3)	Date Assigned (dd-MMM-yy)	Time Assigned (hh:mm) 24-hour clock	Clinic Staff Initials
101				
102				
103				
104				
105				

Appendix 4-1

Screening and Enrollment Log for MTN-020 (ASPIRE)

If you are creating a new entry, complete the first three columns and initial and date in the fourth column. When enrollment or screen fail status is determined, complete the remaining columns and initial and date in the last column. Include all codes for screen failure/discontinuation that apply.

Screening Date	Screening Attempt (1 or 2)	PTID	Staff Initials and Date	Enrollment Date (or NA if not enrolled)	Screen Failure Date (or N/A if enrolled)	Screening Failure/ Discontinuation Codes (or N/A if enrolled)	Comments (as needed)	Staff Initials and Date

Screening Failure/Discontinuation Codes

I1	Not within age range	E1a	Intends pregnancy	E5	Diagnosed with PID/STI/RTI	E7e	PEP within 6 months	E8a	AST or ALT grade 1 or higher
I2	No informed consent	E1b	Plans to relocate	E6	Pelvic finding grade 2 or higher	E7f	Last pregnancy outcome within 90 days	E8b	Creatinine grade 2 or higher
I3	Inadequate locator	E1c	Plans to travel away	E7a	Adverse ring reaction (ever)	E7g	Gyn/genital procedure within 90 days	E8c	Hemoglobin grade 2 or higher
I4	HIV infected	E2	Is pregnant	E7b	Adverse latex reaction (ever)	E7h	Participation other study within 60 days	E8d	Platelet count grade 1 or higher
I5	Not sexually active	E3	Currently breastfeeding	E7c	Chronic vaginal candidiasis	E7i	VOICE/other HIV study within 12 months	E8e	Pap grade 2 or higher
I6	No contraceptive	E4	Diagnosed with UTI	E7d	IVDU within 12 months	E7j	Uncontrolled/chronic condition	E9	Any other condition (IoR/designee)
I7	May participate in other studies								

If a participant declines enrollment or does not return to the clinic within the 28 day window to enroll, please record in the Screening Failure/Discontinuation column.

Page _____

Appendix 4-2

PTID:_____ MTN-020 Eligibility Checklist Date:_____

Instructions: Use the table below to document a participant's eligibility status for MTN-020 study participation at the enrollment visit. Initial and date the bottom of each page. For each item, the reference/source document is listed. If ineligibility status is determined, the form may be stopped and the remaining questions may be left blank. Complete the Eligibility Criteria CRF for all screened participants once the participant's eligibility/enrollment status is determined.

Inclusion Criteria	***Yes***	***No***
I1. Age 18 through 45 years (inclusive) at screening, verified per site SOPs *Source: copy of identification card or other documents as specified in SOP*	☐	☐
I2. Able and willing to provide written informed consent to be screened for and take part in the study *Source: signed/marked Screening and Enrollment consent forms*	☐	☐
I3. Able and willing to provide adequate locator information, as defined by the site SOPs *Source: locator forms as listed in SOP*	☐	☐
I4. HIV-uninfected, based on testing performed by study staff at Screening and Enrollment (per applicable algorithm in Appendix II) *Source: rapid HIV testing logs*	☐	☐
I5. Per participant report, sexually active, defined as having vaginal intercourse at least once in the 3 months prior to Screening *Source: Item 10 of Screening Behavioral Eligibility CRF*	☐	☐
I6. Using an effective method of contraception at enrollment and intending to continue use of an effective method for the duration of study participation; effective methods include hormonal methods (except contraceptive ring), intrauterine device (IUD), and sterilization, (of participant, as defined in site SOPs) NB :Participant may commence family planning method during screening or enrollment prior to randomization *Source: Item 6 of Enrollment Behavioral Eligibility CRF, Item 1 of Baseline Family Planning CRF*	☐	☐
I7. Agrees not to participate in other research studies involving drugs, medical devices, vaginal products, or vaccines for the duration of study participation. Does not include tampons – tampons may be used for the duration of study participation. *Source: Item 11 of Screening Behavioral Eligibility CRF, Item 7 of Enrollment Behavioral Eligibility CRF*	☐	☐

Note: In order for the participant to be eligible, all of the responses to items* I1- I7 *above must be "yes"

Exclusion Criteria	***Yes***	***No***
E1. Per participant report at Screening: a. Intends to become pregnant during study participation *Source: Item 8 of Screening Behavioral Eligibility CRF*	☐	☐
b. Plans to relocate away from study site during study participation in the next 2 years *Source: Item 1 of Screening Behavioral Eligibility CRF*	☐	☐
c. Plans to travel away from the study site for more than 8 consecutive weeks during study participation *Source: Item 2 of Screening Behavioral Eligibility CRF*	☐	☐
E2. Is pregnant, based on testing performed by study staff or participant report *Source: pregnancy testing logs or chart note documenting self-report*	☐	☐
E3. Is currently breastfeeding *Source: Item 7 of Screening Behavioral Eligibility CRF, Item 5 of Enrollment Behavioral Eligibility CRF*	☐	☐
E4. Diagnosed with urinary tract infection (UTI) that has not been treated (treatment has not been completed) and/or has ongoing symptoms *Source: Baseline Medical History Questions, Pre-existing Conditions CRF, urine culture results if done*	☐	☐

Exclusion Criteria	Yes	No
E5. Diagnosed with pelvic inflammatory disease, a sexually transmitted infection (STI) or reproductive tract infection (RTI) requiring treatment per current WHO guidelines that has not been treated (treatment has not been completed) and/or has ongoing symptoms. This includes genital warts requiring treatment. A participant diagnosed with asymptomatic BV or asymptomatic candidiasis is eligible - treatment is not required for eligibility purposes. *Source: Baseline Medical History Questions, Pre-existing Conditions CRF, Pelvic Exam Diagram CRF, STI and RTI laboratory results, Screening STI Test Results*	☐	☐
E6. Has a clinically apparent Grade 2 or higher pelvic exam finding (observed by study staff) per the Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events, Version 1.0, December 2004 (Clarification dated August 2009), Addendum 1, Female Genital Grading Table for Use in Microbicide Studies *Source: Pelvic Exam Diagram, Pre-existing Conditions CRF*	☐	☐
Note: *Cervical bleeding associated with speculum insertion and/or specimen collection judged to be within the range of normal according to the clinical judgment of the IoR/designee is considered expected non-menstrual bleeding and is not exclusionary.* ***Note****: Otherwise eligible participants with exclusionary pelvic exam findings may be enrolled/randomized after the findings have improved to a non-exclusionary severity grading or resolved. If improvement to a non-exclusionary grade or resolution is documented within 28 days of provided informed consent for screening, the participant may be enrolled.*		

Exclusion Criteria	Yes	No
E7. **Participant report and/or clinical evidence of any of the following:** a. Known adverse reaction to any of the study products (ever) *Source: Item 6 and 6a of Screening Behavioral Eligibility CRF*	☐	☐
b. Known adverse reaction to latex (ever) *Source: Item 3 of Screening Behavioral Eligibility CRF*	☐	☐
c. Chronic vaginal candidiasis (4 or more treated episodes in the past year) *Source: Item 5 of Screening Behavioral Eligibility CRF*	☐	☐
d. Non-therapeutic injection drug use in the 12 months prior to Screening *Source: Item 4 of Screening Behavioral Eligibility CRF*	☐	☐
e. Post-exposure prophylaxis (PEP) for HIV exposure within 6 months prior to enrollment *Source: Item 3 of Enrollment Behavioral Eligibility CRF*	☐	☐
f. Last pregnancy outcome 90 days or less prior to enrollment *Source: Item 1 of Enrollment Behavioral Eligibility CRF*	☐	☐
g. Gynecologic or genital procedure (e.g. tubal ligation, dilation and curettage, piercing) 90 days or less prior to enrollment *Source: Item 2 of Enrollment Behavioral Eligibility CRF*	☐	☐
h. Recent participation in any other research study involving drugs, medical devices, vaginal products, or vaccines within 60 days of enrollment *Source: Item 4 of Enrollment Behavioral Eligibility CRF*	☐	☐
i. Participation in the MTN-003, Vaginal and Oral Interventions to Control the Epidemic (VOICE) clinical trial, or any other HIV prevention study using systemic or topical antiretroviral medications, within 12 months of enrollment *Source: Item 16 and 17 Screening Behavioral Eligibility CRF, documentation of participant's termination visit from previous trial/study*	☐	☐
j. As determined by the IoR/designee, any significant uncontrolled active or chronic cardiovascular, renal, liver, hematologic, neurologic, gastrointestinal, psychiatric, endocrine, respiratory, immunologic disorder or infectious disease, including active tuberculosis. *Source: Baseline Medical History Questions, Physical Exam CRF, Pre-existing Conditions CRF*	☐	☐

Exclusion Criteria	Yes	No
E8. **Has any of the following laboratory abnormalities at Screening Visit:** *Source for E8a-E8e: laboratory test results reports* a. Aspartate aminotransferase (AST) or alanine transaminase (ALT) Grade 1 or higher as per the Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events Version 1.0, December, 2004 (Clarification dated August 2009)	☐	☐
b. Creatinine Grade 2 or higher as per Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events Version 1.0, December, 2004 (Clarification dated August 2009)	☐	☐
c. Hemoglobin Grade 2 or higher as per the Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events Version 1.0, December, 2004 (Clarification dated August 2009)	☐	☐
d. Platelet count Grade 1 or higher as per the Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events Version 1.0, December, 2004 (Clarification dated August 2009)	☐	☐
e. Pap result Grade 2 or higher according to the Female Genital Grading Table for Use in Microbicide Studies Addendum 1 of the DAIDS Table for Grading Adult and Pediatric Adverse Events, Version 1.0, December 2004 (Clarification dated August 2009).	☐	☐
Note: *Otherwise eligible participants with an exclusionary test result may be re-tested during the screening process.* ***Note:*** *Women with a documented normal result within the 12 months prior to enrollment need not have Pap smear during the screening period. Women with a Grade 1 abnormal Pap smear can be enrolled upon completion of the initial phase of evaluation if no current treatment is indicated (based on local standard of care for management of abnormal cervical cytology). Need for a repeat Pap within 6 months does not preclude enrollment prior to that result becoming available.*		
Exclusion Criteria	**Yes**	**No**
E9. Has any other condition that, in the opinion of the IoR/designee, would preclude informed consent, make study participation unsafe, complicate interpretation of study outcome data, or otherwise interfere with achieving study objectives *Source: Chart notes or this checklist*	☐	☐

Note: In order for the participant to be <u>eligible,</u> all of the responses to items E1- E9 above <u>must be "no"</u>.

Complete Eligibility Criteria CRF for each participant screened for the study, regardless of enrollment.