SCREENING AND ENROLLMENT CONSIDERATIONS

MTN-038 STUDY-SPECIFIC TRAINING
### SCREENING AND ENROLLMENT VISITS

<table>
<thead>
<tr>
<th>Screening/Visit 1</th>
<th>Enrollment/Visit 2 – Day 0</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Eligibility Criteria initially assessed</td>
<td>• Eligibility Criteria Confirmed</td>
</tr>
<tr>
<td>• Multiple visits, if needed (Split visit)</td>
<td>• No split visit permitted</td>
</tr>
<tr>
<td>• One re-screen attempt permitted</td>
<td>• Start study product use</td>
</tr>
<tr>
<td></td>
<td>• Long visit for PK collection</td>
</tr>
</tbody>
</table>

*45 day window*  

*not to coincide with participant’s menses*
## ADMINISTRATIVE PROCEDURES

<table>
<thead>
<tr>
<th>Screening Visit</th>
<th>Procedure</th>
<th>Enrollment Visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial collection per site SOP</td>
<td>Locator Information collection</td>
<td>Review/update per site SOP</td>
</tr>
<tr>
<td>Conduct process: read, assess, confirm, document</td>
<td>Informed Consent</td>
<td>Review/ reconfirm</td>
</tr>
<tr>
<td>Initial assignment: Complete S&amp;E Log; PTID Name Linkage Log</td>
<td>PTID assignment</td>
<td>Use same PTID; Update S&amp;E Log</td>
</tr>
<tr>
<td>Collect via Demographic CRF</td>
<td>Demographic Information</td>
<td>N/A</td>
</tr>
<tr>
<td>Initial assessment: Age, co-enrollment, Screening Behavioral Eligibility</td>
<td>Eligibility Assessment</td>
<td>Confirmation: Co-enrollment, Enrollment Behavioral Eligibility</td>
</tr>
<tr>
<td>N/A</td>
<td>Study Arm Randomization</td>
<td>Via Medidata; after final eligibility sign-off</td>
</tr>
<tr>
<td>For Enrollment; within 45-days</td>
<td>Next Visit Schedule</td>
<td>Visit 3/ Day 1 (next day)</td>
</tr>
<tr>
<td>Per site SOP</td>
<td>Reimbursement Provision</td>
<td>Per Site SOP</td>
</tr>
</tbody>
</table>
Informed Consent

**Complete 1st part of coversheet**

Read ICF

Assess Comprehension

**Complete 2nd part of Coversheet**

### ICF Discussion Date

**ICF Version Number**

**ICF Date of Approved ICF**

**Is the person of legal age to provide independent informed consent for research?**

- Yes
- No STOP Participant is not eligible for MTN-038.

**Can the person read and understand English?**

- Yes
- No STOP Participant is not eligible for MTN-038.

**Start time (HOUR) of IC process/discussion**

---

**Informed Consent Comprehension Assessment (TRUE/FALSE)**

<table>
<thead>
<tr>
<th>No.</th>
<th>Question</th>
<th>True</th>
<th>False</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>If you decide to join this research study, you will be in the study for about 13 weeks.</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2</td>
<td>The primary purpose of this study is to test how effective a vaginal ring with the</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

---

**Complete Before IC Discussion**

**PTID/Name**

**ICF Discussion Date**

**ICF Version Number**

**Date of Approved ICF**

**Is the person of legal age to provide independent informed consent for research?**

- Yes
- No STOP Participant is not eligible for MTN-038.

**Can the person read and understand English?**

- Yes
- No STOP Participant is not eligible for MTN-038.

**Start time (HOUR) of IC process/discussion**

---

**Informed Consent Comprehension Assessment (TRUE/FALSE)**

<table>
<thead>
<tr>
<th>Open-Ended Question/Statement</th>
<th>Required Points of Comprehension</th>
<th>Assessed (+)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Please tell me your understanding of the purpose of the study.</td>
<td>Testing how study drug (Tenofovir) enters and exits the body and testing safety of ring as compared to a placebo.</td>
<td>☐</td>
</tr>
<tr>
<td>2</td>
<td>Tell me what you understand about the three different groups in the study.</td>
<td>One group will receive a VR with the study drug and the other group will receive a VR with no study drug (placebo) both to wear continuously for 13 weeks.</td>
<td>☐</td>
</tr>
<tr>
<td>3</td>
<td>What are the possible risks for participants in the study?</td>
<td>Wear of one of two rings for a total of 13 weeks.</td>
<td>☐</td>
</tr>
<tr>
<td>4</td>
<td>What will happen if you decide not to join the study?</td>
<td>No change to her access to health care whether she joins the study or not.</td>
<td>☐</td>
</tr>
<tr>
<td>5</td>
<td>How will information about participants in the study be protected?</td>
<td>Information about participants is confidential, private, and locked away.</td>
<td>☐</td>
</tr>
<tr>
<td>6</td>
<td>What are the possible benefits for participants in the study?</td>
<td>Counseling, medical exams, tests, clinical care (must mention at least one).</td>
<td>☐</td>
</tr>
<tr>
<td>7</td>
<td>What should you do if you have questions about your health or the study?</td>
<td>Must state how to contact study staff.</td>
<td>☐</td>
</tr>
</tbody>
</table>

---

**Notes/Comments:**

- No study visit procedures took place prior to obtaining informed consent.
- Initials of staff person obtaining consent.

---

Study staff person completing informed consent process/discussion (and this coversheet):
### Screening and Enrollment Log

MTN-038

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.

<table>
<thead>
<tr>
<th>Screening Date</th>
<th>Screening Attempt</th>
<th>PTID</th>
<th>Staff Initials/Date</th>
<th>Enrollment Date (or N/A if not enrolled)</th>
<th>Screen Failure Date (or N/A if enrolled)</th>
<th>Screening Failure/Discontinuation Codes (or N/A if enrolled)</th>
<th>Staff Initials/Date</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Screening Failure/Discontinuation Codes

1-1 Not assigned female sex at birth
1-2 Under age 18 or older than age 45
1-3 No informed consent
1-4 Inadequate locator
1-5 Not proficient in English
1-6 Not available for all visits/npt willing to comply with study
1-7 Not willing to follow administration requirements prior/after visits
1-8 Not willing to use condom during intercourse for study
1-9 No effective contraceptive
1-10 Not in general good health
1-11 HIV infected
1-12 Irregular menses
1-13 Not willing to refrain from non-study sexual products
1-14 Inadequate/Unsatisfactory Pap documentation for past 3 yrs
1-15 Not willing to refrain from other studies
1-16 Pregnant/plans to become pregnant
1-17 Diagnosed symptomatic UTI
1-18 Diagnosed with acute STI
1-19 Breastfeeding/ plans to breastfeed
1-20 Participation in drug/device/ vaginal product/ hormone trial
1-21 Known study product adverse reaction
1-22 Not willing to refrain from other studies
1-23 Chronic/stress urinary incontinence
1-24 Chronic/recurrent vaginal infections

**Notes:**
- Only complete if ppt provides IC
- Completed immediately after IC completion at Screening and updated after eligibility determination at Enrollment
- One entry for each screening attempt (note if 1st or 2nd screening attempt)
- Fill out all codes that apply
Screening and Enrollment Behavioral Eligibility Worksheet

To confirm eligibility for the study, ask the participant the following questions and mark her responses accordingly:

1. Were you assigned female sex at birth?  
   Yes ☐ No ☐

2. Are you able to speak, read, and write proficiently in English?  
   Yes ☐ No ☐

3. Are you available for all visits and willing and able to comply with all study procedural requirements?  
   Yes ☐ No ☐

4. Are you willing to comply with the abstinence and other protocol requirements as explained to you during the informed consent process?  
   Yes ☐ No ☐

5. Are you willing to use male condoms for penile-vaginal intercourse and penile-rectal intercourse for the duration of study participation?  
   Yes ☐ No ☐

6. If you were to join this research study, would you be willing to use an effective form of contraception for 30 days prior to enrollment and for the duration of the study (about 13 weeks)? Effective methods include: hormonal methods (except contraceptive ring), intrauterine device (IUD), sterilization (you or your partner), having sex exclusively with individuals assigned female sex at birth for 30 days prior to your enrollment visit, or abstinence from penile-vaginal intercourse for 30 days prior to enrollment.  
   Yes ☐ No ☐

7. Do you have regular menstrual cycles with at least 21 days between menses?  
   Yes ☐ No ☐

8. Are you willing to refrain from inserting any non-study vaginal products or objects into your vagina or rectum including, but not limited to spermicides, female condoms, diaphragms, intravaginal rings, vaginal or rectal medications, menstrual caps, cervical caps, douche, lubriband, and sex toys (vibrators, dildos, etc.) for the 24 hours preceding your enrollment visit and for the duration of your study participation?  
   Yes ☐ No ☐

9. Do you agree not to take part in any other research studies involving drugs, medical devices, vaginal or rectal products, or vaccines after this screening visit and for the duration of your study participation?  
   Yes ☐ No ☐

10. Are you willing to abstain from using pre-exposure prophylaxis (PrEP) (Truvada®) for HIV prevention for the duration of your study participation?  
    Yes ☐ No ☐

11. In the past 3 months, have you used PrEP for HIV prevention or post-exposure prophylaxis (PEP) for HIV exposure?  
    Yes ☐ No ☐

12. Are you pregnant or do you plan to become pregnant during your study participation?  
    Yes ☐ No ☐

13. Have you ever had an adverse or bad reaction to any of the study products, including polyurethane?  
    Yes ☐ No ☐

14. Do you have chronic and/or recurrent vaginal candidiasis?  
    Yes ☐ No ☐

15. In the past 12 months, have you used a needle to inject drugs that were not prescribed to you by a medical professional?  
    Yes ☐ No ☐

16. Have you been pregnant within the last 90 days (3 months)?  
    Yes ☐ No ☐

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Enrollment Behavioral Eligibility Worksheet

To confirm eligibility for the study, ask the participant the following questions and mark her responses accordingly:

1. Are you available for all visits and willing and able to comply with all study procedural requirements?  
   Yes ☐ No ☐

2. Are you willing to comply with the abstinence and other protocol requirements?  
   Yes ☐ No ☐

3. Are you willing to use male condoms for penile-vaginal intercourse and penile-rectal intercourse for the duration of study participation?  
   Yes ☐ No ☐

4. Have you used one of the following contraceptive methods for the past 30 days: hormonal methods (except contraceptive ring), intrauterine device (IUD), sterilization (you or your partner), having sex exclusively with individuals assigned female sex at birth for the past 30 days; or abstinence from penile-vaginal intercourse for the past 30 days?  
   Yes ☐ No ☐

5. Are you also willing to continue using the same method for the duration of the study, which is expected to be 13 weeks (about 3 and a half months)?  
   Yes ☐ No ☐

6. Have you refrained from inserting any non-study vaginal products or objects into the vagina or rectum including, but not limited to spermicides, female condoms, diaphragms, intravaginal rings, vaginal or rectal medications, menstrual cups, cervical caps, douche, lubriband, and sex toys (vibrators, dildos, etc.) for the 24 hours preceding this visit?  
   Yes ☐ No ☐

7. Are you willing to continue refraining from these activities for the duration of your study participation?  
   Yes ☐ No ☐

8. Do you agree not to take part in any other research studies involving drugs, medical devices, vaginal or rectal products, or vaccines after this screening visit and for the duration of your study participation?  
   Yes ☐ No ☐

9. Are you willing to abstain from using pre-exposure prophylaxis (PrEP) (Truvada®) for HIV prevention for the duration of your study participation?  
   Yes ☐ No ☐

10. In the past 3 months, have you used PrEP for HIV prevention or post-exposure prophylaxis (PEP) for HIV exposure?  
    Yes ☐ No ☐

11. Are you pregnant or do you plan to become pregnant during your study participation?  
    Yes ☐ No ☐

12. Have you ever had an adverse or bad reaction to any of the study products, including polyurethane?  
    Yes ☐ No ☐

13. Do you have chronic and/or recurrent vaginal candidiasis?  
    Yes ☐ No ☐

14. In the past 12 months, have you used a needle to inject drugs that were not prescribed to you by a medical professional?  
    Yes ☐ No ☐

15. Have you been pregnant within the last 90 days (3 months)?  
    Yes ☐ No ☐

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Screening Behavioral Eligibility Worksheet

Enrollment Behavioral Eligibility Worksheet
### COUNSELING AND BEHAVIORAL PROCEDURES

<table>
<thead>
<tr>
<th>Screening Visit</th>
<th>Procedure</th>
<th>Enrollment Visit</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Behavioral Assessment</td>
<td>Baseline CASI (before HIV and pregnancy testing); Select for IDI (after study arm randomization)</td>
</tr>
<tr>
<td>HIV Pre-Test</td>
<td>HIV/STI Counseling</td>
<td>HIV Pre-Test</td>
</tr>
<tr>
<td>STI Risk Reduction</td>
<td></td>
<td>STI Risk Reduction</td>
</tr>
<tr>
<td>HIV Post-Test</td>
<td></td>
<td>HIV Post-Test</td>
</tr>
<tr>
<td>Contraceptive Component only</td>
<td>Protocol Adherence Counseling</td>
<td>Protocol Adherence, Contraceptive, and Product Use components</td>
</tr>
<tr>
<td>Offer, if indicated</td>
<td>Male Condoms</td>
<td>Offer, if indicated</td>
</tr>
</tbody>
</table>
### HIV Pre- and Post-Test and STI Risk Reduction Counseling

- **Prior to HIV testing:** provide HIV pre-test and STI risk reduction Counseling

- **Refer to SSP Table 11-I for HIV Test interpretation guidance**

- **If HIV test results will not be available during the visit, post-test counseling may occur upon provision of test results over the phone or in person as part of a split visit or at an interim visit, if indicated per local standard of care.**

- **Document on Counseling Worksheet or in chart notes. Initial and date each entry.**

### Counseling Considerations

<table>
<thead>
<tr>
<th>MTN-038</th>
<th>HIV Pre/Post Test and Risk Reduction Counseling Worksheet</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General</strong></td>
<td>Staff Initial &amp; Date:</td>
</tr>
<tr>
<td>- Greet client and establish rapport</td>
<td></td>
</tr>
<tr>
<td>- Review purpose and nature of today’s session</td>
<td></td>
</tr>
<tr>
<td>- Discuss counseling objectives for the day as it pertains to the participant</td>
<td></td>
</tr>
<tr>
<td>- Emphasize confidentiality</td>
<td></td>
</tr>
<tr>
<td>- Address any immediate issues or concerns</td>
<td></td>
</tr>
</tbody>
</table>

**HIV Education and Pre Test Counseling**

- Review difference between HIV and AIDS
- Review modes of HIV transmission and methods of prevention
- Review HIV tests to be done today and tests to be done if today’s tests indicate possible infection
- Review window period and how it may affect test results
- Correct any misconceptions or myths

**Risk Reduction Counseling**

- Use open-ended questions to assess client’s HIV risk factors
- Discuss whether risk factors have changed since the last visit
- Probe on factors associated with higher versus lower risk (e.g., what was different about the times when you could use a condom compared to times when you were not?)
- Develop risk reduction strategies with the participant moving forward
- Verify readiness for testing

**HIV Post-Test Counseling**

- Provide and explain test results, per Protocol appendices II
- Explain additional testing that may be required per protocol
- Assess client understanding of results and next steps
- Provide further information and counseling relevant to client’s test results per site SOP

*Notes: If HIV test results will not be available during the visit, post-test counseling may occur upon provision of test results over the phone or in person per local standard of care.*

**Documentation Instructions:** Notes documenting counseling discussions should be recorded below (continuing on the opposite side if needed). Include any questions raised about HIV and HIV testing discussed with the participant. Document participant understanding of HIV test results and next steps. If relevant, document the participant’s personal risk factors for HIV exposure, experiences with the risk reduction strategies tried, any barriers to risk reduction, and a risk reduction plan for the coming month(s). Initial and date after each entry.

**Counseling Notes (add pages/lines as necessary):**

________
### Counseling Considerations

#### Protocol Counseling Worksheet: Protocol Adherence, Product Use, and Contraceptive Counseling

Counseling Considerations

MTN-036/IPM 047

<table>
<thead>
<tr>
<th>PTID</th>
<th>Visit Code</th>
<th>Staff Initial &amp; Date</th>
</tr>
</thead>
</table>

Use this worksheet to guide and document protocol adherence counseling, which encompasses protocol adherence, product use, and contraceptive counseling. Contraceptive counseling should begin at the screening visit, and protocol adherence and product use counseling should begin at the enrollment visit.

For all follow-up visits (V2-11), all three components of protocol counseling must be provided and documented, but may be abbreviated and content tailored to participant needs. Staff should review the participant’s Protocol Counseling Worksheet from the previous visit to determine the level of counseling needed and issues to revisit.

### Protocol Adherence and Product Use Counseling

- **N/A** (Protocol Adherence/Product Use Counseling not required at Screening Visit)

At enrollment, thoroughly review the Study Adherence Guidelines sheet and the Vaginal Ring Insertion Instructions/Important Information sheet with the participant and give her a copy to reference at home.

At enrollment and all follow-up visits, ask the participant if she has any questions and review any medications, non-study products, and practices that the participant should refrain from before the next visit. Offer copies of the Study Adherence Guidelines at each visit.

- **Study Adherence Guidelines reviewed and discussed**
- **Vaginal Ring Insertion Instructions/Important Information sheet reviewed and discussed**

Any protocol adherence issues/questions/concerns discussed at this visit?

- **None reported**
- **Yes. Describe discussion, indicated counseling provided, and note issues to follow-up at next visit:**

### Contraceptive Counseling

At screening, review protocol contraception requirements as well as the participant’s current contraceptive method(s) and/or preferences, and any questions she may have.

At enrollment and all follow-up visits, ask the participant if she has any questions or concerns, confirm current contraceptive method(s), and ensure participant has adequate contraceptive coverage until her next visit.

Current contraceptive method:

Is this a change from the previous visit?

- **N/A** (Screening visit)
- **No**
- **Yes. Explain change:**

Status of next contraceptive prescription:

- **N/A**
- **Prescription refill/renewal or injection needed by ____________ (Date).**

Any contraceptive information/issues/questions/concerns discussed at this visit?

- **No**
- **Yes. Describe discussion, indicated counseling provided, and note issues to follow-up at next visit:**

---

**Protocol Counseling Worksheet:** Protocol Adherence, Product Use, and Contraceptive Counseling

---
Counseling Considerations

MTN-038 Study Adherence Guidelines

Following all study instructions and requirements is important to ensure your safety as a participant and the validity of the study. Please review this document carefully and keep available for reference at home.

- Attend all Study Visits as Scheduled
  It is important for you to come to every study visit. If you cannot come to the visit, please tell the study staff as soon as possible so that the visit can be rescheduled.

- Use an effective contraceptive method
  You must use an effective contraceptive method for the entire duration of the study. Effective methods include sterilization (yourself or your partner), hormonal methods (except contraceptive rings), IUDs, and abstinence from penile-vaginal intercourse.

- Adhere to vaginal ring use instructions
  Be aware of the instructions for inserting, wearing, and removing the vaginal ring provided by the study staff.

- Refrain from certain activities from during specified periods of time, as follows:

  **Duration of study participation:**
  - Inserting any non-study vaginal products or objects into your vagina or rectum, including:
    - Sex toys (dildos, vibrators, etc.)
    - Female condoms
    - Diaphragm
    - Spermicides
    - Lubricants
    - Contraceptive vaginal rings
  - Taking specific medications*, such as:
    - Anticoagulants or blood thinners (such as heparin, heparin, warfarin, Plavix®/Clopidogrel bisulfate)
    - Pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP)

  **72 hours before each clinic visit**
  - Engaging in:
    - Menstrual cups
    - Contraceptive vaginal rings
  - Receptive anal practices including:
    - Receptive vaginal and anal sexual practices (see column to left for specific examples)
  - Taking Assum (greater than 81 mg)
  - Receptive vaginal and anal sexual practices

  **Additional, 72 hours before and after each biopsy collection visit**
  - Taking Assum (greater than 81 mg)
  - Receptive vaginal and anal sexual practices

**VAGINAL RING INSERTION INSTRUCTIONS**

1. Wash your hands with soap and dry them on a clean cloth.
2. Get in the position that is most comfortable for you to insert the ring.
3. Hold and press the sides of the ring together. You may find it easier to insert the ring if you twist it into the shape of the number "S".
4. Use your other hand to press the ring down.
5. Place the tip of the ring into your vagina.
6. Push it up toward the ridge until it is inserted far enough to push the ring into the vagina.
7. The ring should be your hands when you contact the clinician.

**VAGINAL RING IMPORTANT INFORMATION**

Leave ring inserted, all day, every day: The ring should be kept inserted at all times, including bathing.

If the ring falls or is taken out:

**Somewhere clean:** Try to reinsert the ring as soon as possible. If you cannot reinsert it right away, place the ring in the bag provided to you. Before you reinsert, rinse the ring in clean water (no soap permitted) and follow the insertion instructions on the other side.

**Somewhere dirty** (such as the toilet or the ground): Do NOT reinsert the ring. Instead, place it in the bag provided to you and contact the clinic as soon as possible (do not rinse before putting it in the bag).

Avoid and Abstain: Certain vaginal products, devices, and practices are prohibited during all study participation or at specific time points before and after clinic visits. See the Study Adherence Guidelines handout for detailed information on this topic.

Do not Share: Insert only the ring assigned to you and do not share your ring with other women.

Protocol Adherence Support documents:
- **Study Adherence Guidelines**
- **VR Use Instructions**
<table>
<thead>
<tr>
<th><strong>Screening Visit</strong></th>
<th><strong>Procedure</strong></th>
<th><strong>Enrollment Visit</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Collect baseline medical/ menstrual/ Medications Hx</td>
<td>Medical History Review</td>
<td>Review/update baseline medical/ menstrual/ medications Hx</td>
</tr>
<tr>
<td>Full</td>
<td>Physical Exam</td>
<td>Targeted</td>
</tr>
<tr>
<td>Full exam</td>
<td>Pelvic Exam</td>
<td>Full Exam</td>
</tr>
<tr>
<td>Lab and exam findings for initial eligibility</td>
<td>Review findings</td>
<td>Lab and exam findings for eligibility confirmation</td>
</tr>
<tr>
<td>If indicated</td>
<td>Referrals/Rx for UTIs/RTIs/STIs</td>
<td>If indicated</td>
</tr>
<tr>
<td>Per site SOP (at visit or when available)</td>
<td>Provision of Available Results</td>
<td>Per site SOP (at visit or when available)</td>
</tr>
<tr>
<td>N/A</td>
<td>Study Product</td>
<td>Initial VR provision, digital placement check</td>
</tr>
</tbody>
</table>
Baseline Medical History Guide

- Use guide for assessing baseline medical and menstrual history; document on:

  **Chart Notes**
  **Medical History**
  **Concomitant Medications Log**

Document dates of LMP in **Chart notes or Visit Checklists**

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**General Medical History**

- Does the participant have any health problems?
- Has the participant ever been hospitalized for any reason other than giving birth?
- Has the participant ever had surgery, including a hysterectomy?
- In the past year, has the participant been to the emergency room?
- Has the participant had any medical or health problems in the past year?
- Has the participant had a gynecologic or genital procedure (tubal ligation, dilation and curettage, piercing) in the last 48 days?

**Body System Medical History**

Assess any significant medical problems involving the following organ/systems:

- Nervous system
- Neurologic
- Endocrine/Metabolic
- Infections
- Allergies
- Respiratory
- Gastrointestinal (GI)
- Cardiovascular
- Musculoskeletal
- OB/GYN (pelvic bleeding not associated with menopause or childbirth, uterine fibroids, abnormal PAP, genital infection, hysterectomy or uterus, at least one pregnancy)

**Female Symptoms/Diagnoses**

Assess experiences of any significant medical problem involving the following organ system/disease.

- Pelvic inflammatory disease
- Genital/vaginal warts
- Abnormal pap smear

In the past 3 months, ask if the participant has experienced any of the following genital symptoms:

- Genital/vaginal dryness
- Genital/vaginal itching
- Genital/vaginal pain during sex
- Genital/vaginal burning
- Abnormal genital discharge
- Abnormal genital odor
- Dysuria

Assess menstruation pattern. Document in chart notes or other site-specific form and, as applicable, on the Medical History CRF:

- First and last day of last menstrual period
- Any additional details as needed to describe the participant's baseline menstrual bleeding pattern

**NOTE:** For the purposes of scheduling enrollment visit (if otherwise specified), discuss when the participant anticipates her next menses to start/end, as applicable. Ideally, no bleeding should occur within the first 7 days of product use, e.g., Study Week 1 (Days 0, 1, and 7).
## LABORATORY ASSESSMENTS

<table>
<thead>
<tr>
<th>Screening Visit</th>
<th>Procedure</th>
<th>Enrollment Visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV 1/2</td>
<td>Blood</td>
<td>HIV 1/2</td>
</tr>
<tr>
<td>AST/ALT</td>
<td></td>
<td>Plasma for archive</td>
</tr>
<tr>
<td>Creatinine clearance</td>
<td></td>
<td>HSV 1/2 serology</td>
</tr>
<tr>
<td>CBC with differentials/ platelets</td>
<td></td>
<td>CBC with differentials/ platelets*</td>
</tr>
<tr>
<td>Hep B surface antigen</td>
<td></td>
<td>Creatinine clearance*</td>
</tr>
<tr>
<td>Syphilis serology</td>
<td></td>
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<tr>
<td>Blood</td>
<td></td>
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<tr>
<td>HIV 1/2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plasma for archive</td>
<td></td>
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</tr>
<tr>
<td>HSV 1/2 serology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CBC with differentials/ platelets*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine clearance*</td>
<td></td>
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</tr>
<tr>
<td>Urine</td>
<td>Pregnancy</td>
<td>Pregnancy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dipstick UA, Urine Culture*</td>
</tr>
<tr>
<td>NAAT for GC/CT and trichomonas</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pap Test^</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wet prep/KOH wet mounts*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pelvic</td>
<td>Vaginal swabs for microbiota</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vaginal gram stain</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CVF for anti-HSV-2 and biomarkers</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CVL for PD and biomarkers (prior to insertion)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CVF for TFV(1 &amp; 4 hrs-post ring insertion)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Wet prep/KOH wet mounts*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NAAT for GC/CT and trichomonas*</td>
<td></td>
</tr>
</tbody>
</table>
ELIGIBILITY DETERMINATION

ELIGIBILITY CRITERIA Checklist

Instructions: Starting at the enrollment visit, use the table below to document a participant’s eligibility status for participation by marking “yes” or “no.” If reregistration status is determined, any items not yet completed may be left blank. For an ineligible participant, the checklist must be completed for all items and have staff sign-off at the end of the form to confirm and verify eligibility. Complete the inclusion/exclusion eligibility CRF for all screened participants once a participant’s eligibility enrollment status is determined.

Note: The study eligibility criteria are abbreviated in this checklist; refer to Protocol Sections 5, 6, and 7 for a complete description of the criteria.

<table>
<thead>
<tr>
<th>INCLUSION CRITERIA</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-1 Assigned female sex at birth</td>
<td>Source: Screening Behavioral Eligibility Worksheet Item 1</td>
<td></td>
</tr>
<tr>
<td>1-2 Age 18 through 45 years (inclusive) at Screening</td>
<td>Source: copy of all consent/license to other documents as specified in SOP</td>
<td></td>
</tr>
<tr>
<td>1-3 Able and willing to provide written informed consent</td>
<td>Source: Signed consent form(s)</td>
<td></td>
</tr>
<tr>
<td>1-4 Able and willing to provide adequate locator information</td>
<td>Source: Site specific locator form as listed in site SOP</td>
<td></td>
</tr>
<tr>
<td>1-5 Able to communicate in spoken and written English</td>
<td>Source: Screening Behavioral Eligibility Worksheet Item 2</td>
<td></td>
</tr>
<tr>
<td>1-6 Available for all visits and able to comply with all study procedures and requirements</td>
<td>Source: Screening Behavioral Eligibility Worksheet Item 3; Enrollment Behavioral Eligibility Worksheet Item 1</td>
<td></td>
</tr>
<tr>
<td>1-7 Willing to follow smoking requirements and other protocol requirements as outlined in Sections 6.6 and 6.7</td>
<td>Source: Screening Behavioral Eligibility Worksheet Item 4; Enrollment Behavioral Eligibility Worksheet Item 2</td>
<td></td>
</tr>
<tr>
<td>1-8 Willing to use oral contraceptives for pregnancy prevention during the duration of study participation</td>
<td>Source: Screening Behavioral Eligibility Worksheet Item 5; Enrollment Behavioral Eligibility Worksheet Item 3</td>
<td></td>
</tr>
<tr>
<td>1-9 Regularly using an effective contraception method (as defined in the MTN-038 Protocol) for 30 days prior to enrollment, and intending to continue use for the duration of study participation</td>
<td>Source: Screening Behavioral Eligibility Worksheet Item 6; Enrollment Behavioral Eligibility Worksheet Item 4</td>
<td></td>
</tr>
<tr>
<td>1-10 In general, good health as determined by IG/DS Investigator</td>
<td>Source: Medical History CRF, Pelvic Exam CRF, chart notes at Screening and Enrollment</td>
<td></td>
</tr>
<tr>
<td>1-11 HIV uninfected</td>
<td>Source: Local testing log, laboratory test results report or other sites-specific document at Screening and Enrollment</td>
<td></td>
</tr>
<tr>
<td>1-12 Current blood pressure revealed during study participation at screening with at least 25% abnormal range compared to normal range</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-13 Currently on regular medication monitored by a doctor at screening with at least 75% abnormal range compared to normal range</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Final Sign-off of Participant Eligibility to Enroll:

For the participant to be eligible, all responses to inclusion criteria (Items 1-15) above must be “Yes” and responses to exclusion criteria (Items 16-19) above must be “No.”

Staff Signatures: __________________________
Date: _______/______/______
Time: _______/______

Eligibility Criteria Checklist

- Guide for inclusion/exclusion criteria and source documentation
- Start at Enrollment Visit and complete only if participant is eligible.
- Required before enrollment for eligible participants (2 sign-off signatures)
- At any point the participant is deemed ineligible at Enrollment, no need to continue completing
REQUIRED DOCUMENTATION FOR SCREEN FAILURES

- Completed ICF
- All source documentation complete up until the time that ineligibility was determined indicating what procedures were or were not completed and/or screen failure reasons and date of ineligibility determination noted.
- Visit Checklist
- Chart notes
- Completed Screening and Enrollment Log
- Completed Inclusion/Exclusion Criteria CRF with screen failure reason(s) noted
- 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)
PARTICIPANT ENROLLMENT

Confirm and document eligibility

Randomization to study arm

Complete Post-Randomization Procedures

Post-Randomization Procedures

- IDI randomization/selection
- VR Request/Retrieval from pharmacy
- Ring insertion and placement check
- Specimen collection for TFV level testing (CVF only)
- Schedule visit for next day (generate visit calendar)
- Provide reimbursement, study staff contact information, etc.
- Update Screening and Enrollment Log
QUESTIONS? COMMENTS?