Section 4. Participant Accrual

This section provides information on requirements and procedures for recruiting, screening, and randomizing/enrolling participants in MTN 005.

4.1 Study Accrual Plan and Site-Specific Accrual Targets

The accrual period will be 6 months and 10 months at the US and Pune, India sites, respectively. The accrual targets will be 150 women for the Pune, India site and 102 women total across both US sites.

Table 4-1 presents suggested monthly accrual targets for each 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). See Protocol Section 10.7 for additional detail on Participant Accrual.

Table 4-1
MTN 005 Accrual Plan – Participants Enrolled Per Month

Table: Monthly Accrual Target for MTN-005			
Study Month	**Monthly Accrual Target**	**Monthly Accrual Target**	**Cumulative Accrual Target**
	both US Sites	**Pune, India Site**	
1	12 (6 per site)	6	18
2	18 (9 per site)	16	34
3	18 (9 per site)	16	34
4	18 (9 per site)	16	34
5	18 (9 per site)	16	34
6	18 (9 per site)	16	34
7	0	16	16
8	0	16	16
9	0	16	16
10	0	16	16
Total	**102 (51 per site)**	**150**	**252**

Each site will report the number of participants screened for and enrolled in the study to the MTN CORE on a weekly basis throughout the accrual period. Based on this information, the CORE will distribute a weekly consolidated cross-site accrual report to the Protocol Team. In addition, the SDMC will post regular Enrollment and Retention reports on the Atlas web portal based on data received and entered into the study database.

The Protocol Team will monitor accrual rates during the study to determine if accrual targets need to be adjusted. Site staff are responsible for establishing a standard operating procedure (SOP) for participant accrual and for updating the SOP and recruitment efforts undertaken if needed to meet site-specific accrual goals. The accrual SOP minimally should contain the following elements:

- Site-specific accrual goals
- Methods for tracking actual accrual versus accrual goals

- Recruitment methods and venues
- Methods for identifying the recruitment source of participant who present to the site for screening
- Methods for timely evaluation of the utility of recruitment methods and venues
- Pre-screening procedures (if any)
- Ethical and human subjects considerations
- Staff responsibilities for all of the above (direct and supervisory)
- Staff training requirements (if not specified elsewhere)
- QC/QA procedures related to the above (if not specified elsewhere)

4.2 Screening and Enrollment

4.2.1 Definition of Screening

- The term "screening" refers to all procedures undertaken to determine whether a potential participant is eligible to take part in MTN 005. The study eligibility criteria are listed in protocol Sections 5.3 and 5.4. The screening and enrollment procedures are described in protocol Sections 7.1 and 7.2 and Figure 4-2 provides further information on the timing of assessment for each eligibility criterion.

It is the responsibility of the site Investigator of Record 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 an SOP 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-visit eligibility assessment and confirmation procedures
  - Final confirmation and sign-off procedures prior to enrollment
  - Documentation
- Ethical and human subjects considerations
- Staff responsibilities for all of the above (direct and supervisory)
- Staff training requirements (if not specified elsewhere)
- QC/QA procedures related to the above (if not specified elsewhere)

Should site staff identify that an ineligible participant has inadvertently been enrolled in the study, the Investigator of Record or designee should contact the MTN 005 Management Team (mtn005mgmt@mtnstopshiv.org) for guidance on subsequent action to be taken.

Figure 4-2
Timing of Eligibility Assessments for MTN 005

Inclusion and Exclusion Criteria	Assessed At Screening Visit	Assessed At Enrollment Visit
Inclusion		
Age 18-45 years (inclusive) at Enrollment, verified per site standard operating procedures (SOP)	X	
Willing and able to provide written informed consent to be screened for and to take part in the study	X	X
Willing and able to provide adequate locator information, as defined in site SOPs	X	X
HIV-uninfected at Screening based on testing performed by study staff at Screening (per algorithm in Appendix II) and willing to receive HIV counseling and test results	X	
In general good health at Screening and Enrollment, as determined by the site Investigator of Record (IoR) or designee	X	X
Per participant report at Screening and Enrollment, sexually active, defined as having had penile-vaginal intercourse at least once in the past 30 days prior to Screening and Enrollment	X	X
Per participant report at Screening and Enrollment, expecting to continue penile-vaginal intercourse at least monthly for the duration of study participation	X	X
Per participant report, using an effective method of contraception at Enrollment, and intending to use an effective method for the duration of study participation. Effective methods include hormonal methods (except contraceptive vaginal rings), IUD inserted at least 7 days prior to enrollment, study provided male condoms, and/or sterilization (of participant or her sexual partner(s) as specified in site SOPs)	X	X
Pap result in the 12 calendar months prior to Enrollment consistent with Grade 0 according to the Female Genital Grading Table for Use in Microbicide Studies, or satisfactory evaluation with no treatment required of non-Grade 0 Pap result per American Society for Colposcopy and Cervical Pathology (ASCCP) guidelines or per local standard of care, in the 12 calendar months prior to the Enrollment Visit	X	
At Screening and Enrollment, agrees not to participate in other drug or device research study for the duration of study participation	X	X
Able and willing to abstain from the use of non-study vaginal products and/or practices (other than tampons) including but not limited to spermicides, diaphragms, contraceptive vaginal rings, vaginal antibiotic or antifungal medication, sex toys, lubricants or condoms that contain silicone, menstrual cup and douching, within the 14 days prior to Enrollment through study termination	X	X

Exclusion		
Participant reported history of: a. Adverse reaction to silicone (ever) b. Adverse reaction to latex (as defined per SSP) c. Adverse reaction to titanium dioxide d. Any current male sex partner with known history of adverse reaction to latex, silicone, titanium dioxide or any components of the study product (as defined per SSP) e. Last pregnancy outcome within 30 days or less prior to enrollment f. Hysterectomy	X	X
At Screening or Enrollment, has a clinically apparent Grade 2 or higher pelvic exam finding (observed by study staff)	X	X
Pregnant at Screening or Enrollment, or per participant report intending to become pregnant during the period of study participation	X	X
At Screening or Enrollment: a. Unwilling to comply with study participation requirements b. Has a clinically apparent deep disruption of vulvar, vaginal, or cervical epithelium (colposcopic findings not visible by naked eye are not exclusionary) c. Is diagnosed with a symptomatic urinary tract infection[2] d. Is diagnosed with a reproductive tract infection (RTI) or syndrome requiring treatment per current US Centers for Disease Control CDC) guidelines[2] e. Has any other abnormal physical or pelvic exam finding that, in the opinion of the investigator or designee, would contraindicate study participation	X	X
Severe pelvic relaxation such that either the vaginal walls or the uterine cervix descend beyond the vaginal introitus with valsalva maneuver	X	
Participant report of 3 or more sexual partners in the month prior to Screening	X	
At Screening or Enrollment, has condition that, in the investigator's opinion, would preclude informed consent, make study participation unsafe, complicate interpretation of study outcome data, or otherwise interfere with achieving the study objectives	X	X

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.

Otherwise eligible participants with exclusionary pelvic examination 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 45 days of providing informed consent for Screening, the participant may be enrolled.

Note: RTIs requiring treatment, per site specific treatment guidelines, include BV, vaginal candidiasis, other vaginitis, trichomoniasis, chlamydia (CT), gonorrhea (GC), syphilis, active HSV lesions (HSV-2 seropositive women not excluded except with active lesions), chancroid, pelvic inflammatory disease, genital sores or ulcers, or cervicitis. Otherwise eligible participants diagnosed with RTI and/or UTI during Screening will be offered treatment or a prescription for treatment and may be enrolled after completing treatment and all symptoms have resolved. If treatment is completed and symptoms have resolved within 45 days of obtaining informed consent for Screening, the participant may be enrolled.

4.2.2 Definition of Enrollment

Participants will be considered enrolled in MTN 005 when they have been assigned an MTN 005 Randomization Envelope. Further information on methods and materials for random assignment is provided in Section 4.2.6.

4.2.3 Screening and Enrollment Timeframe

All protocol-specified screening and enrollment procedures must take place within a 45-day period, beginning on the day the potential participant provides written informed consent for screening. For example:

- A potential participant who signs or marks her screening informed consent form on March 1 could be enrolled on any day up to and including April 14.

March 2010						
Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
		1 **Screening Consent**	2	3	4	5
6	7	8	9	10	11	12
13	14	15	16	17	18	19
20	21	22	23	24	25	26
27	28	29	30	31		

April 2010						
Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
					1	2
3	4	5	6	7	8	9
10	11	12	13	14 **Last Day to Enroll**	15	16
17	18	19	20	21	22	23
24	25	26	27	28	29	30
31						

In the above example, the participant signed the screening informed consent form on 01 March 2010 (day 1) and has until 14 April 2010 (day 45) to complete all screening and enrollment procedures. To help ensure that the 45-day screening period is not exceeded, study staff are strongly encouraged to highlight the allowable screening period on their screening and enrollment visit checklists (as shown in Section 7 of this manual).

If all screening and enrollment procedures are not completed within 45 days of obtaining informed consent for screening, the participant must repeat the entire screening process, including the screening informed consent process, except for the PTID assignment. Re-screened participants will retain the assigned PTID from their first screening attempt. The term "screening attempt" is used to describe each time a participant screens for the study.

4.2.4 Screening and Enrollment Logs

The DAIDS SOP for Essential Documents requires study sites to document screening and enrollment activity on screening and enrollment logs. Screening and enrollment logs may be maintained separately or combined into one log. Figure 4-3 presents a sample screening and enrollment log suitable for use in MTN 005. Study sites are encouraged to reference last page of the Screening and Enrollment Logs (see Study Implementation tools on the MTN 005 website) when recording the reason for screening failure/discontinuation on the screening and enrollment logs.

Figure 4-3
Sample Screening and Enrollment Log for MTN 005

	Screening Attempt	Date Screening Consent Signed	PTID	Date Enrollment Consent Signed(or N/A if not enrolled)	Enrollment Date (or N/A ifnot enrolled)	Group (IVR or non-IVR)	Screening Failure/ Discontinuation Date (or N/A if not enrolled)	Reason for Screen Failure/ Discontinuation
1								
2								
3								
4								
5								
6								
7								
8								
9								
10								

4.2.5 Assignment of Participant ID Numbers

SCHARP will provide each study site with a listing of Participant ID (PTID) numbers for use in MTN 005 in the form of a PTID-Name Linkage Log.

Further information regarding the structure and assignment of PTIDs for MTN 005 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, and will be assigned at the Screening Visit. Site staff are responsible for establishing SOPs and staff responsibilities for proper storage, handling, and maintenance of the PTID list such that participant confidentiality is maintained, Figure 4-4 below shows an example of a PTID-Name Linkage Log used to assigned PTIDs.

Figure 4-4
Sample Site-Specific PTID Name-Linkage Log for MTN-005

	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			

4.2.6 Random Assignment

Overview

At each study site, enrolled participants will be randomly assigned to one of the two study arms, IVR or no IVR, in a 2:1 ratio. This means that of the 252 planned enrollments, a total of 168 participants will be randomly assigned to the IVR arm, and 84 to the no IVR arm. The 2:1 randomization ratio is consistent within each site, such that the Pune site will have 100 participants assigned to the IVR arm and 50 to the no IVR arm. Between the two US sites, 68 participants will be assigned to the IVR arm, and 34 to the no IVR arm.

The SDMC will generate and maintain the study randomization scheme and associated materials, which consist of the following:

- MTN-005 Randomization Envelopes (Figures 4-5a, 4-5b, and 4-6)
- MTN-005 Randomization Envelope Tracking Records (Figure 4-7)
- MTN-005 Prescriptions, included in the Randomization Envelopes (Figures 4-8a and 4-8b)

- MTN-005 Site-Specific Pharmacy Dispensing Records

MTN 005 Randomization Envelopes (see Figure 4-5a) will be shipped from the SDMC to each study clinic. They will be stored in the clinic and assigned in sequential order to participants who have been confirmed as eligible and willing to take part in the study. Envelopes must be assigned in sequential order, and 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 security tape to ensure envelopes are not tampered with or opened prior to assignment to a participant. (see Figure 4-6).

Figure 4-5a
Sample MTN 005 Randomization Envelopes

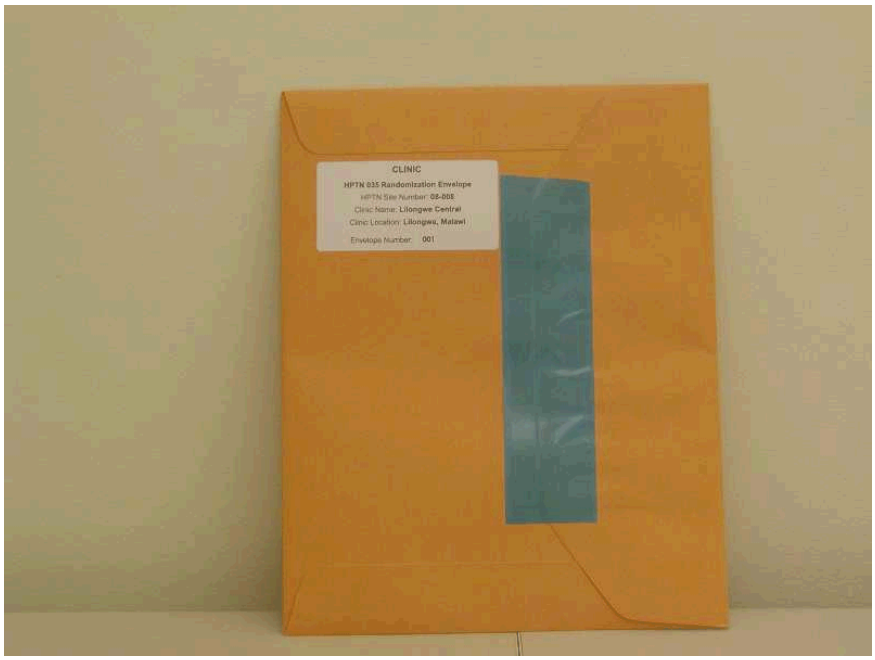


Figure 4-5b
Sample MTN 005 Randomization Envelope — Close-Up View of Label

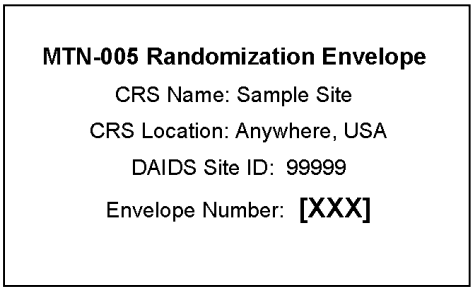
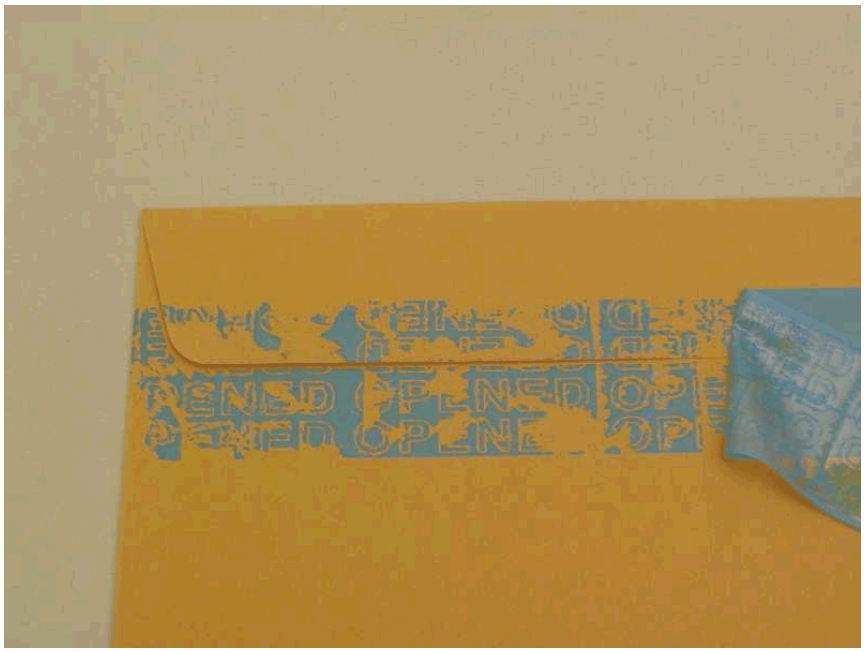


Figure 4-6
Sample Opened MTN 005 Clinic Randomization Envelope



Envelope assignment to eligible participants will be documented on the MTN-005 Randomization Envelope Tracking Records (see Figure 4-7) that will accompany the initial envelope shipment to each site. **The act of assigning an MTN-005 Randomization Envelope to a participant is considered the effective act of randomization and enrollment into the study**. Once a MTN-005 Randomization Envelope is assigned, the participant is considered enrolled in the study.

Each Randomization Envelope will contain an MTN-005 prescription (see Figure 4-8a, 4-8b). Prescriptions will be produced as two-part no carbon required (NCR) forms pre-printed with the site name, site number, clinic name, Randomization Envelope number, and a random assignment (IVR or no IVR). After recording the PTID and other details on the prescription, clinic staff will separate the two parts of the form and deliver the white original form to the pharmacy. The envelope and the yellow copy of the prescription will be retained in the participant's study notebook.

Figure 4-7
Sample MTN-005 Randomization Envelope Tracking Record

CRS Name:	**Pre-print**	**DAIDS Site ID:**	**Pre-print**
CRS Location:	**Pre-print**		

Instructions: Complete one row each time an MTN-005 Randomization Envelope is assigned to a study participant. 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-005 Randomization Envelope #	Envelope Assigned to Participant ID #	Date Assigned (dd-MMM-yy)	Time Assigned (hh:mm) (24-hour clock)	Clinic Staff Initials
Pre-print				

Figure 4-8a
Sample MTN 005 Prescription — IVR

MTN-005 PRESCRIPTION

Instructions: All entries must be made in dark ink. Press firmly when completing this form. Corrections may be made by drawing a single line through incorrect entries, recording correct information, and initialing and dating the correction.

CRS Name:	**Pre-print**	DAIDS Site ID:	**Pre-print**
CRS Location:	**Pre-print**	Randomization Envelope #:	**Pre-print**

Participant ID: ☐☐☐–☐☐☐☐☐–☐

Did the participant provide written informed consent for enrollment into MTN-005? ..... Yes ☐ No ☐ Clinic Staff Initials _____

Assignment: IVR

SIG: Insert one non-medicated intravaginal ring into the vagina at the Enrollment Visit. Leave the ring in place for 12 consecutive weeks.

Quantity: One non-medicated intravaginal ring. Refill only one additional non-medicated intravaginal ring if needed.

Authorized Prescriber Name (please print): _____

Authorized Prescriber Signature: _____

Date: ☐☐–☐☐☐–☐☐
dd *MMM* *yy*

Clinic Staff Instructions: Complete all items on this prescription. After initialing and dating below, deliver original white copy (labeled "Pharmacy") to pharmacy. File yellow copy (labeled "Clinic") in participant study notebook.

Clinic Staff Initials: _____ Date: ☐☐–☐☐☐–☐☐
dd *MMM* *yy*

Pharmacy

Figure 4-8b
Sample MTN 005 Prescription — No IVR

MTN-005 PRESCRIPTION

Instructions: All entries must be made in dark ink. Press firmly when completing this form. Corrections may be made by drawing a single line through incorrect entries, recording correct information, and initialing and dating the correction.

CRS Name:	**Pre-print**	DAIDS Site ID:	**Pre-print**
CRS Location:	**Pre-print**	Randomization Envelope #:	**Pre-print**

Participant ID: ☐☐☐–☐☐☐☐☐–☐

Did the participant provide written informed consent for enrollment into MTN-005? ..... Yes ☐ No ☐ Clinic Staff Initials _____

Assignment: No IVR

Pharmacy Staff Instructions: DO NOT dispense MTN-005 study intravaginal ring to this participant. Complete the date item below, then store this document with the MTN-005 Site-Specific Pharmacy Dispensing Record.

Date this form received in pharmacy: ☐☐–☐☐☐–☐☐
dd *MMM* *yy*

Clinic Staff Instructions: Once form is complete, deliver original white copy (Pharmacy) to pharmacy; retain yellow copy (Clinic) in participant study notebook.

Clinic Staff Name (please print): _____

Clinic Staff Initials: _____ Date: ☐☐–☐☐☐–☐☐
dd *MMM* *yy*

Pharmacy

4.3 Participant-Specific Procedures

For each participant, random assignment will take place after the participant has been confirmed as eligible and willing to take part in the study, as documented by her signing or marking an informed consent form for enrollment. Random assignment also will take place after the participant has completed the ACASI Baseline Behavior Assessment and has provided blood for plasma archive.

4.3.1 In Clinic:

C1. Obtain the next sequential MTN-005 Randomization Envelope and inspect it to verify that the correct envelope has been obtained and there is no evidence that the envelope has previously been opened or otherwise tampered with. Assign the envelope to the participant and document assignment on the MTN-005 Randomization Envelope Tracking Record by recording the PTID, date assigned, time assigned, and authorized clinic staff initials in the row corresponding to the assigned envelope number.

C2. Open the assigned Randomization Envelope; alternatively, allow the participant to open it herself. Remove the prescription and confirm the information pre-printed at the top of the form. In particular, confirm that the envelope number printed on the prescription corresponds to the envelope number on the outside of the envelope. If the envelope does not contain a prescription, or if any information pre-printed on the prescription appears to be incorrect, contact the MTN-005 management team, SDMC Project Manager and the site Pharmacist of Record (PoR) immediately. The PoR will inform the MTN Research Pharmacist. Do not proceed with randomization of this or any other participant until instructed to do so by the SDMC.

C3. Inform the participant of her study arm assignment and provide appropriate information, instructions, and counseling applicable to her assignment. Refer to study-specific informed consent support materials and the Frequently Asked Product Use Questions in Section Appendix 9-1 for reference as needed.

C4. Complete the prescription as follows:

In the top section of the prescription, record the PTID and mark whether the participant provided informed consent to take part in the study. The person who marks the informed consent check box is responsible for confirming the presence of a properly signed/marked and dated informed consent form for enrollment prior to recording his/her initials beside these boxes.

For participants assigned to IVR, the middle section of the prescription must be completed by a study staff member designated in the site's delegation of duties as an authorized prescriber of study product. This person also must be listed as an investigator (either the Investigator of Record or Sub-Investigator) on the current FDA Form 1572. For participants assigned to no IVR, note that the middle section ("Date received in Pharmacy") will remain blank on the clinic (yellow) copy of the completed prescription, as this information is only completed once the NCR form has been separated, and the white copy received in the pharmacy.

The bottom section of both the IVR and no IVR prescription may be completed by any clinic staff member.

C5. Double-check the accuracy of all entries and then separate the two parts of the completed prescription. Retain the yellow copy in the participant study notebook. Also retain the MTN-005 Randomization Envelope in the participant study notebook. Empty Randomization Envelopes may be hole-punched after they have been opened and their contents have been removed.

C6. Deliver the white original prescription to the study pharmacy. This may be done by the participant or by a study staff member.

In the event that pharmacy staff identifies possible errors on the original prescription, they will return the original prescription to clinic staff for clarification or correction. If corrections are required, corrections must be made on both the white original prescription and the yellow copy. A signed and dated note explaining the corrections also should be recorded on both copies. Identical corrections and notes should be recorded on both copies, on the same date, by the same person. Corrections should only be made by study staff authorized to complete original prescriptions, and fully documented in the participant's chart notes.

Section Appendix 4-1
Screening and Enrollment Scenarios for MTN 005

4.1	**Suppose a participant begins the study screening process (i.e., signs or marks the screening informed consent), and that based on the protocol-specified screening visit procedures she appears to be eligible for the study. When her screening lab results are received, however, she is found to have Chlamydia. What do you do?** • When the participant returns for the Enrollment visit, provide results and Chlamydia treatment and continue the enrollment process. Ideally single-dose treatment will be provided, so that if the participant is otherwise eligible for the study and free of STI/RTI symptoms, she may be enrolled at this visit. • If single dose treatment is not provided, schedule the participant to return to the study site to complete the enrollment process immediately after treatment has been completed (assuming she remains free of STI/RTI symptoms at that time). Otherwise eligible participants diagnosed with RTI and/or UTI during Screening will be offered treatment or a prescription for treatment (per site SOPs), and may be enrolled after completing treatment and all symptoms have resolved. If treatment is completed and symptoms have resolved within 45 days of obtaining informed consent for Screening, the participant may be enrolled.
4.2	**Suppose a participant begins the study screening process on May 1, and she appears to be eligible. At her Enrollment visit (on May 15) she does not report any STI/RTI symptoms, and otherwise appears to be eligible for the study, but she is diagnosed with bacterial vaginosis (BV) based on Amsel's criteria. What do you do?** • Enroll the participant in the study on May 15. Asymptomatic BV does not require treatment per CDC guidelines. The participant is free of STI/RTI symptoms and therefore is eligible for the study on May 15 despite having been diagnosed with BV that day.
4.3	**Suppose in Scenario 4.2 that, rather than being asymptomatic, the participant reports abnormal vaginal discharge and is diagnosed with BV based on Amsel's criteria at her Enrollment visit. What do you do?** • Provide treatment for BV (ideally single-dose). Schedule the participant to return to the study site to complete the enrollment process after treatment is expected to be completed and symptoms are expected to have resolved. The enrollment process may continue once treatment is completed and all STI/RTI symptoms have resolved, and the 45-day screening window has not elapsed. • Note: A repeat screening pelvic exam is not required prior to enrollment when she returns to the clinic, since she had no exclusionary pelvic exam findings, and since "no test of cure" is required for treatment of BV. Symptomatic BV requires treatment per CDC guidelines and all STI/RTI symptoms must be resolved prior to enrollment in the study.

Section Appendix 4-1
Screening and Enrollment Scenarios for MTN 005

4.4	**Suppose a participant begins the study screening process on May 1, and that she appears to be eligible. At the enrollment visit on May 9, the clinician observes a deep disruption of the vaginal epithelium during a pelvic exam, but no other STI/RTI signs or symptoms are present. What do you do?** • Schedule the participant to return to the study site for a repeat screening pelvic examination as soon as possible after the observed finding is expected to be resolved. Assuming the finding is resolved at that time, and the 45-day screening window has not elapsed, continue the screening and enrollment process. (Note: If syphilis is suspected, also collect blood and perform syphilis serology.) An observation of a clinically apparent deep disruption of the vulvar, vaginal or cervical epithelim is exclusionary for this study (colposcopic findings not visible by naked eye are not exclusionary).
4.5	**Suppose in Scenario 4.4 that the observed finding involving a deep disruption of the vaginal epithelial disruption is consistent with a genital herpes (HSV-2) outbreak. What do you do?** • Provide the participant with treatment and schedule her to return to the study site for a repeat pelvic examination as soon as possible after treatment is expected to be completed and the finding involving epithelial disruption is expected to be resolved. Assuming the finding is resolved at that time, no STI/RTI symptoms are present, and the 45-day screening window has not elapsed, continue the screening and enrollment process. A pelvic exam finding of deep disruption of the vulvar, vaginal or cervical epithelium is exclusionary for this study. If it is consistent with a genital herpes outbreak, it should be treated per CDC guidelines. If treatment is completed and symptoms resolved within 45 days of obtaining informed consent for screening, the participant may be enrolled.
4.6	**A 28 yo potential participant presents for screening, and reports having had an abnormal pap smear 3 months prior to the screening visit. On review of her records, you see that she had a LGSIL pap smear followed by colposcopy 2 weeks later (2.5 months prior to the screening visit). The colposcopy was reported as satisfactory and a biopsy of the endocervix was obtained. The final biopsy pathology was read as CIN 1. Per the gynecologist's records and the participant's understanding, the participant is to have a repeat pap smear done 6 months after the LGSIL pap smear. Is she eligible?** • This participant is eligible as she has a non grade 0 pap smear that has been adequately evaluated per ASCCP guidelines and does not require further treatment. A follow-up pap smear is not considered "treatment," but rather surveillance.

Section Appendix 4-1
Screening and Enrollment Scenarios for MTN 005

4.7 A 28 yo potential ppt presents for screening, and has not had a pap smear in over one year. Per protocol, a pap smear is performed as part of her screening procedures. The results are returned as satisfactory for evaluation, ASCUS-HPV. Is she eligible?

- Answer: At this point she is not eligible as she has not had a thorough evaluation of this abnormal pap smear. Per ASCCP guidelines, an ASCUS/HPV positive pap smear should be followed with colposcopy. You should refer her for colposcopy.
- If she undergoes a colposcopy and a biopsy is NOT performed as her lesion appears low-grade, she is eligible to enroll in the study. She has had thorough evaluation of her pap smear and no further treatment is required. Likely she will have been instructed to have another pap smear in 6 months from her ASCUS/HPV pap smear for surveillance; this is not considered "treatment."
- If she undergoes a colposcopy and a biopsy is performed, she may still be eligible for the study depending on the timing of events. Deep epithelial disruption is an exclusion criterion so this participant will need another pelvic exam after the biopsy to confirm adequate healing prior to being enrolled