

## **MTN-013/IPM 026 Frequently Asked Questions (FAQs)**

This document offers introductory answers to frequently asked questions about the MTN-013/IPM 026 protocol and related study implementation.

Click on a subject heading below to view questions and answers relating to that selection. Links throughout the answers will guide you to further information on the [MTN-013/IPM 026 webpage](#) or from other sources.

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Should you have any further questions, please contact the MTN-013/IPM 026 Study Management Team ([mtn013mgmt@mtnstopshiv.org](mailto:mtn013mgmt@mtnstopshiv.org)).

## MTN-013/IPM 026 Frequently Asked Questions (FAQs)

### General Questions

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1. If a participant screens out for more than one reason, do we report all these reasons on the screen-failure report or only the primary reason? How often do these reports get sent to FHI? Is there a standard set of screen failure reasons that we should be categorizing by?
  - a. Only the primary reason for screen failure should be included in the report. For example, if during the screening visit, a participant tests positive for pregnancy and once the remaining lab test results are received, she also has exclusionary laboratory test results, the primary reason for screen out should be the pregnancy test because it was the first indicator that the participant was not eligible for the study. In other words, only send one screen failure reason per participant.
2. After the vaginal ring has been dispensed and inserted by the participant, can the foil pouch be discarded that contained the ring?
  - a. The foil pouch can be discarded only after site staff ensures the pharmacist has removed the coded label. Site staff are reminded that the randomization envelope should be maintained in the participants notebook and the coded label maintained in the pharmacy.
3. Per protocol, women with an exclusionary lab test result during screening will be excluded from the study. However, otherwise eligible participants with an exclusionary test result may be retested during the screening process. If a participant is re-tested and a non-exclusionary result is documented within 45 days of providing informed consent for screening, the participant may be enrolled. What is the limit to the number of times a participant can be retested for an exclusionary lab result within the 45-day screening-enrollment window?
  - a. Participant can be retested one time. If the participant still has an exclusionary result on the second lab test, she should be considered a screen fail. If the participant is willing and able, per protocol, she may be re-screened one time. If a second screening attempt is made, the same re-testing criterion applies.
4. How is recurrent and/or chronic candidiasis defined?
  - a. Per [2010 CDC Sexually Transmitted Diseases Treatment Guidelines](#), recurrent vulvovaginal candidiasis is defined as four or more episodes of symptomatic infections in 1 year.
5. What should site staff do if during the tear test strip collection, they notice there are 2-3 tear strips stuck together in the glass tube the strips were supplied?
  - a. If more than one strip is detected prior to sampling, remove the extra strip and perform the pre-weight with only one tear strip in the tube. Continue specimen collection per protocol.
  - b. If more than one strip is detected after to sampling has already occurred, continue to place the strips in the glass tube and perform the post weight. Note on the Tear Test Strip Weights CRF that more than one strip is in the tube.

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6. Per protocol, sexual abstinence is defined as ‘abstaining from receptive sexual activity including receptive penile intercourse, anal intercourse, receptive oral intercourse and the use of sex toys.’ Participants must be willing to abstain from receptive sexual activity for the 14 days prior to enrollment and for the duration of study participation to be eligible for participation. Are participants restricted from ‘giving’ oral sex to their sexual partner?
  - a. No. The participant is able to ‘give’ oral sex to their partner. This is defined as the participant putting her mouth or tongue on her partner's penis, vagina or anus (or butt).
  - b. For study eligibility purposes, the following definitions apply to receptive sexual activity:
    - Vaginal Sex: When a man inserts his penis into the study participants’ vagina.
    - Receptive Anal Sex: When a man puts his penis into the study participants’ anus (or butt).
    - Receiving Oral Sex: When a partner puts his or her mouth or tongue on the study participants’ vagina, or anus (or butt).
7. On the screening and enrollment reports, who should be counted in the ‘In Pipeline’ category? Why do we need to report this number?
  - a. The ‘In Pipeline’ category should include only those participants who are still undergoing the screening process and still have the potential to enroll. In other words, participants who have completed all required Screening procedures, and have not screened out, but who have yet to enroll. It is expected that not all participants “in screening” will enroll. The rationale behind including this information is because the protocol team is interested in knowing the total number screened and how many still have the potential to enroll. They cannot get this information from the reported "total no. screened" as this includes both screen-outs and those still undergoing the screening process.
8. In the event a participant reports a history of chronic and/or recurrent candidiasis but does not have an active infection at the time of the visit, how is this graded?
  - a. Participant eligibility is first assessed at Screening. If a participant does not have an active infection but reports a history of recurrent infections, it should be graded using the category “Estimating Severity Grade” located on Page 3 of the Table for Grading the Severity of Adult and Pediatric Adverse Events Version 1.0 - December 2004 (Clarification dated August 2009) Toxicity Table. For the [DAIDS Adverse Event Grading Tables](#), please visit the DAIDS Regulatory Support Center website.

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1. Is there an allowable time window for the 1, 2, 4, and 6 hour PK blood draws at Enrollment (Day 0) and Day 28?
  - a. Sites should make every effort to collect the 1, 2, 4, and 6 hour post ring insertion blood draws at the protocol defined times. However, there is an allowable window of +/- 15 minutes prior to and following each designated time point to allow for flexibility. A PK Timepoint Calculator was developed to help sites calculate the timing for collection of blood specimens at the Enrollment and Day 28 study visits. This tool is available on the [MTN-013/IPM 026 webpage under Study Implementation Materials](#).
  
2. On item #12 on the Pharmacokinetics Specimens (PKS-1) case report form (CRF), sites should record the start and stop dates of the participants' last menstrual period at the Enrollment, Day 28, and Day 52 visits. However, what should be recorded if a participants experiences episodes of irregular bleeding throughout the study?
  - a. The purpose of Item #12 is to capture menstrual dates only. This information will be assessed to determine if menses or stage of menstrual cycle affects vaginal tissue absorption of study product. Only the dates of menses (regardless of cause) should be recorded; not dates of spotting or breakthrough non-menstrual bleeding.
  
  - b. If the participant has not had a menstrual period since this item was last completed, mark "none." If, at Enrollment, the participant has not had a period within the last 30 days, mark "none."
  
3. At Day 28, can site staff collect the blood samples for the required CBC with differential and platelets and chemistries testing and HIV serology, if clinically indicated, at the same time blood is collected for the PK hour 0 (within 15 minutes prior to VR removal) time point?
  - a. Yes. At the Day 28 visit, it is acceptable to collect the blood sample for the CBC with differential and platelets, Creatinine, AST, ALT and HIV (if indicated) at the same time you collect the 0-hour PK blood draw.

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### Behavioral Assessments

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1. On the behavioral assessment training PowerPoint presentation, slide #7 states that the Baseline CASI should be administered after the Enrollment CRFs have been completed, but before ring insertion and product use counseling. However, completion of the Enrollment CRF requires the participant to already be randomized and the Enrollment Visit Checklist states that the CASI questionnaire must be performed prior to randomization. Is this a discrepancy? Please clarify?
  - a. The PowerPoint training slide is actually referring to the 'Enrollment Behavioral Eligibility' Non-Data Fax CRF not the 'Enrollment' Data-Fax CRF'. The 'Enrollment' CRF is completed to document the participant's enrollment/randomization and yes should be done after randomization. A portion of the baseline CASI questionnaire is measuring the participant's initial attitude towards the vaginal ring prior to her exposure so it is done prior to her inserting the ring and receiving the associated product use counseling.

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1. How are abnormal or normal healing biopsy sites recorded following the Day 28 study visit?
  - a. If or when the clinician conducts a pelvic examination after Day 28, it is not unusual to see evidence of the previous biopsies. Evidence of a normal-healing biopsy site within several weeks of the biopsy is considered expected and therefore does not meet the requirement for adverse event reporting. A normal-healing biopsy site does not require documentation as an abnormal finding. This should be considered a normal finding that does not require mention on the Pelvic Exam CRF. Please note this on the Pelvic Exam Diagram CRF and/or in a signed and dated chart note (for example: cervical biopsy site healing normally at ... (specify location)).

However, abnormally healing biopsy site(s), which should prompt adverse event reporting, include biopsy site(s) with evidence of infection or any other characteristics which the IoR or clinician deems to be abnormal and reason for concern. If at any time the investigator deems the biopsy site(s) to be healing inappropriately, please consult the MTN Safety Physicians ([mtn013safetymd@mtnstopshiv.org](mailto:mtn013safetymd@mtnstopshiv.org)) with any questions or concerns.

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#### Visit Scenarios

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1. During a Day 21 study visit, when discussing ring use over the previous week, a participant reports her vaginal ring was partially expelled while having a bowel movement. The ring did not completely come out of the vagina and she was able to push the ring back into place with her finger. Should this be considered an instance where the ring has not been used? How should this participant-reported information be documented?
  - a. All instances of complete and/or partial expulsion of the ring should be documented on the Ring Adherence (RA-1) CRF and on the Ring Use Log, as applicable.

Ring Adherence (RA-1) CRF Completion Instructions: For this case scenario only.

- Item 2 should be marked 'yes'.
  - Item 2a should be '01' for the # of times.
  - Item 3 should be recorded as follows: '00' for days; '00' for hours; and '00' for minutes.
  - For the removal/expulsion code, use the appropriate code that caused the partial expulsion. In this case, the expulsion code should be '02' for 'having a bowel movement'.
  - In the 'Comments' section, site staff should include a note that item 3a (or appropriate sub-item 3) is a 'partial expulsion – ring did not come out completely'.
2. A participant has her Day 7 (visit code 7.0). Two days later, she contacts site staff to discuss some new symptoms she is experiencing. Site staff requests that she come into the clinic the next day to assess her concerns. Will the phone contact placed two days after the Day 7 visit in addition to her in-clinic visit to assess any concerns or findings be considered interim visits?
    - a. It is dependent on when site staff will complete the AE Log CRF. If the AE Log CRF is completed at the time the participant contacts the clinic by phone, then the phone call should be assigned an Interim Visit code (7.1). When the participant comes to the clinic for an assessment, the in-clinic visit should be assigned the next sequential Interim Visit code (7.2).
    - b. However, if the AE Log CRF is completed after the in-clinic visit is completed and no other CRFs require completing based on the earlier phone call, then the in-clinic visit should be assigned the Interim Visit code (7.1). The phone call can be noted in a signed and dated chart note as long as no other CRFs are completed.
  3. What steps should be taken if a participant reports she experienced symptoms during interviewer-administered semi-structured Interview (SSI) that she did not report previously to site staff.
    - a. Study staff must document in source documents and case report forms all AEs reported by or observed in study participants. Clinical evaluations including a pelvic exam as appropriate should be conducted to assess her symptoms. Site staff should follow up and record as an AE(s) as appropriate. In her progress notes and on the AE Log site staff can note that it was first reported by the participant during the SSI. At each follow-up visit, an authorized study clinician should review all previously identified ongoing AEs and evaluate and document their current status in participants chart notes.

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4. A participant was provided written informed consent for screening prior to the site receiving IRB approval for LoA#01 thus HBsAg and Anti-HCV testing was not done. The Enrollment ICF was revised to add *“If you did not have Hepatitis B or C tests at your Screening visit, you will need to have these tests performed at an upcoming visit. These tests will require a blood sample.”* Is the participant required return to the clinic for HBsAg and Anti-HCV testing prior to her scheduled enrollment visit?
  - a. No. Unless the participants' labs indicate ineligibility and retesting is required, sites are not required to bring the participant back in for Hepatitis B and C testing prior to enrollment. She can proceed to her enrollment visit at which time she can be tested for Hepatitis B and C. If hepatitis B or C infection is confirmed, product use must be permanently discontinued. Refer to [Section 6.13 of the MTN-013/IPM 026 SSP Manual](#) for modified follow-up procedures to be completed for participants who are found to be infected with Hepatitis B and/or C.