Section 5. Participant Follow-up/Visit Checklists

This section provides information on requirements and procedures for participant follow-up in MTN-012/IPM 010. Examples of visit checklists detailing the protocol-specified procedures and data collection forms that must be completed at MTN-012/IPM 010 study visits are also available in this section.

5.1 Study Follow-up Plan and Participant Retention Targets

Once enrolled, each participant will undergo 7 days of study product use, and one additional day of follow-up off study product for a total study duration of approximately 8 days.

As this is a short-term Phase 1 study, a retention rate of 100% is targeted across sites. Further information on retention definitions and procedures for MTN-012/IPM 010 is provided in Section 6 of this manual.

5.2 Types of Follow-up Visits

Scheduled Visits are those visits required per protocol. The protocol specifies that, after Screening and Enrollment visits, participants will have one Follow-up Phone Assessment, and a Final Clinic Visit/Termination Visit.

Interim Visits are those visits that take place between scheduled visits. More specifically, a visit is considered an interim visit when a participant presents for additional procedures or assessments beyond the required procedures for a scheduled visit. There are a number of reasons why interim visits may take place (see protocol Section 7.6). Site staff may be required to assign visit codes to interim visits for purposes of data management as described in Section 10 of this manual.

Additional information related to the scheduling and conduct of scheduled and interim visits is provided in the remainder of this section.

5.3 Follow-up Visit Scheduling

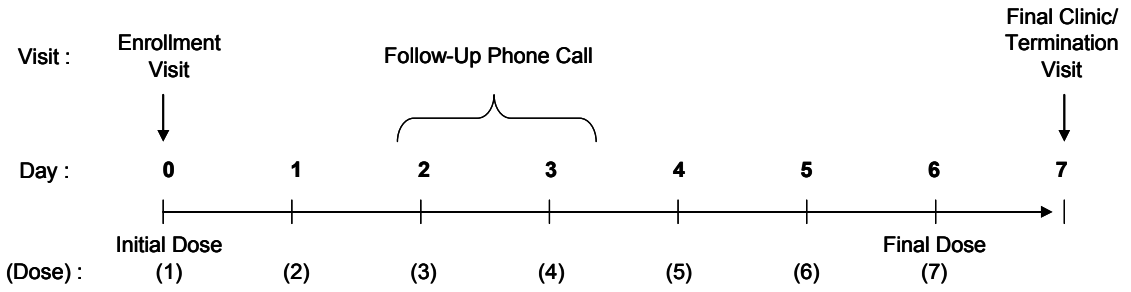
5.3.1 Target Visit Dates and Visit Windows

For MTN-012/IPM 010, randomization is the effective point of enrollment and enrollment is considered Day 0. Enrolled participants will have 2 scheduled visits in MTN-012/IPM 010:

- Follow-up Phone Assessment, targeted within 48-72 hours following enrollment
- Final Clinic Visit (Day 7) /Termination Visit, targeted within 24 hours of final application of study product

Figure 5-1 depicts a timeline of the scheduled follow-up visits for MTN-012/IPM 010 in relation to the 7 days of study product use. Given this schedule, a participant's Final Clinic Visit will be targeted on the same day as enrollment of the subsequent week (i.e. if enrollment is on a Monday, the targeted Final Clinic Visit will be the following Monday). Additionally, the MTN Statistical and Data Management Center (SDMC) will provide each site with a visit scheduling tool that can be used to generate follow-up visit schedules for enrolled participants.

Figure 5-1
Follow-up Visit Schedule for MTN-012/IPM 010



Participants who miss one application of the product should be instructed to complete the missed application on the evening of Day 7, and then present for their final visit within 24 hours following their last dose (Day 8, not shown in figure 5-1). Should a participant miss more than one dose, contact the MTN-012/IPM 010 management team and the MTN-012/IPM 010 Protocol Chair for further guidance.

Acknowledging that it will not always be possible to complete the Final Clinic Visit on the targeted date, a visit window of 7 additional days (through day 14) will be permitted. Study visit windows for MTN-012/IPM 010 are outlined further in Section 10 of this manual.

As MTN-012/IPM 010 is a short term study which includes a pharmacokinetic measurement at the Final Clinic Visit, every effort should be made to schedule participants within the timeframes as specified above. The MTN SDMC will provide the Protocol Team with routine visit adherence reports for purposes of monitoring adherence to the visit schedule.

5.3.2 Visits Conducted Over Multiple Days: "Split Visits"

Split visits will not be allowed in MTN-012/IPM 010. All procedures specified by the protocol to be performed at the Final Clinic Visit should be completed at a single visit on a single day. In the event that all required procedures cannot be completed on a single day, contact the management team for further guidance.

5.3.3 Missed Visits

For participants who do not complete any part of a scheduled visit within the visit window, the visit will be considered "missed" and a Missed Visit case report form will be

completed to document the missed visit. Section 10 gives detailed information regarding the completion of the Missed Visit form.

5.4 Follow-up Visit Locations

All visits will be conducted at the site clinics. No study specific assessments may be completed off-site. The exception to this is the Follow-up Phone Assessment. Site staff will contact the participant by phone to evaluate if they have experienced any adverse events.

5.5 Study Product Supply/Dispensing during Follow-up

Because of the nature of the short dosing period and follow-up in MTN-012/IPM 010, there will be no routine product re-supplies. The supply of study product at the Enrollment Visit encompasses the full dosing for this study (7 days) plus one extra applicator. Product replacement will occur only in the event of lost or damaged product that must be replaced. For complete details of study product replacement during follow-up please see Section 7.4 of this manual.

5.6 Follow-up Visit Procedures

Required follow-up visit procedures are listed in protocol Section 7 and Appendix I. Further operational guidance on completing protocol-specific follow-up procedures is incorporated into the following sections.

5.6.1 Follow-up Phone Call

Participants should be contacted by phone within 48-72 hours of the enrollment visit to inquire about potential adverse events (AEs). This contact should be documented using the Follow-up Phone Call visit checklist, participant chart notes and/or site-specific forms according to site SOPs.

If indicated, site staff should record reported AEs on the Adverse Experience Log (AE-1) and complete an Interim Visit form (IV-1). If indicated, site staff should schedule an in-person interim visit to follow-up on reported AEs. If permanent discontinuation may be warranted in response to AEs reported over the phone, participants should be instructed to stop product use and be scheduled for evaluation at the study clinic as soon as possible. In this situation, the Product Hold/Discontinuation Log (PH-1) should also be completed to document the temporary hold. Refer to Section 8 for additional guidance regarding AE reporting and management, and Section 10 for data management considerations.

Additional product use instructions, adherence, and/or abstinence counseling can be provided over the phone as needed. All participants should be encouraged to contact the clinic before their next scheduled visit as needed to report symptoms and/or request information or counseling. Staff should also remind participant of final clinic appointment, to bring used and unused applicators, and to record date and time of their last dose for PK.

5.6.2 Final Clinic Visit/Termination Visit

Participants will have one scheduled in-clinic visit during study follow-up. The protocol section 7.4, Appendix I, and the visit checklists provided in this section outline required procedures as well as procedures to be done when clinically indicated. Additional guidance is provided below.

- All used and unused **study product** should be collected from the participant early in the visit. Used product should be counted, documented, and then placed in a biohazard container for destruction in accordance with the sites biohazard materials policy. Unused study product should be counted, documented, and then sent to the Pharmacist of Record (PoR) for documentation and quarantine. NO used applicators should be sent to the pharmacy. Participants should also inform the clinic staff of any used and unused study product that they were unable to bring with them to the clinic (e.g., left at home or thrown away), which should be documented in the chart notes. For participants who do not bring all used and unused supplies to their Final Clinic Visits, arrangements must be made to collect the remaining supplies as soon as possible. If the study product is not collected within seven working days after the Final Clinic Visit, the MTN-012/IPM 010 Protocol Safety Review Team (PSRT) must be informed, using the PSRT Query Form. Participants should also communicate the exact date and time (including hours and minutes) of their last product use to the clinic staff. Detailed study product considerations can be found in section 7 of this SSP manual.

- The **Product Acceptability and Adherence Questionnaire (CASI)** should be administered prior to risk reduction counseling. The entire CASI interview must be completed in one sitting. Refer to section 12 for detailed guidance regarding CASI administration.

- **HIV Counseling and Testing** during follow-up will only occur if indicated, based on suspected infection reported by the participant. Due to the short duration and abstinence requirements of MTN-012/IPM 010, it is expected that HIV testing during follow-up will be extremely rare. However, should it be warranted, the algorithm for this testing can be found in Appendix II of the protocol. Full information on the procedural and documentation requirements of the algorithm and the processing of the HIV test can be found in Section 9 of this SSP Manual.

- **Urine and Blood** should be collected for protocol specified and as-indicated testing per sections 8 and 9 of this SSP Manual. Additional details are also provided in the template visit checklists at the end of this section.

- Updates to **Medical History** and **Current Medications** should be made according to section 8 of this SSP Manual.

- **Physical and Genital Exams** should be conducted according to section 8 of this SSP Manual.

- All identified **AEs** should be documented and reported according to section 8 of this SSP Manual. If an STI or RTI is diagnosed, participants should be referred for treatment per site SOPs. Additional visits may need to be scheduled to follow all

AEs to resolution or stabilization. As needed, sites should provide referrals to care outside the clinic per site SOPs.

- Although the Final Clinic/Termination Visit is the last scheduled study visit, a final contact will be required afterwards to provide the participant with his final laboratory test results, and any post-test counseling, and referral treatment, if needed. Additional contacts also are required for participants with AEs that are ongoing at study exit. Study staff may complete final contacts at the study site, by telephone, or at community-based locations, depending on site capacities and site and participant preferences. All final contacts must be documented in participant study records, but no case report forms are completed for these contacts.

- Participants who permanently discontinue study product will not routinely be withdrawn from the study. Rather, every effort will be made to complete all protocol-specified visits and procedures with these participants.

5.7 Visit Checklists

5.7.1 Use of Visit Checklists

The visit checklists included in this section (Appendix I) are designed to guide site staff in proper study procedures as well as to serve as source documentation of procedures performed at study visits. Note, however, that checklists alone may not be sufficient for documenting all procedures. For example, chart notes may be required to:

- Explain why procedures in addition to those listed on a checklist were performed
- Explain why procedures listed on a checklist were not performed
- Document procedures performed at interim visits
- Document the content of counseling sessions and/or other in-depth discussions with participants (e.g., related to adherence to protocol requirements)

See Section 3 of this manual for detailed information on source documentation requirements. Tips for completing visit checklists in accordance with these requirements are as follows:

- Enter the participant identification number (PTID) and visit date in the top section of each checklist. If information is written on the front and back of the checklist, enter the PTID and visit date on both sides.

- For screening visits, enter the screening attempt number in the top section of the checklist.

- For interim visits, enter the visit code in the top section of the checklist.

- Enter your initials only beside the procedures that you perform. Do not enter your initials beside procedures performed by other staff members. If other staff members are not available to initial checklist items themselves, enter, initial, and date a note on the checklist documenting who completed the procedure, e.g., “done by {name}” or “done by lab staff.”

- If all procedures listed on a checklist are performed on the date entered in the top section of the form, the date need not be entered beside each item. If procedures listed on a checklist are performed on multiple dates, enter the date upon which each procedure is performed beside each item.

- If a procedure listed on the checklist is not performed, enter "ND" for "not done" or "NA" for "not applicable" beside the item and record the reason why on the checklist (if not self-explanatory); initial and date this entry.

5.7.2 Sequence of Procedures

The sequence of procedures presented on the visit checklists is a suggested ordering. In consultation with the MTN CORE (FHI), site staff may modify the checklists included in this section to maximize the efficiency of site-specific study operations. Sites may alter the sequence of procedures to suit local staffing and logistical requirements, with the following exceptions:

- Informed consent for screening must be obtained before any screening procedures are performed. Screening procedures are listed in protocol Sections 7.1.

- Informed consent for enrollment must be obtained before any study enrollment or follow-up procedures are performed. Enrollment procedures are listed in protocol Section 7.2. Follow-up procedures are listed in protocol Section 7.3 and 7.4

- On the day of enrollment, random assignment must take place **after** administration of the Baseline Behavioral Computer Assisted Self-Interview (CASI) Questionnaire, collection of blood for plasma archive, and final confirmation of eligibility.

- At the final clinic visit, the CASI Product Acceptability and Adherence Questionnaire must be administered prior to risk reduction counseling.

Section Appendix I
Sample Visit Checklists

PTID:	Visit Date:
Screening Attempt:	Visit Code: 01.0

Initials	Procedures
	1. Confirm identity per site SOPs and determine whether an MTN-012/IPM 010 PTID has previously been assigned to participant.
	2. Determine whether participant is ≥ to 18 years old.
	3. Explain, conduct, and document screening informed consent process per site SOPs.
	4. Assign a MTN-012/IPM 010 PTID (if not done during a previous screening attempt).
	5. Determine last possible enrollment date for this screening attempt: ☐☐ ☐☐☐ ☐☐ DD MON YY
	6. Explain procedures to be performed at today's visit.
	7. Obtain locator information and determine adequacy per site SOPs
	8. Administer Demographics form.
	9. Administer Behavioral Eligibility form
	10. Collect urine (15-60 mL) ❒ Perform dipstick urinalysis for protein, blood, glucose, nitrites and LE; complete testing logs; transcribe results onto Safety Laboratory Results form ❒ Prepare remaining urine for gonorrhea and chlamydia NAAT ❒ If indicated, perform urine culture
	11. Provide and document HIV counseling and testing per site SOPs: ❒ Provide HIV pre-test counseling ❒ Provide HIV/STI risk reduction counseling and condoms ❒ Explain abstinence requirements for study ❒ Collect blood: ❒ 1 x 6 mL lavender top (EDTA) tube ❒ 1 x 5 mL red top (no additive) tube ❒ 1 x 10 mL red top (no additive) tube Volumes shown are approximate. Tailor this item to reflect site-specific tube types and volumes. ❒ Perform and document HIV testing per site SOPs. ❒ Provide HIV test results in the context of post-test counseling

PTID:	Visit Date:
Screening Attempt:	Visit Code: 01.0

Initials	Procedures
	12. Prepare remaining blood for required testing: • Complete blood count with differential and platelets • AST, ALT, creatinine • Syphilis serology
	13. Collect baseline medical history with documentation of current medications; document on relevant source documents and case report forms per site SOPs.
	14. Perform physical exam, including height measurement; document per site SOPs
	15. Perform genital exam; document per site SOPs ❒ Inspect via naked eye and hand-held magnifying glass: ❒ internal and external foreskin (if present) ❒ penile shaft ❒ glans ❒ urethral meatus ❒ scrotum ❒ inguinal lymph nodes (right and left) ❒ gently evert both meatal lips to inspect for discharge ❒ Document all findings on the Genital Exam form.
	16. Determine whether participant has current RTI/STI symptoms.
	17. Provide and explain all available findings and results.
	18. If RTI/STI is diagnosed, refer for treatment per site SOPs
	19. Complete Enrollment Eligibility form
	20. Provide study informational material: [add site-specific list if desired]
	21. Provide contact information and instructions to contact the site for additional information and/or counseling if needed before the next visit.
	22. If applicable, schedule next visit.
	23. Provide reimbursement.

PTID:	Visit Date:
Screening Attempt:	Visit Code: 01.0

Initials	Procedures
	24. Review all visit documentation. *NOTE: The STI Laboratory Results and Laboratory Results CRFs (including HIV Test Results CRF) should be completed when all required test results are available, prior to the Enrollment Visit. Do not fax any forms to SCHARP until the participant is randomized. If the participant is deemed ineligible, retain all DataFax forms on site but do not fax any of them to SCHARP.*

PTID:	Visit Date:
Screening Attempt:	Visit Code: 02.0

Initials	Procedures
	1. Confirm identity and verify PTID per site SOPs
	2. Confirm that the 30-day screening to enrollment window has not been exceeded for current screening attempt.
	3. Provide and explain all prior screening test results.
	4. Explain procedures to be performed at today's visit.
	5. Review/update locator information and re-assess adequacy per site SOPs.
	6. Explain, conduct, and document enrollment and specimen storage informed consent process per site SOPs.
	7. If indicated, collect urine for urine culture.
	8. Administer Behavioral Eligibility form.
	9. Actively review participant's baseline medical history and current medications. Document all updates on relevant source documents and case report forms.
	10. Perform physical exam; document per site SOPs
	11. Perform genital exam; document per site SOPs ❒ Inspect via naked eye and hand-held magnifying glass: ❒ internal and external foreskin (if present) ❒ penile shaft ❒ glans ❒ urethral meatus ❒ scrotum ❒ inguinal lymph nodes (right and left) ❒ gently evert both meatal lips to inspect for discharge ❒ Document all findings on the Genital Exam form.
	12. Determine whether participant has current RTI/STI symptoms.
	13. Provide and explain all available findings and results.
	14. If RTI/STI is diagnosed, refer for treatment per site SOPs
	15. Review all screening documentation and determine eligibility. Review and update Enrollment Eligibility form

PTID:	Visit Date:
Screening Attempt:	Visit Code: 02.0

Initials	Procedures
	16. Verify participant eligibility per site SOPs
	17. Administer CASI Baseline Behavioral Questionnaire
	18. Collect 10 mL blood in lavender top (EDTA) tube; refrigerate pending delivery to lab for plasma archive.
	19. Complete Enrollment form and LDMS Specimen Tracking Sheet.
	20. Verify documentation of enrollment informed consent and assign next sequential Randomization Envelope to participant per site SOPs. Note: Obtain Randomization Envelope for the appropriate circumcision status.
	21. Complete prescription.
	22. Give completed white original prescription to participant to bring to pharmacy to obtain study product. Retain envelope and yellow copy of prescription in participant's study notebook.
	23. Verify participant received study product. Review product use instructions with participant in detail, using visual aids as needed.
	24. Provide adherence and abstinence counseling per site SOPs.
	25. Provide HIV risk reduction counseling.
	26. Schedule next visit and remind participant to bring all used and unused study product to the Final Clinic visit and to record the exact date and time of last dose prior to final visit
	27. Inform participant of follow-up phone call which will occur in 48-72 hours
	28. Provide contact information and instructions to report symptoms and/or request information, counseling, or study product, before next visit.
	29. Provide reimbursement.

PTID:	Visit Date:
Screening Attempt:	Visit Code: 02.0

Initials	Procedures
	30. Fax all required DataFax forms to SCHARP DataFax: ❒ Demographics ❒ Enrollment ❒ Pre-existing Conditions ❒ Concomitant Medications Log ❒ Genital Exam ❒ STI Laboratory Results ❒ Laboratory Results If applicable: ❒ HIV Test Results

PTID:	Call Date:

Initials	Procedures
	1. Confirm participant identity and PTID per site SOPs
	2. Collect AEs if indicated and document on Adverse Experience Log form
	3. If indicated, schedule interim visit for follow-up of identified AEs
	4. If indicated, instruct participant to stop product use until further evaluation can be completed in the clinic. Document on Product Hold/Discontinuation Log.
	5. If indicated, provide additional product use instructions, adherence, and/or abstinence counseling.
	6. Provide instructions to report symptoms and/or request information or counseling, before next visit.
	7. Provide reimbursement if applicable.
	8. Remind participant of next visit and to: • Bring used and unused applicators • Record the exact date and time of last dose prior to final visit
	9. If applicable, fax all completed DataFax forms to SCHARP DataFax: ❒ Interim Visit (if new AE(s) are reported or updated) ❒ Adverse Experience Log ❒ Product Hold/Discontinuation Log

PTID:	Visit Date:	Visit Code: 03.0

Initials	Procedures
	1. Confirm participant identity and PTID per site SOPs.
	2. Collect used and unused study product; document on the Study Product Returns form.
	3. Explain procedures to be performed at today's visit.
	4. Review/update locator information.
	5. Administer CASI Product Acceptability and Adherence Questionnaire.
	6. Collect urine (15-60 mL) ❒ Perform dipstick urinalysis for protein, blood, glucose, nitrites and LE; complete testing logs; transcribe results onto Safety Laboratory Results form ❒ If indicated, perform urine culture
	7. Provide HIV/STI risk reduction counseling per site SOPs. ❒ If indicated, provide and document HIV counseling and testing per site SOPs ❒ Provide condoms ❒ Collect blood: ❒ 1 x 10 mL lavender top (EDTA) tube ❒ 1 x 6 mL lavender top (EDTA) tube ❒ 1 x 5 mL red top (no additive) tube ❒ 1 x 10 mL red top (no additive) tube Volumes shown are approximate. Tailor this item to reflect site-specific tube types and volumes.
	8. Prepare remaining blood for required testing: • Complete blood count with differential and platelets • AST, ALT, creatinine • Dapivirine level • If indicated, HIV serology
	9. Collect interval medical with documentation of current medications; document on relevant source documents and case report forms per site SOPs.
	10. Perform physical exam; document per site SOPs.

PTID:	Visit Date:	Visit Code: 03.0

Initials	Procedures
	11. Perform genital exam; document per site SOPs ❒ Inspect via naked eye and hand-held magnifying glass: ❒ internal and external foreskin (if present) ❒ penile shaft ❒ glans ❒ urethral meatus ❒ scrotum ❒ inguinal lymph nodes (right and left) ❒ gently evert both meatal lips to inspect for discharge ❒ Document all findings on the Genital Exam form.
	12. Determine whether participant has current RTI/STI symptoms.
	13. Provide and explain all available findings and results.
	14. If RTI/STI is diagnosed, refer for treatment per site SOPs.
	15. If required based on all available information, complete AE Log form(s).
	16. If indicated, schedule next visit.
	17. Provide reimbursement.
	18. Ensure that chart notes and all other required visit documentation is completed.
	19. Fax all required DataFax forms to SCHARP DataFax: ❒ Final Clinic Visit ❒ Study Product Returns ❒ Genital Exam ❒ Laboratory Results ❒ Adverse Experience Log ❒ End of Study Inventory ❒ Termination If Applicable: ❒ Concomitant Medications Log (new and/or updated form pages) ❒ STI Laboratory Results ❒ HIV Test Results

PTID:	Visit Date:	Visit Code:

Initials	Procedures
	1. Confirm participant identity and PTID per site SOPs.
	2. Based on the primary reason for the interim visit, explain procedures to be performed at today's visit.
	3. Review/update locator information.
	4. Review/update interval medical history with documentation of current medications; document per site SOPs.
	5. Collect AEs. If applicable, complete AE Log form(s).
	If indicated, perform procedures in italics below
	6. Perform physical exam; document per site SOPs
	7. Perform genital exam; document per site SOPs
	8. Collect urine (15-60 mL) ❒ *Perform dipstick urinalysis for protein, blood, glucose, nitrites and LE; complete testing logs; transcribe results onto Safety Laboratory Results form* ❒ *Prepare remaining urine for gonorrhea and Chlamydia NAAT* ❒ *Perform urine culture*
	9. Provide and document HIV counseling and testing per site SOPs: ❒ *Provide HIV pre-test counseling* ❒ *Provide HIV/STI risk reduction counseling and condoms* ❒ *Collect blood:* ❒ *1 x 6 mL lavender top (EDTA) tube* ❒ *1 x 5 mL red top (no additive) tube* ❒ *1 x 10 mL red top (no additive) tube* ❒ *Perform and document HIV testing per site SOPs.* ❒ *Provide HIV test results in the context of post-test counseling*
	10. Prepare remaining blood for required testing: • *Complete blood count with differential and platelets* • *AST, ALT, creatinine* • *Syphilis serology*
	11. Provide and explain all available findings and results.
	12. If RTI/STI is diagnosed, refer for treatment per site SOPs

Volumes shown are approximate. Tailor this item to reflect site-specific tube types and volumes.

PTID:	Visit Date:	Visit Code:

Initials	Procedures
	13. Provide study product and complete the Replacement Product Dispensation form.
	14. Review product use instructions
	15. Provide adherence and abstinence counseling per site SOPs.
	16. Schedule or reinforce scheduling of next visit and remind participant to bring all used and unused study product to next visit
	17. Provide contact information and instructions to report symptoms and/or request information, counseling, or study product, before next visit.
	18. Provide reimbursement as needed/indicated.
	19. Ensure that chart notes and all other required visit documentation is completed.
	20. If applicable, fax all completed DataFax forms to SCHARP DataFax: ❒ Interim Visit If applicable: ❒ Concomitant Medications Log (new and/or updated form pages) ❒ Adverse Experience Log ❒ Genital Exam ❒ STI Laboratory Results ❒ Laboratory Results ❒ HIV Test Results ❒ Product Hold/Discontinuation ❒ Replacement Product Dispensation