Section 6. Participant Follow-up

This section provides information on requirements and procedures for participant follow-up.

6.1 Study Follow-up Plan and Participant Retention Targets

Each enrolled participant will be followed for sixteen weeks post her enrollment date. The target accrual is expected to be completed within six months of site activation at the US sites, and within ten months of activation at the Pune, India site. The protocol team will actively monitor and manage the study accrual process to ensure that the enrollment occurs within the specified timeframe.

To minimize bias and ensure accuracy of study results, each study site will target a minimum retention rate of 95% of all enrolled study participants. Further information on MTN 005 retention definitions and procedures is provided in Section 8.

6.2 Types of Follow-up Visits

Throughout the study follow-up period, two types of follow-up visits may be conducted:

- **Scheduled visits** are those visits required per protocol. The protocol specifies that follow-up visits occur at: enrollment, 4-week, 8-week, 12-week, and 16-week. All scheduled follow-up visits are pre-assigned a visit code for purposes of data management as described in the Data Collection section of this manual.

- **Interim visits** are those visits that take place between scheduled visits. 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 the Data Collection section of this manual.

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

6.3 Follow-up Visit Scheduling

6.3.1 Target Visit Dates

Enrolled participants will be scheduled to complete follow-up visits throughout their participation in the study. For each participant, all follow-up visits are targeted to take place every 4 weeks (28 days) based on the participant's enrollment date (Enrollment = Day 0, see Figure 6-1). Each participant's enrollment date is defined as the date upon which she is assigned an MTN-005 Randomization Envelope.

6.3.2 Visit Windows

Acknowledging that it will not always be possible to complete follow-up visits on the targeted dates, the MTN 005 protocol allows for visits to be completed within a visit window of ± 7 days of the target date. For example, the visit window for the 4-Week visit (target day 28) is day 21 to 35. Sites are encouraged to complete required study visits on the target day if at all possible. If it is not possible to complete the required visit on the target day, the visit may be completed within the visit window. Visits completed within the visit window will be considered completed ("retained") visits.

Although the visit windows allow for some flexibility, the intent of the protocol-specified visit schedule is to conduct follow-up visits on the target day, and every effort should be made to do so. The MTN SDMC will provide study sites with an Excel tool that may be used to generate participant follow-up visit calendars, acknowledging that follow-up visit scheduling is ultimately the site's responsibility. The MTN SDMC will also make available routine retention reports for purposes of monitoring adherence to the required visit schedule (see the Study Reporting Plan section of this manual).

Figure 6-1
MTN 005 Target Days and Visit Windows

Visit	Visit Code	Window Opens	Target Day	Window closes
Week 4	3.0	21	28	35
Week 8	4.0	49	56	63
Week 12	5.0	77	84	91
Week 16	6.0	105	112	119

Note: All windows are listed in days, with Enrollment = Day 0.

Figure 6-2
Example Visit Windows for MTN 005

December-2008						
Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
						1
2	3	4	5	6	7	8
9	10	11	12	13 **Enrollment Day**	14	15
16	17	18	19	20	21	22
23	24	25	26	27	28	29
30	1					

January-2009						
Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
		2	3	4 4W Target Window Opens	5	6
7	8	9	10	11 **4W Target Day**	12	13
14	15	16	17	18 4W Target Window Closes	19	20
21	22	23	24	25	26	27
28	29	30	31			

6.3.3 Visits Conducted Over Multiple Days: "Split Visits"

All procedures specified by the protocol to be performed at a particular follow-up visit ideally will be completed at a single visit on a single day. In the event that all required procedures cannot be completed on a single day, (for example because the participant must leave the study site before all required procedures are performed or the participant has her menses), ACASI questionnaires, behavioral assessments (including the Ring Adherence CRF), and the pelvic exam must be conducted on the same day, and the remaining procedures may be completed on subsequent day(s) within the visit window.

For the Enrollment visit, ideally this visit will be conducted on the same day; however, split enrollment visits are allowable if necessary. The participant may be rescheduled for another Enrollment visit. She does not have to resign the Enrollment ICF, but she will have to repeat all other procedures from her first Enrollment visit.

For the non-DataFax Enrollment Behavioral Eligibility form, obtain the originally-completed form, administer all questions again, and update the form as needed. A note should be written on the form to indicate it was re-administered and the reason why should be noted in the participant's chart notes. A new Pelvic Exam Diagrams form should be completed for the new pelvic exam, and all required specimens should be collected at this second Enrollment Visit. If there are other CRFs which were completed at the first Enrollment visit, please email SCHARP and the Management team for further guidance.

The ACASI should also be re-administered, and this will create two records for the participant. The original record should be indicated as a 'duplicate'. To do this, please refer to pages 27-30 of the ACASI Manual (Section 16 of the SSP Manual). When indicating the reason for the change, 'other' may be selected and details entered in the comments section. The ACASI team and the Management team should be consulted for further guidance.

6.3.4 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 (see the Data Collection section).

6.3.5 Follow-up Visit Scheduling Scenarios

Presented in Section Appendix 6-1 are several follow-up visit scenarios that may occur during MTN 005. These scenarios illustrate that the visit windows impact whether a completed visit will be considered a scheduled visit or an interim visit. The examples also illustrate the complexities that may be encountered when scheduling and completing study follow-up visits in a "real world" setting.

6.4 Follow-up Visit Procedures

Required follow-up visit procedures are listed in protocol Sections 7.3, 7.4 and 7.5. Protocol Tables 6 and 7 list all required procedures.

6.5 Follow-up Visit Locations

All visits must take place on-site.

6.6 Product Re-Supply During Follow-up

Participants in the IVR cohort are expected to use the same IVR for 12 weeks without self-removal. Therefore only one study ring should be dispensed to each participant in the IVR cohort, occurring at the enrollment visit. If the IVR is removed by the participant or comes out involuntarily (expelled), the participant should rinse the ring and re-insert it if possible. If she is unable or unwilling to re-insert the ring, she should place it in a study-provided re-sealable bag and return to the clinic as soon as possible. Site staff will document return of the used ring and decide if it will be re-inserted or disposed of based on the situation. If it is determined by site staff that a new ring must be inserted, an MTN 005 Study Ring Request Slip will be completed to obtain a new IVR. Section 9 of this Study-Specific Procedures Manual contains detailed information on clinic staff procedures for the dispensation of study product, as well as the return of used study products.

At each follow-up visit, study staff will determine whether a participant remains eligible for continued study product use per protocol specifications. Protocol Section 9.4 lists conditions under which participants should be discontinued from study product use, either temporarily or permanently. The site Investigator of Record (IoR) is responsible for ensuring that these protocol specifications are followed for all participants.

6.7 HIV Testing During Follow-Up

At all sites, HIV testing during follow-up will be performed only at the 16-Week/ Termination Visit. At all other follow-up visits, HIV testing will be performed if clinically indicated. HIV testing will be performed according to the algorithm in protocol Appendix II. Further information on the procedural and documentation requirements of the algorithm is provided in the remainder of this section.

Further instructions for performing HIV tests during follow-up are provided in Section 12. All tests must be documented on local laboratory log sheets or other laboratory source documents. A second independent clinic or laboratory staff member trained in proper HIV testing and result recording procedures must review, verify, and sign-off on test results within the timeframe of the tests and prior to disclosure of results to participants. For positive/reactive results, review, verification, and sign-off must be performed by a nurse, clinician, or physician. In addition to initialing or signing the testing logs to document review and verification of the results, the second staff member must also record the time at which the results were reviewed and verified.

6.8 Modified Follow-up Procedures for Participants Who Become Infected with HIV

Participants who become infected with HIV during follow-up will be maintained in follow-up according to their original study follow-up schedule. All participants who become infected with HIV will be counseled and referred to available sources of medical and psychosocial care and support, as well as to any available research studies for HIV-infected persons. For any participants who become HIV-infected and also become pregnant during follow-up, every effort will be made to facilitate access to current prevention of mother to child transmission regimens to reduce the probability of HIV transmission to the participant's infant.

While in scheduled follow-up, all protocol-specified study procedures will continue to be conducted for participants who become infected with HIV, with the following exceptions:

- After HIV infection is confirmed per the algorithm in Protocol Appendix II, HIV testing will be discontinued.

- IVR use will be permanently discontinued starting at the visit where the participant has a positive or indeterminate HIV EIA result. Site staff will make every effort to recover study product immediately after the site becomes aware of the positive or indeterminate HIV EIA result.

- Counseling will be tailored to primary and secondary HIV/STI prevention for infected women.

- IVR use and adherence counseling will be discontinued for participants in the IVR cohort.

6.9 Modified Follow-up Procedures for Participants Who Become Pregnant

At all sites, pregnancy testing during follow-up will be performed only at the 16-Week/ Termination Visit. At all other follow-up visits, pregnancy testing will be performed if clinically indicated. Participants who become pregnant during follow-up will be maintained in follow-up according to their original study follow-up schedule. Participants who are pregnant at the termination visit will continue to be followed until the pregnancy outcome is ascertained (or, in consultation with the PSRT, it is determined that the pregnancy outcome cannot be ascertained).

While in scheduled follow-up, all protocol-specified study procedures, including pregnancy testing at the 16-Week/ Termination visit, will continue to be conducted for pregnant participants, with the following exceptions:

- Study IVR use and adherence counseling for participants in the IVR cohort will be discontinued

.

- Pelvic Exam will not be performed

- For all participants who become pregnant, regardless of study treatment group, a Pregnancy Report form must be completed to report the pregnancy. A Pregnancy Outcome form also must be completed to document the outcome of the pregnancy. Whenever possible, pregnancy outcomes should be ascertained based on medical records or other written documentation from a licensed health care practitioner. When medical records cannot be obtained, however, outcomes may be ascertained based on participant report. Contact the MTN 005 study management team with any questions related to reporting of pregnancy outcomes, including AE/EAE reporting related to pregnancy outcomes.

All study sites are strongly encouraged to use a pregnancy management worksheet similar to the sample in Section Appendix 6-4 to ensure proper documentation of the pregnancy and timely discontinuation of IVR use.

6.10 Resumption of Study Participation after Voluntary Withdrawal

As stated in protocol Section 9.5, participants may voluntarily withdraw from the study for any reason at any time. The protocol also allows for participants who voluntarily withdraw from the study to reverse their decision and re-join the study during their planned 16-week follow-up period at the discretion of the investigator. If such cases arise, study staff are advised to contact the MTN 005 study management team for additional guidance on how to manage various aspects of protocol implementation and data collection as the participant resumes participation in the study. In general, however, the following instructions and requirements should be adhered to:

- The participant's original PTID and follow-up visit schedule will remain unchanged. Her random assignment also will remain unchanged and she will continue product use per her random assignment.

- An interval (since the last visit) medical/menstrual history should be taken and a pregnancy test should be performed before the participant resumes study participation. Product use will be resumed only among participants who are not currently pregnant.

- A pelvic exam should be performed as soon as possible, and prior to reinstating IVR use. A pelvic exam and other clinically-indicated evaluations also should be performed if the participant reports current genital symptoms. IVR use will be reinstated (if applicable) only after any genital symptoms have resolved, any STIs/RTIs requiring treatment per World Health Organization guidelines have been treated, and any pelvic exam findings involving deep epithelial disruption have resolved.

- Clinic staff will communicate any re-instatement of product use to the study pharmacy in writing as outlined in Section 9 of this manual, using the MTN 005 Study Product Prescription and Study Ring Request Slip.

6.11 Study Exit Considerations

Procedural requirements for conducting study exit (termination) visits are specified in protocol Sections 7.4 and 7.13 and protocol Table 7. Further procedural guidance is incorporated in the Week-16/Termination Visit checklist in Section 7 of this manual. Provided in the remainder of this section is additional information related to key aspects of study exit visits.

6.11.1 Participant Locator Information

Accurate participant locator information will be needed for post-study contact with study participants. As such, locator information should be actively reviewed and updated at all study exit visits and all participants should be counseled to contact the study site should their locator information change after study exit.

6.11.2 Final Study Contacts

Although the study exit visit is the last scheduled study visit, a final contact may be required after the exit visit to provide the participant with her final study test results, post-test counseling, and treatment, if needed. Additional contacts also are required for:

- Participants who are pregnant at study exit (see Section 6.9 above)
- Participants with positive or indeterminate HIV EIA or Western blot (WB) test results (see Section 6.11.3 below)
- Participants with AEs that are ongoing at study exit (see Section 6.11.6 below)

For each participant, a final contact should be scheduled as needed based on the participant's overall clinical picture at study exit, as well as the time required to obtain all final study test results. 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. It is recommended that final contact plans be documented on a study exit worksheet similar to the sample provided in Section Appendix 6-6.

All final contacts must be documented in participant study records, but no case report forms are completed for these contacts.

6.11.3 HIV Counseling and Testing

HIV testing is performed at the study exit visit per the algorithm in protocol Appendix II and HIV pre- and post-test counseling provided at the study exit visit should emphasize that additional counseling and testing will be provided to the participant after her study exit visit if needed to clarify or confirm her HIV status.

6.11.4 AE Management and Documentation

All AE Log forms completed for each participant should be reviewed at the study exit visit and updated as needed. For AEs that are ongoing at the exit visit, the status/outcome of the AE should be updated to "continuing at end of study participation" and the AE Log form should be re-faxed to SCHARP DataFax.

For any AEs requiring expedite reporting (according to *the Manual for Expedited Reporting of Adverse Events to DAIDS, January 2010*) that are continuing at a participant's study exit visit, the IoR/designee must establish a clinically appropriate follow up plan for the AE (see Section 11 of this manual for more information AE reporting and safety monitoring). At a minimum, the AE must be re-assessed by study staff 30 days after the participant's study exit visit. Additional evaluations also may take place at the discretion of the IoR/designee. The same approach must be taken for any AEs that are found to have increased in severity at the study exit visit. It is recommended that AE follow-up plans be documented on a study exit worksheet similar to the sample provided in Section Appendix 6-6.

For those AEs requiring re-assessment, if the AE has not resolved or stabilized at the time of re-assessment, study staff will continue to re-assess the participant at least once per month while the study is ongoing. After the study has ended, all AEs requiring re-assessment will be re-assessed at least once within the 30-60 days after the study end date. The MTN 005 PSRT may advise study staff as to whether any additional follow-up may be indicated on a case by case basis.

For AEs that are re-assessed after study exit, information on the status of the AE at the time of re-assessment will be recorded in source documents only — no updates should be made to AE Log case report forms based on the re-assessments. All information related to the re-assessment of AEs should be documented in the participant's chart notes, including all efforts to contact the participant.

6.11.5 Referral to Non-Study Service Providers

After completing their study exit visits and final study contacts, participants will no longer have routine access to services provided through the study, such as reproductive health care and HIV counseling and testing. Participants should be counseled about this — ideally before and during their study exit visits — and provided information on where they can access such services after study exit. It is strongly recommended that all study sites develop a sample script which can be used when discussing this issue with exiting participants, as well as written referral sheets that can be given to participants at their study exit visits (after obtaining IRB/EC approval of the written information). A sample script which may be tailored for use at each site is provided in Section Appendix 6-7.

6.11.6 Post-Study Contacts

It is expected that all participants will be re-contacted by study staff approximately three to nine months after study completion, when it is expected that study results will be available for dissemination to all participants.

To facilitate post-study contact with participants, locator information should be updated at the study exit visit, and participants should be counseled to contact the study site should their locator information change after study exit. In addition, participant preferences for methods to be used for contacting them when study results are available should be documented in participant study records. It is recommended that participant preferences be recorded on a study exit worksheet similar to the sample provided in Section Appendix 6-6.

Lastly, for participants whom study staff may wish to contact regarding participation in future studies, permission for such contact should be sought from the participant and documented. It is recommended that participant permission (or lack thereof) for future studies be documented on a study exit worksheet similar to the sample provided in Section Appendix 6-6. In addition, for ease of retrieving information on participant permissions, it is recommended that study staff maintain future study contact permission logs similar to the examples provided in Section Appendix 6-8.

Section Appendix 6-1
Follow-up Visit Scheduling Scenarios for MTN 005

6.1 **Suppose Participant X enrolls in the study on 3 July. What are the target dates for her visits in study weeks 3, 6, 7, and 10?**

	Target
4-Week	31 July
8-Week	28 August
12-Week	25 September
16-Week	23 October

Why? Target dates are set based on the participant's study enrollment date (day 0) and occur at 4, 8, 12 and 16 weeks after enrollment.

6.2 **Continuing from scenario 6.1, what are the allowable and target windows for this participant?**

	Allowable Window
4-Week	24 July – 7 August
8-Week	21 August – 4 September
12-Week	18 September – 2 October
16-Week	16 October – 30 October

Why? The allowable visit windows ±7 days from the target day for the visit.

6.3 **Suppose Participant X completes her 4-Week visit on 6 August. What are the target and allowable dates for her visits in study weeks 8, 12 and 16?**

	Target	Allowable
8-Week	28 August	21 August – 4 September
12-Week	25 September	18 September – 2 October
16-Week	23 October	16 October – 30 October

Why? Target dates always remain linked to the enrollment date. Target dates do not shift when a previous visit does not take place on the target date.

6.4 **Suppose Participant X does not complete her 8-Week visit on the target date of 28 August, but presents to the study site on 1 September. What do you do?**

- Complete a 8-Week visit per protocol on 1 September.

Why? 1 September is within the allowable 8-Week visit window.

6.5 **Suppose Participant X does not complete her 8-Week visit between 21 August – 4 September, but presents to the study site on 8 September. What do you do?**

- On 4 September, consider the 8-Week visit missed.
- On 8 September complete an interim visit per protocol.

Why? The 8-Week visit window closed on 4 September, the 12-Week visit window does not open until 25 September, therefore this visit is considered an interim visit. Appendix I of the protocol lists the procedures that are required at each interim visit. .

Section Appendix 6-1
Follow-up Visit Scheduling Scenarios for MTN 005

6.6	**Suppose Participant X completes all her 8-Week visit procedures on 21 August, but presents to the study site on 9 September to report genital bleeding. What do you do?** • On 9 September, complete interim visit required procedures • Perform pelvic exam to assess symptoms and manage accordantly. • Complete necessary documentation such as chart notes and AE log form. • Confirm and reinforce the scheduling of 12-Week visit. Why? The 8-Week visit procedures were completed, and the window for the 12-Week visit does not open until 18 September.
6.7	**Continuing from scenario 6.6, suppose Participant X comes to the study site for follow-up on the genital bleeding on 19 September. What do you do?** • On 19 September, complete a 12-Week visit per protocol. Why? The 12-Week visit opened on 18 September. A pelvic exam is a required procedure at the 12-Week study visit. Clinician should assess whether or not the genital bleeding has resolved and update documentation as appropriate.
6.8	**Suppose Participant X does not complete her 8-Week visit between 21 August and 4 September, but presents to the study site on 19 September. What do you do?** • On 4 September, consider the 8-Week visit missed. • On 19 September, complete a 12-Week visit per protocol. • Why? The 8-Week visit window closed on 4 September and the 12-Week visit window opened on 18 September.
6.9	**Suppose Participant X presents to the study site for her 8-Week visit on 21 August, and completes some but not all of the protocol-specified procedures for the 8-Week visit. What do you do?** • Document all procedures performed on 21 August as usual. Explain in chart notes why all protocol-specified procedures were not completed. • Schedule Participant X to return to the study site as soon as possible to complete the remaining 8-Week procedures. • When Participant X returns to the study site, provided the 8-Week visit window has not elapsed, perform an interval medical/menstrual history and all remaining 8-Week visit procedures. • Take care to document the actual date of all procedures performed in visit chart notes, on visit checklists, and all other documents and forms. • Confirm and reinforce the scheduling of 12-Week visit. Why? Since Participant X could not complete all protocol-specified procedures in a single visit, her 8-Week visit is considered a split visit. Split visits may be conducted over two or more days, provided the allowable visit window does not elapse. DataFax forms completed for all parts of a split visit are assigned the same scheduled visit code.

Section Appendix 6-1
Follow-up Visit Scheduling Scenarios for MTN 005

6.10	**A participant comes in for her enrollment visit, was consented, went through the behavioral CRF's and also completed the baseline ACASI questionnaire. During the clinical exam an abnormal finding was identified, because of which she was not enrolled. Investigators decide that they would like to schedule her for a rescreening/reevaluate her for enrollment at a later date. When she returns for the rescreening, should the baseline ACASI assessment be re-administered?** Yes, the baseline ACASI assessment should be re-administered for this participant. This will create 2 records for the participant. The original record should be indicated as a 'duplicate'. To do this, please refer to pages 27-30 of the ACASI Manual (Section 16 of the SSP Manual). When indicating the reason for the change, 'other' may be selected and details entered in the comments section. Why? ACASI questionnaires include questions about sexual behavior and ring use that correspond to specific time points.
6.11	**(NARI only) A participant returns for her enrollment visit and needs to receive her screening HIV test results (as well as pre and post test counseling). Since counseling must occur after ACASI interviews are administered, when should site staff conduct post test counseling?** Conduct pre-test counseling and provide the participant with her screening HIV test result first. If she is HIV-/eligible and chooses to enroll: 1) inform the participant that post-test counseling will occur later in the visit; 2) administer the enrollment ICF; 3) administer the baseline ACASI assessment. Post-test counseling can occur any time after the ACASI interview has been administered. Why? The post-test counseling session might influence the participants' responses to ACASI questions.
6.12	**It is a busy day at the clinic. A participant is ready to do her ACASI interview but all of the ACASI computers are being used by other participants. What else can the staff do with the participant while she is waiting to do her ACASI interview?** ACASI questionnaires must be administered before the participant goes through counseling and diary card review. In other words, other study procedures can be conducted before the ACASI questionnaire is administered, but counseling and diary card review can only occur after ACASI questionnaires are administered. Why? The counseling session and diary card review might influence the participants' responses to ACASI questions.
6.13	**Please see section 6.3.3 of the SSP for details regarding the handling of "Split visits". What if a participant wants to leave the clinic: while she is in the middle of her ACASI interview OR before initiating her ACASI interview OR immediately after completing her ACASI interview?** ACASI questionnaires, behavioral assessments (including the Ring Adherence CRF), and the pelvic exam must be conducted on the same day, and the remaining procedures may be completed on subsequent day(s) within the visit window. Why? ACASI questionnaires include questions about sexual behavior and ring use that correspond to specific time points.

Section Appendix 6-1
Follow-up Visit Scheduling Scenarios for MTN 005

6.14 A participant comes in for her Week 12 visit. Which ACASI questionnaire should be administered?

- If randomized to the No IVR arm: The No IVR Follow-up ACASI questionnaire should be administered.
- If randomized to the IVR arm: Both the IVR Follow-up and IVR Week 12 (Final Acceptability Assessment) should be administered.

Why? Even though the ring is removed at the Week 12 visit per protocol, the IVR Follow-up questionnaire should still be administered as well as the Week 12 specific assessment.

6.15 A participant randomized to the IVR arm misses her Week 4, 8 and/or 12 visits. She comes for her Week 16/termination visit, and tells the site staff that the ring is no longer in place/she lost the ring. Which ACASI questionnaires should be administered at the Week 16/termination visit?

The participant should complete 3 ACASI questionnaires: 1) IVR follow-up, 2) Week 12 follow-up, and 3) Week 16-Termination. Please ensure that a note is made on the Ring Adherence CRF about why Week12 procedures are being administered at the Week 16 Visit.

Why? The IVR follow-up questionnaire contains questions about her actual ring use as well as sexual behavior; the Week 12 follow-up questionnaire contains questions about ring acceptability (actual ring use); the Week 16/Termination questionnaire contains hypothetical questions about future ring use.

6.16 A participant terminates the study early/is withdrawn from the study at her Week 4, 8 or 12 visit. Which ACASI questionnaires should be administered?

- If randomized to the No IVR arm: The participant should complete 2 ACASI questionnaires: 1) No IVR follow-up and 2) Week 16/Termination
- If randomized to the IVR arm: The participant should complete 3 ACASI questionnaires: 1) IVR follow-up, 2) Week 12 follow-up/Final Acceptability, and 3) Week 16/Termination.

Why? The IVR follow-up questionnaire contains questions about her actual ring use as well as sexual behavior; the Week 12 follow-up questionnaire contains questions about ring acceptability (actual ring use); the Week 16/Termination questionnaire contains hypothetical questions about future ring use.

Section Appendix 6-2
MTN 005 Study Ring Request Slip

MTN005 Study Ring Request Slip

Clinic Name:

Participant ID

☐☐☐-☐☐☐☐☐-☐

Clinic Staff Instruction: *Mark whether this is a study ring re-supply, hold, resume, or permanent discontinuation request. Deliver the original white copy (labeled "Pharmacy") to the pharmacy. File the yellow copy (labeled "Clinic") in the participant study notebook.*

☐ **RE-SUPPLY** → **Pharmacy:** Dispense one non-medicated placebo intravaginal ring.

☐ **HOLD** → **Pharmacy:** Do not dispense further study rings to the participant unless another MTN 005 Study Ring Request Slip marked "Resume" is received, or another MTN005 Prescription is received.

☐ **RESUME** → **Pharmacy:** Dispense one non-medicated placebo intravaginal ring.

☐ **PERMANENT DISCONTINUATION** → **Pharmacy:** Do not dispense any further study rings to participant.

Clinic Staff Name (please print): _____

Clinic Staff Signature: _____

Date: ☐☐ ☐☐☐ ☐☐
dd *MMM* *yy*

Pharmacy

Section Appendix 6-3
Product Use Management Scenarios for participants in the IVR cohort in MTN 005

1. Suppose Participant X is randomized on 2 September 2008 and on her Week 4 Visit she indicates that her period is ten days late. The study clinician decides to perform a pregnancy test, and the result of the pregnancy test is positive. What do you do? Clinic Staff: Although the pregnancy test is not a required procedure for the Week 4 Visit, the pregnancy test should be performed because it is clinically indicated. Once a positive pregnancy test result is obtained, if the participant is in the IVR cohort, Study IVR use must be permanently discontinued. If the participant agrees, she should continue follow up in the study with modified procedures for participants who become pregnant (Protocol 7.5.2). Complete an MTN 005 Study Ring Request Slip marked "PERMANENT DISCONTINUATION" to inform pharmacy staff that no other IVR will be dispensed. Also complete a Product Hold/Discontinuation Log case report form. The IVR should be removed by the study clinician and processed for assays by the MTN Network Lab.
2. Suppose Participant X tests HIV EIA positive at her Week 16 Visit. What procedures do you follow? Schedule an appointment with the participant to inform her of her HIV results and follow the HIV testing algorithm provided in the protocol. Provide post-test counseling and referrals.

Section Appendix 6-4
Sample Pregnancy Management Worksheet for MTN 005

PARTICIPANT ID:			
BACKGROUND INFORMATION			
First day of last menstrual period			
Date of positive pregnancy test			
Estimated week 16 and full term pregnancy dates		**Week16:**	**Full Term:**
PREGNANCY MANAGEMENT INFORMATION		**Mark ✓ When Done**	**Initials/Date/Comments**
1	**Pregnancy Report form completed and faxed to SCHARP**		
2	**Pharmacy informed of permanent discontinuation of product use via MTN 005 Study Ring Request Slip.**		
3	**Product supplies retrieved from participant and prepared for Network Lab analyses.**		
4	**Product Hold/Discontinuation form completed and faxed to SCHARP**		
5	**Pregnancy outcome and outcome date ascertained, based on:** **❒ medical records or other written documentation from a licensed non-study health care practitioner** **❒ participant self-report** **❒ negative pregnancy test performed by study staff** **❒ other (specify in comments)** ***(medical records should be obtained whenever possible)***		
6a	**Pregnancy Outcome form completed and faxed to SCHARP**		
6b	**If applicable, AE Log form completed and faxed to SCHARP**		
6c	**If applicable, EAE Report completed via DEAERS**		

Section Appendix 6-5
MTN 005 Study Exit Worksheet

PTID:	**Exit Visit Date:**
Plan for providing participant with final study test results	
Method by which participant wishes to be contacted when study results are available	
Does participant have study product remaining in her possession? ❒ No, per participant report, all product supplies have been used/collected/returned ❒ Yes ⇒ describe plan for product collection (continue on back if needed) ❒ Completed _____	
Is participant currently pregnant? ❒ No ❒ Yes ⇒ describe plan for ascertaining pregnancy outcome (continue on back if needed) IoR approval: _____ ❒ Completed: _____	
Does participant have any ongoing SAEs/EAEs or any AEs at this visit? ❒ No ❒ Yes ⇒ describe plan for AE follow-up (continue on back if needed) IoR approval: _____ ❒ Completed: _____	
Is participant willing to be contacted about future studies for which she may be eligible? ❒ No ❒ Yes	
Staff Signature and Date:	

Section Appendix 6-6
Sample Script for Study Exit Visits

Before we finish your visit today, I would like to take some time to sincerely thank you for taking part in this study. By taking part, you have made an important contribution to the fight against HIV/AIDS.

I also would like to review a few more details with you:

• *If applicable, reinforce plans to collect remaining product supplies.*

• Your appointment to receive your final exam and test results is scheduled for [date]. This appointment will take place [here at the clinic / other specify]. If you need to change this appointment for any reason, please contact us to let us know.

• Although your scheduled study visits have now been completed, the study is planned to be ongoing for another [X] months. After that, we expect it will take about 9 months to have the results of the study available to share with all study participants. In order for us to share this information with you, we need to be able to keep in touch with you. Therefore we ask you to please inform us if you move to a new home, change your phone number, or have any other new details that would help us keep in touch with you. [Give contact card.]

• As you know, [project name] is involved in many different types of research studies. We would like to be able to contact you in the future about other studies that you may be eligible for. Are you willing to give us your permission to do that? [Record response on study exit worksheet; if permission is granted, explain that information recorded on the participant's locator form would be used for this purpose and enter participant on future contact permission log.]

• *If applicable, reinforce plans to determine pregnancy outcome.*

• *If applicable, reinforce plans for AE follow-up.*

• Lastly, we would like to give you some information on places where you can go for different types of services now that you will not be coming here for regular study visits [give referral sheet]:

- For HIV counseling and testing
- For family planning and other reproductive health care
- For other types of health care
- Other

• Please feel free to contact us if you have any questions about the study that we have not answered today, or if you encounter any problems related to your participation in the study. Once again, we sincerely thank you for your contributions to the study and we look forward to sharing the results with you when they become available.

Section Appendix 6-7
Sample Future Study Contact Permission Log

MTN 005 Participants Willing to Be Contacted for Future Studies
By Participant Name

No	Name	Date of Contact Approval