Section 17. Counseling Considerations

This section contains guidance on the following types of counseling provided in MTN-013/IPM 026:

- HIV risk reduction counseling
- Contraception counseling
- Study product adherence counseling
- Protocol adherence counseling

Each of these types of counseling is required at most if not all study visits. All counseling should be provided in a non-judgmental client-centered manner that responds to current participant needs for information, education, support, skills-building, and/or referrals. Participants' needs are likely to change over time; counseling provided should also change over time accordingly. To support ongoing client-centered counseling over time, documentation of each counseling session should include sufficient information and detail to inform and guide the participant's next counseling session

17.1 HIV Pre and Post Test Counseling

HIV testing is required at Screening, Enrollment, and the Day 52 Final Clinic/Early Termination Visit. HIV pre-test and post-test counseling is therefore required at Screening, Enrollment, and the Day 52 Final Clinic/Early Termination Visit. All HIV counseling should be provided in accordance with local counseling standards and study staff who provide HIV counseling should be trained to do so per local practice standards. Counseling staff should also be trained on study-specific HIV testing methods and interpretation of test results per the testing algorithms in protocol Appendix II. Additional information on HIV testing is provided in Section 12 of this manual.

Client-centered approaches should be used to assess participant knowledge of relevant information, dispel any misconceptions, ensure participant readiness for HIV testing, and ensure participant understanding of test results. In the context of repeated HIV-negative test results, care should also be taken to dispel any misconceptions related to the unknown effectiveness of the study products for prevention of HIV infection and the importance of abstaining from receptive intercourse to avoid infection.

17.2 Risk Reduction Counseling

Risk reduction counseling is required per protocol at each scheduled visit. Client-centered approaches should be used when assessing participant risk for HIV infection and providing risk reduction counseling. The counselor should ask open-ended questions, actively listen to participant responses, probe as needed for further information, and guide the participant in identifying her risk factors and barriers to risk reduction, as well as strategies and action plans to try to address these.

Supported and facilitated by the counselor, the risk reduction plans identified by the participant should reflect and respond to her current risk assessment and should be practical, yet challenge the participant toward risk reduction. For participants whose risk reduction barriers are significant, risk reduction plans may need to be incremental. For participants whose risk reduction barriers change over time (e.g., due to a partner change), risk reduction plans may need to change over time. Importantly, all risk reduction plans should be agreed upon by the participant and should be documented in the participant's study records, with a copy made available to the participant if she wishes.

At each counseling session, the risk factors and risk reduction plans identified at the previous sessions should be reviewed and discussed with the participant to determine her experience since her last session, was she able to carry out her strategies and plans, and what were the outcomes. Risk reduction plans identified and agreed upon with the participant at the current session should then build on experience since the last session. Additional or alternative strategies may be identified to achieve further risk reduction if current strategies were not successful.

Risk reduction counseling sessions should also offer skills building to the participant when indicated, how to discuss sensitive issues with partners and other influential persons. HIV counseling for partners should always be offered, either as an individual session or as a couple's session.

Referrals are expected components of risk reduction plans when indicated based on participant needs. When referrals are provided, these should be fully documented in participant study records and should be actively followed up at subsequent counseling sessions to determine whether the participant sought the services to which she was referred, what the outcome of the referral was, and whether additional referrals are needed. All such follow-up should also be fully documented in participant study records.

17.3 Contraception Counseling

Participants are required to be sexually abstinent for the 14 days prior to enrollment and for the duration of study participation. Sex for this study is defined as receptive penile, anal, and receptive oral intercourse. Contraception counseling is required at all scheduled study visits, with the exception of the Final Clinic/Early Termination Visit. All contraception counseling should be provided in accordance with local counseling standards. Study staff who provide contraception counseling should be trained to do so per local practice standards and should also be trained on MTN-013/IPM 026 protocol specifications related to contraception.

Participants must have no intention to become pregnant within the 4 months following Screening. Participants should be counseled regarding the necessity of using an effective method of birth control. Per protocol, these include birth control pills, continuous combination oral contraceptive pills or another hormonal-based method (except for vaginal rings), or an intrauterine device (IUD), unless they are sterilized or identify as a woman who has sex with women exclusively; and/or have been sexually abstinent for more than 90 days. For those participants who report sterilization, study staff must verify the sterilization per site SOPs; all sites are strongly encouraged to obtain credible medical records as part of their verification procedures. At Screening and throughout Enrollment and Follow-up, contraception may be provided on site; however, sites may opt to refer participants to non-study providers for contraception. Condoms will be provided to study participants at their final clinic visit.

All contraception counseling should be provided in a client-centered manner and should guide and support each participant in making the best contraceptive method choice for her and in maintaining adherence to an effective method. When providing information on various contraceptive methods to study participants, in addition to standard information on how each method is taken or administered, mechanism of action, and level of effectiveness, information on the potential advantages and disadvantages of each method should be provided in the context of daily use.

At screening and enrollment visits, contraception counseling should be provided in the context of the study eligibility criteria related to pregnancy intentions and willingness to use an effective contraceptive method. Counseling provided at these visits should therefore explain which methods are acceptable for study purposes and emphasize that women who cannot commit to use of these methods for the duration of the study should not enroll in the study (this is part of their contraceptive choice).

At follow-up visits, client-centered counseling should continue. Issues discussed at the previous counseling session should be reviewed and discussed with the participant as needed and the counselor should determine whether the participant has any current issues, questions, problems, or concerns with her current contraceptive method. For participants with no issues or problems, counseling sessions during follow-up may be brief but should always provide clear method use instructions and always reinforce key adherence messages. For participants with issues or problems with their current method, counseling sessions during follow-up may require more time. In some cases, only counseling and reassurance may be required to address the issues or problems. In other cases, consideration of method switching may be indicated.

All contraception counseling sessions should be fully documented in participant study records. For each session, sufficient information and detail should be recorded to support review and appropriate follow-up at each subsequent visit. A sample of a contraception counseling worksheet and discussion guide is provided in section appendix 17-5.

17.4 Study Product Use Adherence Counseling

17.4.1 Study Product Use Adherence Counseling at Enrollment

Participants will be provided ring use adherence counseling for the first time at their study enrollment visit. Ring use adherence counseling will continue to be provided through the participants Day 28 Visit, at which time the vaginal ring is removed. Prior to receiving this counseling, participants will receive their dispensation of the vaginal ring, be provided with and insert the vaginal ring at the study clinic. Study participants will be given detailed instructions in the clinic on proper vaginal ring insertion and removal procedures.

In addition to verbal instructions, a copy of the illustrated instructions should be provided to each participant. Other visual aids, such as sample vaginal rings, pelvic models, product photographs, and the study-specific fact sheets should be used as needed when providing instructions to help ensure participant understanding of proper product use.

Adequate time should be taken to thoroughly explain the product use instructions and answer any questions the participant may have. Any questions or concerns raised by the participant should be documented in her study records so this information is easily available for reference at follow-up visits.

Site staff should help ensure participant understanding, comfort, and confidence with vaginal ring use from the very beginning of study participation. In particular, any questions or concerns that arise in the context of ring insertion can be addressed by study staff before the participant leaves the clinic.

Participants should be provided with a private space to insert the vaginal ring, with study clinician standing by in case the participant requests guidance or technical assistance. If after three unsuccessful attempts by the participant to self-insert the ring, the study clinician can then assist the participant with insertion. If assistance is required, study clinicians should take time and talk through each step and whenever possible, demonstrate the insertion steps by guiding participant's hands through the process.

Following insertion of the ring, the study clinician should check placement, regardless of who inserted it to confirm correct placement. This can be verified in a variety of methods including:

- The participant should walk around prior to verification of correct ring placement
- The participant should then lie comfortably on the examination couch in supine position
- On genital inspection, the ring must not be visible on the external genitalia. If the ring is visible, this is not correct placement and the ring should be reinserted correctly. In addition, the ring should not press on the urethra

After correct placement is confirmed, the clinician should ask the participant to feel the position of her ring. This will help ensure that she understands what correct placement feels like should she need to check this outside of a study visit.

Key Messages: The following key messages should be discussed with each participant during counseling sessions:

- Refrain from removing the ring for the entire period of 28 days except when instructed by clinic staff. The ring should remain in place during menstruation.
- If the ring accidentally comes out of the vagina before their next clinic visit, it should be rinsed with clean water and put it back in the vagina.
    - If participants have any problems putting the ring back in the vagina, they should contact and/or come to the clinic.
    - Participants should always wash their hands with clean water and soap before and after inserting or removing the vaginal ring, or when checking to ensure the ring is correctly in place.
- If the participant, experiences any of the following the VR should be removed immediately and the study site staff should be contacted: rash, itching, or other skin trouble, joint pain, or difficulty breathing occurs as these may be signs of an allergic reaction or any other problems (i.e. partner or family issues).
- It should not be necessary to check on correct placement between regular visits.
    - However, if the participant feels the need to make sure the ring is still inserted, or is inserted correctly, she should first wash her hands with clean water and soap.

At the discretion of the IoR/designee, women who have previously experienced an expulsion may be advised to check on the ring whenever the precipitating event reoccurs. This advice should be documented in the participant's chart notes. Participants may also be advised to try and adopt the habit of visually checking the toilet after passing a hard stool, lifting heavy objects, or during the heaviest days of menses if such events are the cause of expulsion. Adequate time should be taken to counsel the participant on all key messages, answer any questions and address any concerns the participant may have, and work with the participant in a client-centered manner to identify

operational strategies to assist her in inserting the ring, and removing the ring if necessary. She should be encouraged to ask questions and raise issues or problems at any time.

17.4.2 Study Product Use Adherence Counseling during Follow Up

During follow up, product use adherence counseling is required at Days 1, 2, 3, 5, 7, 14, and 21. At these visits, the client-centered counseling approach initiated at Enrollment should continue. Each counseling session should include the following components:

- Assess product use adherence to study product use since the last counseling session based on participant report and discuss challenges with ring use adherence
- Reinforce key adherence messages
- Document the counseling session

Sites are encouraged to use Neutral Assessment and Next Step Counseling methods when discussing participants' product use in the previous month. Further guidance for the adherence counseling session is provided below.

- Review documentation of previous product use adherence counseling sessions in preparation for a new counseling session.
- Emphasize the importance of open communication about ring use at the beginning of each session.
- Remind the participant that one of the reasons we are doing this study is to find out if women are able to use this ring on a regular basis.
- Use open-ended questions and probes to assess the participant's self-reported adherence since her last counseling session. Note how often the participant reports having removed or expelled the study ring. This will help guide the adherence counseling that she will receive.

- When providing adherence counseling:
    - Ask the participant what her experience has been using the ring. If it was bad, ask why and when. If it was good, ask how and why.
    - Review and discuss with the participant any current barriers to ring use.
    - When needed, review ring use insertion and/ or removal instructions with the participant, using the illustrated instruction sheet and any other visual aids that may be helpful to ensure participant understanding of proper product use.
    - When needed, provide skills building to the participant, e.g., on how to discuss ring use with partners or other influential persons.

- Reinforce key messages provided in section 17.4.1 of this manual.

Adequate time should be taken to counsel the participant on all key messages, answer any questions and address any concerns the participant may have, and work with the participant in a client-centered manner to identify operational strategies to assist her in inserting the ring, and removing the ring if necessary. She should be encouraged to ask questions and raise issues or problems at any time. Each counseling session should be fully documented in chart notes as needed.

At visits Day 7, 14, 21, and 28, ring non-use will be documented by site staff on the Ring Adherence CRF. However, during study visits at Days 1, 2, 3, and 5, site can use the Ring Use Log located in Section Appendix 17-6 to document all instances of non-ring use (regardless of reason) identified at visits other than Day 7, 14, 21, and 28. Information may be added to this log at the time it becomes available including during phone contacts and at interim contacts/visits.

17.4.3 Study Product Use Instructions

At Enrollment, participants will have the study product dispensed to them and be provided with detailed product use and insertion instructions. Product insertion instructions will be provided based on the instructions shown in Section 9 Figure 9-1 of this manual. In addition to verbal instructions, a copy of the illustrated instructions should be provided to each participant. Other visual aids, such as sample rings, pelvic models, and product photographs, should be used as needed when providing instructions to help ensure participant understanding of proper product use. Adequate time should be taken to thoroughly explain the product use and insertion instructions and answer any questions the participant may have; any questions or concerns raised by the participant should be documented in her study records so this information is easily available for reference at follow-up visits.

17.5 Protocol Adherence Counseling

As safety is of the utmost importance, site staff will counsel participants to refrain from engaging in certain practices and/or using prohibited medications during the course of study participation which could potentially increase the possibility of adverse events due to agents other than the study ring and product.

17.5.1 Prohibited Practices

During study participation, participants must abstain from sexual activity which includes engaging in vaginal and/or anal intercourse and receiving oral.

Participants should be counseled to avoid the use of prohibited non-study vaginal products or objects. These products are restricted in order to protect the integrity of the lower genital tract and reduce the possibility of adverse events due to agents other than the study vaginal rings. These medications and practices include:

- spermicides
- female condoms
- diaphragms and/or contraceptive vaginal rings
- vaginal medications for the treatment of STIs (with the exception of single dose fluconazole (diflucan) for the treatment of symptomatic Candida vaginitis)
- menstrual, cervical caps or any other vaginal barrier method
- Other products used in the vagina such as douches, lubricants, tampons, and sex toys (e.g. vibrators, dildos, etc.)

17.5.2 Prohibited Medications

Site staff should counsel study participants to refrain from using CYP3A inhibitors and inducers. These medications are restricted because both dapivirine and maraviroc are CYP3A substrates. Co-administration with CYP3A inhibitors and inducers may increase and/or decrease the concentration of either drug within the blood and/or vagina. Participants are asked to refrain from using CYP3A inhibitors and CYP3A inducers however allowances will be made to treat symptomatic Candida vaginitis. Below are several types of CYP3A inhibitors and/or inducers that are PROHIBITED during study participation.

- Antibiotics or antifungals, such as:

- Clarithromycin (Biaxin®)
- Itraconazole (Sporanox®)
- Ketoconazole (Nizoral®)
- Telithromycin (Ketek®)
- Nefazodone
- Saquinavir
- aprepitant
- erythromycin
- grapefruit juice
- verapamil
- diltiazem
- cimetidine
- amiodarone
- NOT azithromycin
- chloramphenicol
- ciprofloxacin
- delaviridine
- diethyldithiocarbamate
- fluvoxamine
- gestodene
- imatinib
- mibefradil
- mifepristone
- norfloxacin
- norfluoxetine
- star fruit
- voriconazole

- Anticonvulsants, such as:
  - Carbamazepine (Carbatrol®, Epitol®, Equetro™, Tegretol®, Tegretol XR®)
  - Phenobarbital (Luminal®)
  - Phenytoin (Dilantin®, Phenytek®)

- Most protease inhibitors, such as:
  - Amprenavir (Agenerase®)
  - Atazanavir (Reyataz®)
  - Darunavir (Prezista®)
  - Fosamprenavir (Lexiva®)
  - Indinavir (Crixivan®)
  - Lopinavir and ritonavir (Kaletra®)
  - Nelfinavir (Viracept®)
  - Ritonavir (Norvir®)
  - Saquinavir (Fortovase®, Invirase®)

Other:

- Delavirdine (Rescriptor®)
- Efavirenz (Sustiva®)
- Nefazodone (Serzone®)
- Rifampin (Rifadin®)
- St. John's wort

Appendix 17-1
Enrollment Product Use Counseling Checklist

Enrollment Product Use Counseling Checklist

Instructions: Designated staff are to use this checklist for documentation of any product use counseling provided to participants at Enrollment.

PTID:	**Visit Date:**

❒ **De-brief with participant about her ring insertion experience**:

- Was she able to insert the ring?
- Did she have any difficulties?
- Does she have any questions?
- Does she have any concerns about possibly re-inserting the ring at home if necessary?
- Would she like any additional information or instructions?

❒ **Remind participant the ring should not be removed at anytime during the entire 28-day period of the vaginal ring use even during menses, except as directed during study visits.**

☐ **Discuss key adherence messages to the participant**

☐ If the ring accidentally comes out of the vagina before their next clinic visit, it should be rinsed with clean water and re-inserted in the vagina immediately.

☐ If participants have any problems putting the ring back in the vagina, they should contact and/or come to the clinic.

☐ Always wash hands with clean water and soap before and after re-inserting or removing the vaginal ring, or when checking to ensure the ring is correctly in place.

☐ Remove ring immediately if she experiences any of the following:
rash, itching, or other skin trouble, joint pain, or difficulty breathing occurs as these may be signs of an allergic reaction

❒ **Provide instructions to contact study staff:**

- To report symptoms or problems she may be experiencing
- Needs additional counseling
- Has any other problems, concerns, or questions (such as partner or family issues)

_____
Staff Initials and Date

Appendix 17-2
Enrollment Protocol Adherence Counseling Checklist

Enrollment Protocol Adherence Counseling Checklist	
PTID:	**Visit Date:**
☐ **Agrees to abstain from sexual activity including engaging in <u>receptive intercourse</u> (penile, anal, and/or oral) during study participation**	
☐ Agrees to refrain from using the following products in order to protect the integrity of the lower genital tract and reduce the possibility of adverse events due to agents other than the study vaginal rings: ☐ Tampons ☐ Spermicide ☐ Female Condoms ☐ Contraceptive Vaginal Rings ☐ Diaphragms ☐ Vaginal Medications for the treatment of STIs ☐ CYP3A Inducers and/or Inhibitors ☐ Sex toys (vibrators, dildos, etc.) ☐ Lubricants ☐ Douching ☐ Menstrual, Cervical Caps or any other vaginal barrier method	

Additional Counselors

Notes:_____

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Staff Initials and Date

Appendix 17-3
Follow Up Product Use Adherence Counseling Checklist

Follow Up Product Use Counseling Checklist

PTID:	**Visit Date:**

❒ **Discuss and assess adherence to vaginal ring use since the last counseling session based on participant report. Examine the following:**

What were the participant's experiences with the ring since the last counseling session?
What are things that seem to have made keeping the ring in or re-inserting (if applicable) easy or challenging?
Note how often the participant reports having removed or expelled the study ring.

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☐ **Reinforce key adherence messages, if necessary**

- ☐ Refrain from removing the ring for the entire period of 28 days except when instructed by clinic staff. The ring should remain in place during menstruation.
- ☐ If the ring accidentally comes out of the vagina before their next clinic visit, it should be rinsed with clean water and put it back in the vagina.
- ☐ If participants have any problems putting the ring back in the vagina, they should contact and/or come to the clinic.
- ☐ Participants should always wash their hands with clean water and soap before and after re-inserting or removing the vaginal ring, or when checking to ensure the ring is correctly in place.
- ☐ If the participant, experiences any of the following the VR should be removed immediately and the study site staff should be contacted: rash, itching, or other skin trouble, joint pain, or difficulty breathing occurs as these may be signs of an allergic reaction or any other problems (i.e. partner or family issues).

❒ Provide instructions to contact study staff if you have any questions, problems or need another study vaginal ring between visits.

- Problems re-inserting in the vaginal ring
- Any other problems (such as partner or family issues)

❒ Remind participant to:

- Record on her appointment card (or other designated site-specific document) the days and times the ring was out of her vagina prior to her next study visit. (Days 7, 14, 21 and 28)
- Bring appointment card to next visit

_____
Staff Initials and Date

Appendix 17-4
Follow Up Protocol Adherence Counseling Checklist

Follow Up Protocol Adherence Counseling Checklist	
PTID:	**Visit Date:**
☐ **Agree she is abstaining from sexual activity including engaging in <u>Receptive Intercourse</u> (penile, anal, and/or oral)**	
☐ Agree she is refraining from using the following products: ☐ Tampons ☐ Spermicide ☐ Female Condoms ☐ Contraceptive Vaginal Rings ☐ Diaphragms ☐ Vaginal Medications for the treatment of STIs ☐ CYP3A Inducers and/or Inhibitors ☐ Sex toys (vibrators, dildos, etc.) ☐ Lubricants ☐ Douching ☐ Menstrual, Cervical Caps or any other vaginal barrier method	

Additional Counselors

Notes:_____

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Staff Initials and Date

Appendix 17-5
Contraceptive Counseling Checklist

Contraceptive Counseling Checklist	
Review participant's reproductive history documentation and previous entries on this flow sheet to inform and guide contraceptive counseling provided at each visit. For all protocol specified acceptable methods of contraception, discuss: how each method is taken or administered, mechanism of action, and level of effectiveness.	
PTID:	**Visit Date:**
What method of contraception is she currently using?	
Has she experienced any issues/questions/concerns regarding your current form of contraception?	
Issues to follow up at next visit:	
Does she intent to continue using the method listed above throughout study participation?	

Staff Initials and Date

Appendix 17-6
Ring Use Log

Details from participant (date, duration, reason ring not used)	Staff Initials/Date