Section 10. Counseling Considerations

All counseling should be provided in a non-judgmental client-centered manner that responds to current participant needs for information, education, support, motivation, skills-building, and/or referrals. Participants' needs are likely to change over time; thus the content and focus of counseling discussions should also responsively change over time. Because of this, specific content to cover or skills to emphasize are not standardized. Rather, the process for these discussions is standardized to allow for appropriate tailoring and targeting to an individual participant's needs at a given point in time.

All counseling and referrals should be documented in participant study records. Proper documentation may be achieved through the use of counseling checklists/worksheets, and/or chart notes. To support continuity in the ongoing client-centered counseling over time, documentation of each counseling session should include sufficient information and detail to inform subsequent counseling sessions.

10.1 HIV and Risk Reduction Counseling

HIV testing is required at Screening, Enrollment, and the Day 35 Final Clinic/Early Termination Visit. HIV pre-test, post-test, and risk reduction counseling is therefore required at these visits, as well as when HIV testing is clinically indicated. All HIV counseling should be provided by trained study staff in accordance with local counseling standards. Counseling staff should also be trained on study-specific HIV testing methods and interpretation of HIV test results per the testing algorithms in protocol Appendix II. Sites are required to develop SOPs which outline site-specific procedures for HIV/Risk Reduction Counseling, Testing, and Referral.

10.1.1 HIV Pre and Post-Test Counseling

When providing pre-test and post-test counseling, participant-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. A sample HIV counseling worksheet is available for use on the MTN-028 webpage under Study Implementation Materials. This worksheet provides a guide to the minimum requirements for HIV testing and counseling sessions and may be tailored for use at each study site. Counselors should provide and explain test results in a private setting per site SOPs. Counselors should assess participant understanding of results and provide clarification and further information as necessary. Regardless of status, continued risk-reduction should be emphasized.

Table 10-1
Interpretation of HIV Test Results Per Protocol Appendix II

Test Result	Counseling Message(s)
Sample 1 Immunoassay negative	HIV-uninfected; test results indicate that you are not infected with HIV.
Sample 1 Immunoassay positive or indeterminate	HIV status not clear; test results indicate that you may be infected with HIV but additional testing is needed to confirm your status. No additional blood collection is needed for this testing. Provide estimated turnaround time for results.
Sample 1 Confirmatory Test positive	**If Screening or Enrollment Visit**: HIV-infected; test results indicate that you are infected with HIV. You are not eligible for enrollment in this study. Provide counselling and referrals for HIV positive participants per site SOPs. **If during study follow-up**: HIV-infected; test results indicate that you are infected with HIV. Additional testing may be needed for study purposes and to see how your body is responding to the virus. This additional testing will be done from a new blood sample. It is common for HIV research studies to do additional testing in this situation, and unusual for this testing to show a different result. Provide counseling and estimated turnaround time for results.
Sample 1 Confirmatory Test negative or indeterminate	HIV status not clear; test results indicate that you may be infected with HIV but additional testing is needed to confirm your status. Consult the LC for specific testing and counseling guidance.
Sample 2 Confirmatory Test positive	HIV-infected. Test results have confirmed that you are HIV infected. Provide counselling and referrals for HIV positive participants per site SOPs. Counsel participant that regular study visits will discontinue at this time.
Sample 2 Confirmatory Test negative or indeterminate	HIV status not clear; test results indicate that you may be infected with HIV but additional testing is needed to confirm your status. Consult the LC for specific testing and counseling guidance.

10.1.2 Risk Reduction Counseling

Risk reduction counseling is required per protocol at the enrollment visit, and should also occur whenever HIV testing is done. More frequent counseling could be done per site SOP. 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. Abstinence requirements for the duration of the study may also be emphasized during risk-reduction counseling.

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.

As participants are expected to remain sexually abstinent during participation in MTN-028, and use of other vaginal products is prohibited, condoms will only be offered during HIV/Risk Reduction counseling at the Day 35 Final Clinic/Early Termination Visit.

10.2 Protocol Counseling

Per protocol, protocol requirements counseling will include adherence, product use, and contraceptive counseling. Counseling is required at Screening and Enrollment Visits, and at follow-up visits if indicated. If indicated in this case means that given the frequency of the visits, it is not necessary to go over all aspects of the counseling messages, but rather review or clarify with the participant important information relevant to their situation. Guidance about these types of counseling are described in detail in the sections that follow.

10.2.1 Contraceptive Counseling

Contraceptive counseling is required at Screening and Enrollment visits, and at other study visits if indicated. Study staff who provide contraceptive counseling should be trained to do so per local practice standards and should also be trained on MTN-028 protocol specifications related to contraception. Contraception may be provided on site or sites may opt to refer participants to non-study providers for contraception.

To be eligible for MTN-028, potential participants must report use of an effective method of contraception at enrollment and intend to use an effective method for the duration of study participation. Per protocol, effective methods include hormonal methods (except for contraceptive IVRs), intrauterine device (IUD) inserted at least 28 days prior to enrollment, engaging in sex with women exclusively, self or partner sterilization, and/or being sexually-abstinent for the past 90 days. For those participants who report sterilization, study staff must verify the sterilization per site eligibility SOPs; the site is encouraged to obtain medical records as part of their verification procedures.

All contraceptive 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. When providing information on various contraceptive methods to study participants, standard information should include how each method is taken or administered, mechanism of action, potential side effects, and level of effectiveness.

At Screening and Enrollment, 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). Participants must have no intention to become pregnant within the 3 months following screening or enrollment.

During follow-up, contraceptive counseling should be offered if indicated. 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 and supportive. For participants with issues or problems with their current method, counseling sessions during follow-up include discussion of the specific problems encountered and identify potential strategies to address these, which may include switching methods.

All sites should offer emergency contraception to study participants when applicable. The term emergency contraception refers to back-up methods for contraceptive emergencies which can be used within the first few days after unprotected intercourse to prevent unwanted pregnancy. The WHO-recommends two methods of emergency contraception: emergency contraceptive pills and copper bearing IUDs. Please see the WHO Fact Sheet (dated July 2012) for more information on emergency contraception: http://www.who.int/mediacentre/factsheets/fs244/en/.

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 is provided on the MTN-028 Study Implementation webpage.

10.2.2 Product Use Instructions and First Product Use

During the enrollment visit, participants will be provided with detailed instructions regarding vaginal ring insertion and removal (see MTN-028 Ring Insertion Instructions available on the MTN-028 Study Implementation webpage). Staff should actively review these instructions with participants, and use visual aids and pelvic models (if available) to help explain ring insertion and removal. A copy of the illustrated instructions should be offered to each participant.

Participant Instructions for Ring Insertion: See MTN-028 Ring Insertion Instructions available on the MTN-028 website.

Participant Instructions for Ring Removal (provide verbally to participants):

1. Before removing the ring, wash and dry your hands.
2. Choose a comfortable position (can reference ring insertion instructions for illustrations of different positions).
3. Put a finger into your vagina and hook it through the ring.
4. Gently pull down and forward to remove the ring.
5. If you will be reinserting the ring, follow the ring insertion instructions, and wash your hands when you are done. If you will not be reinserting the ring, continue to steps 6-9 and contact the study clinic.
6. Place the used ring in the bag provided by clinic staff or other suitable container if the bag is not available.
7. Wash your hands.
8. Place used ring and container in a safe and private area out of reach of children or other occupants of the home.
9. Bring any used ring (in its container) with you to the clinic during your next study visit.

In addition to receiving ring insertion and removal instructions, staff should provide adherence counseling as outlined in section 10.2.3. This can be done before or after first product use.

After providing product insertion instructions and answering any questions the participant may have, study staff will ask the participant if she is ready to try inserting the vaginal ring herself. Insertion should be performed in a private space, with study staff standing by in case the participant requests guidance or technical assistance.

Difficulties in inserting the vaginal ring are expected to be rare. At the Enrollment Visit, study staff are required to confirm proper placement of the VR by a digital examination (see Section 10.2.2.1). For all other follow-up visits, this procedure should be done only if indicated (i.e. the participant is having discomfort potentially due to improper VR placement). For participants who have difficulty or who have inserted the ring incorrectly, study staff should provide further information and guidance to address the difficulty encountered. After guidance is provided, the participant should try again to insert the vaginal ring at the enrollment visit. If she is unable, study staff may insert the ring for the participant.

It is recommended that staff also confirm that the participant is able to remove and reinsert the VR. This is to encourage comfort with removal procedures, and additional practice in case the VR is removed or accidentally falls out prior to her next clinic visit.

NOTE: If ring is remove for this purpose, timing for PK purposes starts when the ring is first inserted.

After the VR is inserted, study staff should de-brief with the participant on her experience. Any issues or problems raised by the participant should be addressed by the study staff and documented in participant study documents so the information is easily available for reference at study follow-up visits.

10.2.2.1Clinician Instructions for Checking Ring Placement

At the enrollment visit, following insertion of the VR, the study clinician should check placement of the VR, regardless of who inserted it, to confirm correct placement. The following is the procedure that should be used to verify ring placement:

1. After ring placement, the participant should walk around prior to verification of correct ring placement.
2. The participant should then lie comfortably on the examination couch in supine position (on her back).
3. Upon genital inspection, the ring must not be visible on the external genitalia. If the ring is visible, the placement is not correct.
4. The ring should not press on the urethra.
5. On digital examination, the ring must be placed at least 2cm above the introitus beyond the Levator Ani muscle.
6. If, on inspection, the ring is found to be inserted incorrectly, the ring should be removed and reinserted correctly by the participant or the study clinician.

At the Enrollment visit, after correct placement is confirmed, staff 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 between study visits. This instruction may be repeated at any visit, as needed.

10.2.3 Study Product Adherence Counseling

Per protocol, participants will be provided product adherence counseling at their enrollment visit. At their discretion, sites may also review adherence counseling messages or product use instructions during the screening visit (e.g. as part of education on study requirements), and throughout follow-up as needed.

When discussing adherence, it is important that the topic be addressed using a neutral approach, so as to leave the participant feeling comfortable/free with discussing instances of non-adherence. Participants should be encouraged to ask questions and raise issues or problems at any time. Participants should also be encouraged to pay attention to their experiences using the ring, and to share these experiences with staff.

A MTN-028 Protocol/Product Adherence Counseling Worksheet is available for use on the MTN-028 Study Implementation Materials webpage. This worksheet provides a guide to the minimum requirements for protocol/product use counseling messages at enrollment; this

worksheet may be tailored for use. As each point is addressed, site staff should mark each message on the worksheet. Discussion points, participant questions should also be noted on the worksheet and/or in chart notes and used for future counseling sessions. These key counseling messages are also available as printed materials on the reverse side of the Ring Insertion Instructions for participants to take home. These printed materials should be IRB approved before use.

During follow-up visits, adherence counseling should be provided if indicated. At a minimum, it is recommended that staff briefly check in with participants at regular intervals (about once per week) to see how ring use is going and if they have any questions or concerns. If the participant reports ring removals or expulsions, is experiencing discomfort, and/or has any questions or concerns about ring use, these issues should be addressed in a neutral and non-judgmental way. Further guidance for the adherence counseling 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.
- Use open-ended questions and probes to assess the participant's experiences with ring use. For example, "What has your experience with ring use been so far?" or, "How has ring use been going for you?" If her experience was bad, ask why and when. If it was good, ask how and why.
- Work with participants to develop strategies and goals to either maintain good adherence, or to overcome adherence barriers if encountered.
- When needed, review ring use insertion instructions or key adherence messages 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 and/or study protocol requirements.
- When needed, provide skills building to the participant, e.g., on how to discuss ring use with partners or other influential persons.

Adequate time should be taken to counsel the participant and address any questions or concerns the participant may have. Each counseling session should be fully documented per site SOPs for source documentation.

During follow-up, adherence counseling (if indicated) should occur after administration of the Ring Adherence CRFs. Sites may choose to conduct adherence counseling prior to completion of clinical/lab assessments to improve visit flow. Note that in this situation, some participants may receive adherence counseling, but may subsequently be put on product hold during the visit.

10.2.4 Biopsy Collection for PK Counseling

Participants will also undergo collection of cervical tissue (biopsies) for PK at the Day 28 visit. As part of the provision of protocol adherence counseling, study staff will explain what procedures will be performed at the visit and what to expect. The participant will be counseled and informed that in order to collect cervical biopsies, a clinician will use an instrument called a speculum. Once the speculum is inserted, the clinician will take one or two small tissue samples from the participant's cervix, each about the size of a grain of rice. These samples will be used to see how much of the study drug is in her tissue.

Participants should be counseled to abstain from inserting anything in the vagina, including engaging in vaginal intercourse, as she may be at increased risk for STIs and HIV acquisition, if exposed. Participants should also be counseled that they may experience some pressure or discomfort in her genital area during the pelvic examination and sample collection. During the collection of biopsies, the participant may feel slight to moderate pain (similar to the feeling of being pinched) which usually resolves within a few hours following tissue collection. The participant should be informed that she may have spotting (small amounts of bleeding) for 1 – 2 days following the biopsies and that there is a small risk of the biopsy area becoming infected or having bleeding that is heavier than spotting. The participant should be instructed to contact the study clinic immediately if she experiences heavy bleeding, more than a usual menstrual period, a foul odor or a heavier vaginal discharge (more than usual).

10.2.5 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. Note that protocol adherence counseling may be reviewed and documented as part of the study product adherence counseling session at enrollment (specifically, refer to the "AVOID" section of the adherence counseling messages worksheet). If sites wish to conduct protocol and product adherence counseling separately, worksheets/tools may be modified to suit this approach (e.g. if different staff members will be assigned these responsibilities).

10.2.5.1 Prohibited Practices and Medications

Participants will be counseled to avoid the following prohibited practices and medications during participation in the study:

- Receptive intercourse (vaginal, anal, or oral intercourse, finger stimulation and the use of sex toys) should be avoided for duration of study and for 5 days preceding Enrollment, i.e., participants should be sexually abstinent.
- Tampons should not be used during the first week of study participation (starting at the enrollment visit) and for 24 hours prior to each clinic visit following enrollment.
- Non-study vaginal products and other devices should be avoided. This includes, but is not limited to: spermicides, female condoms, diaphragms, contraceptive intravaginal rings, vaginal medications (with the exception of single dose fluconazole (diflucan) for the treatment of vaginal fungal infections), menstrual cups, cervical caps, douches, lubricants, and sex toys (e.g., vibrators, dildos, etc.).
- Participation in other research studies involving drugs, medical devices, or vaginal products for the duration of study participation
- Use of female-to-male transition medications (i.e. cross gender hormonal therapy) during the study is prohibited.
- Avoid using certain CYP3A inhibitors and CYP3A inducers (see SSP Section 7)

Site staff should counsel study participants to refrain from using CYP3A inhibitors and inducers. These medications are not recommended because VCV (MK-4176) is a CYP3A substrate. 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. Several types of CYP3A inhibitors and/or inducers that are PROHIBITED during study participation are listed in section 7 of this manual.