

Section 9. Study Product Considerations for Non-Pharmacy Staff

This section provides information and instructions for non-pharmacy staff related to the request, transport, and delivery of MTN 005 study product for study participants. Record keeping requirements for non-pharmacy staff also are provided. Associated instructions for pharmacy staff are provided in the *MTN 005 Pharmacy Policy and Procedure Manual*, which will be made available to each study site Pharmacist of Record (PoR) by the MTN Protocol Pharmacist. Please also refer to related information in Sections 4 and 6 of this manual.

9.1 Intravaginal Ring (IVR) Use Instructions

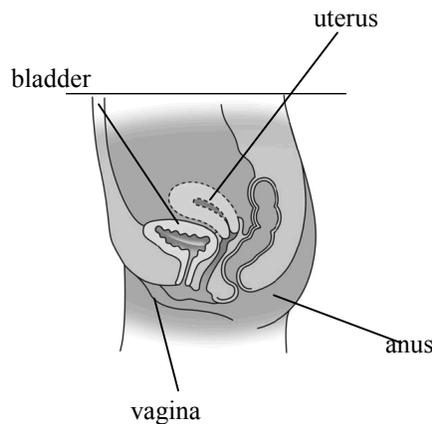
At the Enrollment visit, participants assigned to the IVR group will receive instructions on study IVR insertion and use. The participant will self insert (or by clinician, if necessary), the study IVR. The study IVR will remain in place for 12 consecutive weeks.

Detailed instructions for IVR insertion are listed in Figure 9-1 below. A listing of frequently asked IVR insertion questions, and answers to these questions, is provided in Section Appendix 9-1.

Figure 9-1
IVR Insertion Instructions for MTN 005

VAGINAL RING INSERTION INSTRUCTIONS

HOW DO I USE THE VAGINAL RING?



TO INSERT THE RING INTO YOUR VAGINA:

1. Wash and dry your hands.
2. Remove the ring from its package.
3. Choose the position that is most comfortable for you. For example, lying down or standing with one leg up. (See **Diagrams 1a and 1b**, respectively).

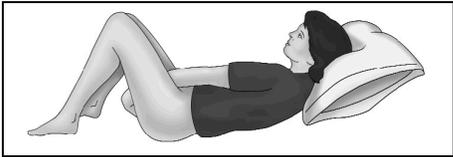


DIAGRAM 1a

OR



DIAGRAM 1b

4. Use your thumb and index finger (pointer finger) to press the sides of the ring together. You may find it easier to insert the ring if you twist it into a figure-of-eight shape. (See **Diagram 2**)

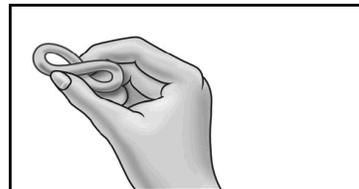


DIAGRAM 2

5. Use your other hand and hold open the folds of skin around your vagina. (See **Diagram 3**)



DIAGRAM 3

6. Place the tip of the ring in the vaginal opening and then use your index finger to push the folded ring gently into your vagina. Push it up towards your lower back as far as you can. (See **Diagram 4**)

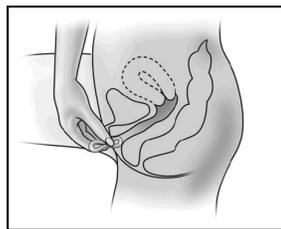


DIAGRAM 4

If the ring feels uncomfortable, you probably did not push it into your vagina far enough. Use your index finger to push the ring as far as you can into your vagina (See **Diagram 5**). There is no danger of the ring being pushed too far up in the vagina or getting lost.

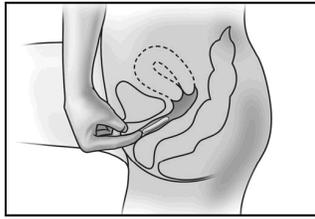


DIAGRAM 5

The ring should now be in your upper vagina (See **Diagram 6**).

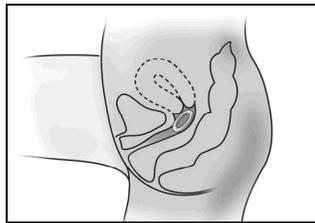


DIAGRAM 6

7. Wash your hands when you are done.

TO REMOVE THE VAGINAL RING:

1. Wash and dry your hands.
2. Choose the position that is most comfortable for you (See **Diagrams 1a** and **1b**).
3. Put a finger into your vagina and hook it through the ring. (See **Diagram 7**)

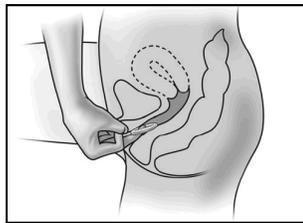


DIAGRAM 7

4. Gently pull downwards and forwards to remove the ring.
5. Wrap the used ring in tissue or toilet paper and give it to the clinic staff for disposal.
6. Wash your hands.

IMPORTANT INFORMATION

- If possible, you should try not to remove the ring for the entire 12 week period of the Vaginal Ring regimen. If the ring accidentally comes out of your vagina before your next clinic visit, e.g., during sex, clean it with warm water and put it back in your vagina.

- If you have any problems putting the ring back in your vagina, call or come to the clinic.

9.2 Dispensing Non-Medicated Intravaginal Rings

Refer to Section 4 and 6 of this manual for further procedures for participant randomization, initial ordering and dispensation of non-medicated intravaginal rings for enrolled participants.

Upon receipt of a completed and signed MTN 005 Prescription, or a completed and signed MTN 005 Study Ring Request Slip, pharmacy staff will dispense one non-medicated intravaginal ring per instructions in the MTN 005 Pharmacy Policy and Procedure Manual. One non-medicated intravaginal ring will be dispensed in a pouch contained in an individual box. The clinic staff must also provide the participant with a resealable bag for use if the used ring needs to be returned to the clinic.

Non-medicated intravaginal rings may be dispensed to participants in one of two ways:

- From the pharmacy directly to the participant
- From the pharmacy to authorized clinic staff who will then deliver the study product to the participant

Each study site must designate its dispensing method in MTN 005 standard operating procedures (SOPs) for dispensing the non-medicated intravaginal ring and, if necessary, product re-supply during follow-up. The SOP (Chain of Custody) should be developed with input from both pharmacy and clinic staff.

9.2.1 Dispensing of Study Product from Pharmacy

At sites choosing to dispense study gel cartons directly from the pharmacy to participants, prescriptions and Study Ring Request Slips are expected to be delivered to the pharmacy by the participants themselves, although this may be done by clinic staff or a runner. Upon receipt of a completed and signed prescription or Study Ring Request Slip, the PoR will prepare one non-medicated intravaginal ring. The ring may be prepared based on either original documents or faxed (scanned) copies, but will not be released to participants until the original prescription or original Study Ring Request Slip is received by the site pharmacy.

9.2.2 Dispensing of Study Product from Clinic Staff

At sites choosing to dispense the non-medicated intravaginal ring to clinic staff who will then deliver the ring to participants, prescriptions and Study Ring Request Slips are expected to be delivered to the pharmacy by clinic staff or a runner. Upon receipt of a completed and signed prescription or Study Product Re-Supply Slip, the PoR will prepare one non-medicated intravaginal ring. The ring may be prepared based on either original documents or faxed (scanned) copies, but the ring will not be released to clinic staff until the original prescription or request slip is received by the site pharmacy.

The MTN 005 Record of Receipt of Participant-Specific Non-medicated Intravaginal Rings (see Section Appendix 9-2) must be used to document dispensing of rings to clinic staff. Pharmacy staff will complete the top section (site name, site number, clinic name) and the

first four columns on the Record of Receipt. When receiving the ring from the pharmacy, clinic staff will verify the PTIDs, confirm the ring received for each PTID, and complete the remaining three columns on the Record of Receipt for each PTID. Comments may be recorded in the designated column and, if additional space is needed, on the back of the record. All Records of Receipt will be retained in the pharmacy. Clinic staff are responsible for controlling access to the rings dispensed into their custody and ensuring that the rings are delivered to the participants for whom they were dispensed. Clinic staff also must document delivery of the rings to designated participants in the participants' study charts. Delivery may be documented in chart notes, on visit checklists, or on other source documents designated for this purpose by clinic staff. In the event that a ring dispensed for a participant is not delivered to the participant, clinic staff will document this in the participant's study chart and return the ring to the pharmacy as soon as the participant's visit is completed.

9.3 Return of Study IVR

Clinic staff will provide participants with re-sealable plastic bags or other suitable containers in which to store their IVR in case the IVR is expelled spontaneously or is taken out by the participant and they are unable to re-insert it. Clinic staff should not return used rings to the pharmacy.

9.3.1 Used IVR Supplies

Once the initial ring is inserted it should remain in place for 12 weeks. If the ring has been expelled in such a way that it is no longer useable (e.g., in the toilet, etc.), the participant should be instructed to notify the clinic immediately and a new ring will be dispensed. The used ring should be returned to the clinic. The participant should be instructed by the clinic to place the used ring in the resealable plastic bag that they received when the ring was inserted. If this bag is no longer available, participants should be encouraged to obtain a suitable substitute and return the ring to the clinic. If the ring is intentionally removed by the participant for more than a few hours, the ring should be rinsed with clean water, dried with a clean (paper) towel, and stored in the resealable plastic bag provided by the clinic. The ring should be rinsed with clean water prior to reinsertion by either the participant or the study clinician.

In the event that a participant is temporarily or permanently discontinued from study product use, every effort should be made to collect the used IVR within five working days. The participant should be asked to report to the study clinic in order for the study clinician to remove the ring. If the ring is removed by the study staff and it will not be reinserted (because of permanent or temporary product use discontinuation), it should be prepared for culture and biofilm assessment by the Network Lab (see Section 12 Laboratory Considerations). If the ring is removed by the participant prior to the clinic visit and will not be reinserted, it should be discarded in a proper biohazard receptacle.

NO USED RINGS SHOULD BE RETURNED TO THE PHARMACY. Return of the used ring to the clinic should be documented as determined by the site clinic.

9.4 Study Product Hold/Resume Supply Slip

The MTN 005 Study Ring Request Slip is a two-part no carbon required (NCR) document that will be provided to the clinic staff by SCHARP (see Section Appendix 6-2 for illustration). This slip will be used to request replacement IVR or to inform the pharmacy if product needs to be held (permanently or temporarily) or resumed.

Complete the Study Ring Request Slip as follows:

- Record the clinic name.
- Record the PTID assigned to the participant in the boxes provided.
- Mark the box for RESUPPLY, HOLD, RESUME or PERMENANT DISCONTINUTAION, to indicate the action to be taken by the study pharmacy.
 - When resuming product, a new prescription for the IVR will need to be completed and sent to the pharmacy along with the Study Product Slip. Study product will not be dispensed from the pharmacy unless/until another slip marked RESUME is subsequently completed and received in the pharmacy, along with the new prescription.
- The clinic staff name, signature, and signature date must be completed by a clinic staff member authorized to order product supplies for participants during follow-up. DAIDS does not require that an authorized prescriber sign and date the Study Product Slips; however site-specific pharmacy regulations may be more stringent than DAIDS requirements. All sites must comply with local requirements.
- Double-check the accuracy of all entries and then separate the two parts of the completed Study Product Slip. Retain the yellow copy in the participant study notebook. Deliver the white original to the study pharmacy in the same manner that original prescriptions are delivered to the pharmacy. Both the original and clinic copy of the slip may be hole-punched.

9.5 Product-Related Scenarios

For illustrative purposes, a number of product-related scenarios are provided in Sections 4 and 6 of this manual (see Section Appendix 4-1 and Section Appendix 6-3).

Section Appendix 9-1 Frequently Asked IVR Use Questions

SCENARIO 1

A ring is dispensed to a participant in the study IVR cohort on March 15th. After one week of use, she finds that the ring is uncomfortable, and calls the clinic to ask for advice.

What do you tell her?

- Ask the participant if she is experiencing any other symptoms that might suggest she should come in for a physical/pelvic exam
- If the participant calls to complain that she feels discomfort from the ring in her vagina, first advise the participant to wash her hands and try to gently push the ring higher up into the vagina

OR

- If the ring has been expelled from the vagina, advise her to wash her hands and, using the bottled water or other clean water, rinse and gently reinsert the ring into the vagina
- (Explain to her that this is not unusual to occur and give some examples of cases (Refer to FDA article examples - straining on bowel movement)
- If repositioning the ring does not improve her discomfort, advise her to follow up in clinic for evaluation.

SCENARIO 2

A participant calls the clinic between her Week 4 and 8 visits to say that her partner tells her that he can feel the ring during sexual intercourse. What steps should you take?

Possible Answer:

- If the participant is concerned that something is wrong, provide her reassurance that while most partners don't notice the ring, many will and usually it is not bothersome to the partner.
- Ensure that the participant has inserted the ring in the correct position. If the ring has moved down the vaginal canal, advise the participant to wash her hands and try to gently push the ring higher up into the vagina.
- Inquire whether she has removed the ring and document periods where the IVR was not used.

SCENARIO 3

After the participant speaks to the clinic, she decides that she will try to reposition the IVR and resume use. After one week of resuming use, her partner complains that the ring is bothersome during intercourse, and she calls the clinic to say that she is going to remove the ring and leave it out. What should you do?

Possible Answer:

- If the participant insists on voluntarily stopping use of the IVR, follow modified procedures for product use completion as specified in the protocol.
- Encourage her not to remove the ring herself, but to come in to have the IVR removed by a clinician. At the visit, prepare the ring for Network Laboratory analyses.

- If she insists on removing the IVR prior to coming into the clinic, advise her to do the following:
 - Store the IVR in a bag
 - Return the IVR to the clinic as soon as possible
 - [Participant should not discard the IVR]
- Document via a chart note the participant's decision to stop using study product. Attempt to keep participant in study follow-up as scheduled until the Week 16/Termination visit. Follow modified procedures for completion of product use as specified in the protocol.
- Document conversation in the participant chart notes.
- Document return of the IVR for accountability and dispose of IVR if IVR was returned by participant.

SCENARIO 4

On her week 4 visit, a study participant reports that she removed the IVR for a duration of one week due to use of tampons for her menses. She did not think that it was possible to use both the tampon and the IVR at the same time. After cessation of her menses, she resumed IVR use and followed instruction for reinsertion. What do you do?

Possible Answer:

- Advise the participant that she can use the tampon and the IVR at the same time, and that the IVR should not be removed at any time, unless she is experiencing discomfort or pain.
- Document IVR removal (duration, date, etc.) on the Ring Adherence case report form.

SCENARIO 5

A participant contacts the clinic between her week 8 and week 12 visit to report vaginal itching. Upon further probing, you discover that she removed the ring, washed it with detergent, and re-inserted it for hygienic purposes. What do you do?

Possible Answer:

- Ask the participant if she is experiencing any other symptoms that might indicate infection or pathology. Schedule in-clinic pelvic exam for follow-up if indicated.
- Remind the participant not to remove the IVR, and to only use clean water, such as the study-provided bottled water, to rinse it in the event of ring expulsion.

SCENARIO 6

A participant contacts the clinic and states the ring has fallen out and she refuses to rinse and reinsert it. She wants to come to the clinic to receive a new ring.

Possible Answer:

- Advise the participant to return to the clinic as soon as possible to receive a new IVR.
- Complete an MTN 005 Study Ring Request Slip and obtain a new IVR from the pharmacy. Document return of the IVR for accountability and dispose of IVR (do not process for Network Lab analyses).

