MTN-036/IPM 047
Study Product Considerations

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Microbicide Trials Network
Pittsburgh, PA
USA
Presentation Overview

- Prescription Completion
- Vaginal Ring Supply and Labeling
- Chain of Custody and Accountability
- Vaginal Ring Request Slip Completion
- Vaginal Ring Retrievals
- Vaginal Ring Complaints
Reference Materials

- MTN-036/IPM 047 Protocol, Version 1.0
  - Section 6
- MTN-036/IPM 047 SSP Manual
  - Section 7
- Site-Specific Clinic Study Product Accountability and Destruction SOP (non-pharmacy) for MTN-036/IPM 047
- Participant will self-insert vaginal ring at Visit 2/Day 0: Enrollment. IoR/authorized clinician, if necessary.
- New 25 mg DPV VR is inserted approx. Q4W for the first 8 weeks, and third VR will be worn for approx. 5 weeks for total of 13 weeks.
- 100 and 200 mg DPV VRs are inserted once and worn continuously for approx. 13 weeks.
Visit 2/Day 0: Enrollment

- A supply of prescriptions is provided to the clinic staff by the MTN LOC Pharmacy via site PoR

- Completion of prescription by clinic staff/authorized prescriber will occur at the Visit 2/Day 0: Enrollment
  - Prescription is a 2 part no carbon required (NCR) paper document. The top white is the original (pharmacy) and the bottom is yellow (clinic).
Visit 2/Day 0: Enrollment Visit

- The study database (via the Medidata Balance module) will assign the participant to a study product and the Randomization Date and Time will appear automatically on the Randomization CRF.

- Completion of prescription by clinic staff/authorized prescriber is the next step
One prescription for each participant for the entire study.
MTN-036/IPM 047 Prescription

- When completing the prescription, place the cardboard flap under the copy (clinic prescription)
- Double check the accuracy of all entries
- Errors may be corrected in blue or black ink by putting a line through and initialing/dating
- Retain the yellow copy for the participant study notebook in the clinic
- Deliver white copy to pharmacy
- The pharmacist will review the prescription.
  - Compare to VR indicated on Pharmacy Dispensation CRF

- If an error is noted, the white and yellow copies must be individually corrected by an authorized prescriber with identical information on both copies (correction, initials, date).

- If no problems are noted, the pharmacist will dispense the vaginal ring (VR).
Dapivirine Vaginal Rings

25 mg
Sustained drug release over a minimum of one month

100 mg
Sustained drug release over 90 ± 3 days

200 mg
Dapivirine Vaginal Rings

- 56 mm outer diameter and 7.7 mm cross-sectional diameter
- Storage: 20°C-25°C, with allowable excursions between 15°C-30°C
MTN-036/IPM 047 VR Pouch Label

Strength is indicated on each label.

100mg and 200mg will not be disclosed to the participant.

PoR to indicate
MTN-036/IPM 047 Returned Used VR Label (on white bag)

PoR to indicate

Clinic Staff to indicate

<table>
<thead>
<tr>
<th>MTN-036/IPM 047 FOR USED RING ONLY</th>
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</thead>
<tbody>
<tr>
<td>Date Dispensed:___________________  PTID #: ____________________</td>
</tr>
<tr>
<td>Contents: 1 used vaginal ring containing up to 200 mg Dapivirine.</td>
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<tr>
<td>Keep out of reach of children and pets</td>
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<tr>
<td>For clinical trial use only</td>
</tr>
<tr>
<td>IND Sponsor: International Partnership for Microbicides, Silver Spring, MD USA.</td>
</tr>
<tr>
<td>Phone: 00 + 1 301-608-2221</td>
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<tr>
<td>Emergency Contact Name:</td>
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<tr>
<td>Phone Number:</td>
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Chain Of Custody

- The VR must be tracked with documentation, from the pharmacy to the participant, all steps in between and the return documented in the clinic.

- Study product may be prepared by the pharmacist based on either original documents or faxed copies, but will not be released to the clinic staff until the original prescription is received.

- Upon receipt of a completed and signed prescription, the PoR will **dispense one study VR**.
Chain Of Custody

- Study Product is dispensed by pharmacy staff to:
  - Clinic staff who will:
    - Provide to the participant for self-insertion
    - Insert the VR into the participant’s vagina or
  - Runner who delivers the VR to clinic staff
  - Courier who delivers the VR to clinic staff

- Depends on pharmacy site-specific Chain of Custody SOP

- Chain of Custody from pharmacy staff to clinic staff/runner/courier is documented on the Record of Receipt of Site-Specific Vaginal Rings at time of VR dispensation
  - This record is stored in the pharmacy
MTN-036/IPM 047 RECORD OF RECEIPT OF SITE-SPECIFIC VAGINAL RINGS

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<tr>
<th>CRS Name:</th>
<th>CRS ID:</th>
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<tr>
<th>PHARMACY STAFF</th>
<th>CLINIC STAFF/RUNNER/COURIER</th>
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<tr>
<td>Date/Time dispensed from pharmacy dd-MMM-yyyy (hh:mm) 24 hr clock</td>
<td>PTID</td>
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</table>
Chain of Custody

Clinic Staff Responsibilities

- Control access to the VRs in clinic staff custody
- Clinic staff must document provision of the VR to the designated participant on the **Site-Specific Clinic Study Product Accountability Log**
Instructions: Complete one row for each ring provided to and returned from a participant (PTID). At the time of ring provision: record the PTID, Date Provided, Visit Code, and Staff Initials. Comments can be included, if necessary. When the same participant (PTID) returns the ring (or is expected to return the ring), complete the Date Returned, Visit Code, the appropriate Ring Status, and Staff Initials for that PTID. This information should also be recorded in the event of an off-site visit if the ring is collected. Recording the Ring Status: If a ring is returned and set aside for storage, check the box for that option and record the date that the ring was sent to the lab. If a ring is returned and set aside for destruction, check the box for that option and record the destruction bin #. If an unused ring was returned, check the box for that option and return the ring to the pharmacy on the same day. If a ring is not returned as expected, check the box for that option. Update the ring status, if the ring is returned. All entries must be made in dark ink. Corrections may be made by drawing a single line through incorrect entries, entering correct information, and initialing and dating the correction. Comments may be entered at any time.

<table>
<thead>
<tr>
<th>PTID</th>
<th>Date Provided (dd-MMM-yy)</th>
<th>Visit Code (#.#.#)</th>
<th>Staff Initials</th>
<th>Comments</th>
<th>Date Returned (dd-MMM-yy)</th>
<th>Visit Code (#.#.#)</th>
<th>Ring Status</th>
<th>Staff Initials</th>
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</tbody>
</table>

- Used ring for destruction: bin #________
- Used ring for testing: date to lab________
- Unused ring to pharmacy
- Ring not returned

- Used ring for destruction: bin #________
- Used ring for testing: date to lab________
- Unused ring to pharmacy
- Ring not returned

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- Unused ring to pharmacy
- Ring not returned
Chain of Custody

**Clinic Staff Responsibilities**

- If a VR dispensed for a participant is not provided to the participant, clinic staff must document this on the **Site-Specific Clinic Study Product Accountability Log** and return the **unused VR** to the **pharmacy** as soon as participant’s visit is completed.
Additional VR Dispensation

- A participant should not require more than one **100 mg OR 200 mg DPV VR** during study participation.

- Reasons for an additional 100 mg or 200 mg DPV VR dispensation at enrollment or a follow-up visit:
  - VR dropped on floor prior to insertion
    - No PSRT consultation required
  - VR removed or expelled during follow-up and cannot be reinserted
    - Provisions for the dispensation of additional VRs will be at the discretion of the IoR and in consultation with the PSRT as needed.
Participants receiving the **25 mg DPV VR** will receive a new VR approximately every 4-5 weeks for a total of 3 dispensations of the 25mg DPV VR per participant in this study product arm.

- Vaginal Ring Request Slip marked RE-SUPPLY
  - Visit 8
  - Visit 9
Additional VR Dispensation

- If an additional VR dispensation is necessary
  - Clinic staff will request a new VR from the pharmacy by completing MTN-036/IPM 047 Vaginal Ring Request Slip
  - Mark **VR dose** and **RE-SUPPLY** of one (1) VR
  - A supply of **Request Slips** is provided to the clinic staff by the MTN LOC Pharmacy via site PoR
  - A Request Slip is a 2 part no carbon required (NCR) paper document. The top white is the original (pharmacy) and the bottom is yellow (clinic).
**MTN-036/IPM 047 VAGINAL RING REQUEST SLIP**

**Instructions:** Mark whether this is a study vaginal ring re-supply, clinical hold, resume (after a clinical hold), participant decline, clinical permanent discontinuation, or product use period completion notification. Deliver the original white copy (labeled “Pharmacy”) to the pharmacy. File the yellow copy (labeled “Clinic”) in the participant’s study notebook.

**Participant ID:**

<table>
<thead>
<tr>
<th>CHECK ONE (for RE-SUPPLY and RESUME only):</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ 25mg dapivirine VR</td>
</tr>
<tr>
<td>□ 100mg dapivirine VR</td>
</tr>
<tr>
<td>□ 200mg dapivirine VR</td>
</tr>
</tbody>
</table>

| RE-SUPPLY ➔ Pharmacy: Dispense one (1) VR. |
| HOLD ➔ Reason: |
| Pharmacy: Do not dispense further VRs to the participant until another MTN-036/IPM 047 Vaginal Ring Request Slip marked “RESUME” is received. |

| RESUME ➔ Pharmacy: Dispense one (1) VR. Only an authorized prescriber can indicate RESUME. |
| PARTICIPANT DECLINE ➔ Pharmacy: Do not dispense at this visit – participant is refusing VR. |

| PERMANENT DISCONTINUATION ➔ Reason: |
| Pharmacy: Do not dispense any further VRs to the participant. |

| PRODUCT USE PERIOD COMPLETED ➔ Pharmacy: Do not dispense any further VRs to the participant. |

**Clinic Staff Name (please print):**

**Clinic Staff Signature:**

**Date:**

*dd MMM yy*
VR Request Slip Completion

- This slip can be completed by any authorized clinic staff except in the case of indicating “RESUME”
  - Only authorized prescribers to indicate “RESUME”
- Insert cardboard flap behind the clinic copy
- Double check the accuracy of all entries
- Errors may be corrected in blue or black ink by putting a line through and initialing
- Retain the yellow copy for the participant study notebook in the clinic
- Deliver white copy to pharmacy
- Once the white and yellow copies are separated errors must be corrected on each sheet separately
VR Request Slip – Other Actions

- **HOLD**
  - Used by clinic staff to communicate to pharmacist that the participant has a temporary VR hold due to a clinical/safety reason(s)
  - Record reason for hold
  - Pharmacy will not dispense any VRs until RESUME
VR Request Slip – Other Actions

- **RESUME**
  - Once a product hold is in effect, the pharmacist will not dispense any study product to that participant until a subsequent request slip is received and “RESUME” is marked on that request slip.
  - Mark VR dose and pharmacy will dispense one (1) VR.
  - Only an authorized prescriber indicated on the FDA 1572 form can initiate a VR resume.
VR Request Slip – Other Actions

☐ PARTICIPANT DECLINE

- If a participant decides that she does not want to use the VR, then the box for “PARTICIPANT DECLINE” is marked
- This is not a clinical hold and does not require a “RESUME’”
- When the participant wants to continue the product the clinic staff will complete a request slip for “RE-SUPPLY”
  - Mark VR dose and pharmacy will dispense one (1) VR
PERMANENT DISCONTINUATION

- If study clinician determines that a participant should permanently stop VR use, then the box for “PERMANENT DISCONTINUATION” is marked
- Indicate reason for permanent discontinuation
- Future VR requests slip will no longer be completed at the participant’s remaining study visits
VR Request Slip – Other Actions

- PRODUCT USE PERIOD COMPLETED
  - Used by clinic staff to communicate to the pharmacy when the participant has completed or withdrawn from the study
  - PUEV, Visit 10
Retrieval of VR

- Protocol Section 6.4.4
- SSP Section 7.5
- Document all efforts to retrieve VR
  - VR retrieval may occur by the participant returning the VR to study staff or attempts should be made by study staff to contact the participant to retrieve VR
Retrieval of VR

- VR must be retrieved within 5 working days of the PUEV/Early Termination Visit.
- If the VR is not retrieved within the timeframes stated, the MTN-036/IPM 047 PSRT must be informed.
- All attempts to retrieve study product should be documented.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Timeframe for Retrieval</th>
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<tbody>
<tr>
<td>Permanent discontinuation or temporary hold due to potential HIV infection or pregnancy</td>
<td>Within 24 hours</td>
</tr>
<tr>
<td>Permanent discontinuation for any other reason or IoR discretion</td>
<td>Within 5 working days</td>
</tr>
<tr>
<td>Temporary hold for reasons with expected duration of at least 7 days</td>
<td>Within 7 working days</td>
</tr>
</tbody>
</table>
USED Vaginal Ring Return/Destruction

- Follow your Site-Specific Clinic Study Product Accountability and Destruction SOP (non-pharmacy) for MTN-036/IPM 047
  - **Site-Specific** Clinic Study Product Accountability Log
  - Clinic Study Product Destruction Log
    - Expect this to be very rare
MTN-036/IPM 047 Site-Specific Clinic Study Product Accountability Log

<table>
<thead>
<tr>
<th>CRS Name</th>
<th>CRS ID</th>
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Instructions: Complete one row for each ring provided to and returned from a participant (PTID). At the time of ring provision: record the PTID, Date Provided, Visit Code, and Staff Initials. Comments can be included, if necessary. When the same participant (PTID) returns the ring (or is expected to return the ring), complete the Date Returned, Visit Code, the appropriate Ring Status, and Staff Initials for that PTID. This information should also be recorded in the event of an off-site visit if the ring is collected. Recording the Ring Status: If a ring is returned and set aside for storage, check the box for that option and record the date that the ring was sent to the lab. If a ring is returned and set aside for destruction, check the box for that option and record the destruction bin #. If an unused ring was returned, check the box for that option and return the ring to the pharmacy on the same day. If a ring is not returned as expected, check the box for that option. Update the ring status, if the ring is returned. All entries must be made in dark ink. Corrections may be made by drawing a single line through incorrect entries, entering correct information, and initialing and dating the correction. Comments may be entered at any time.

<table>
<thead>
<tr>
<th>PROVIDED</th>
<th>RETURNED</th>
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<tbody>
<tr>
<td>PTID</td>
<td>Date Provided (dd-MMM-yy)</td>
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</table>

- Used ring for destruction: bin #__________
- Used ring for testing: date to lab __________
- Unused ring to pharmacy
- Ring not returned

- Used ring for destruction: bin #__________
- Used ring for testing: date to lab __________
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- Used ring for testing: date to lab __________
- Unused ring to pharmacy
- Ring not returned

- Used ring for destruction: bin #__________
- Used ring for testing: date to lab __________
- Unused ring to pharmacy
- Ring not returned
### MTN-036/IPM 047 Clinic Study Product Destruction Log

<table>
<thead>
<tr>
<th>Name of Site:</th>
<th>DAIDS Site Number:</th>
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<tbody>
<tr>
<td>Protocol Title:</td>
<td>MTN-036/IPM 047: A Phase 1, Randomized Pharmacokinetics and Safety Study of Extended Duration Dapivirine Vaginal Rings</td>
</tr>
<tr>
<td>Site Investigator:</td>
<td>Phone Number:</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Destruction Container Code/Bin #</th>
<th>Date Sent for Destruction</th>
<th>Clinic Staff Initials</th>
<th>Date of Destruction</th>
<th>Clinic Staff Initials</th>
<th>Comments</th>
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**Unused Vaginal Ring Return**

- ONLY unused study product should be returned to the pharmacy
  - NO USED RINGS should be returned to the pharmacy
  - Used rings will be forwarded to lab or for destruction

- Unused VR is returned to the pharmacy by:
  - Clinic staff member, runner, or courier
  - Depends on pharmacy site-specific Chain of Custody SOP

- Documented on **Record of Return of Site-Specific Unused Vaginal Rings**
  - This record is stored in the pharmacy
Chain Of Custody

- If returning unused VR because damaged or contaminated, record the details on the record.

- The pharmacy will document and quarantine any returned unused VRs.
MTN-036/IPM 047 RECORD OF RETURN OF SITE-SPECIFIC UNUSED VAGINAL RINGS

<table>
<thead>
<tr>
<th>CLINIC STAFF/RUNNER/COURIER</th>
<th>PHARMACY STAFF</th>
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</thead>
<tbody>
<tr>
<td>Date Returned to Pharmacy (dd-MMM-yy)</td>
<td>PTID</td>
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Prohibited Medications

- Protocol Section 6.6
- PEP
- PrEP
- Anticoagulants or blood thinners
  - Heparin, Lovenox (enoxaparin), Coumadin (warfarin), Plavix (clopidogrel bisulfate)
- Aspirin (greater than 81mg) within 72 hours before and after cervical biopsy collection visits (Visits 8 and 10).
Vaginal & Rectal Meds, Products, and Practices

- Participants will be counseled to avoid the use of non-study vaginal and rectal products and other devices.

- Participants are asked to abstain from receptive vaginal and anal sexual activities for 72 hours prior to each clinic visit and to abstain from vaginal sexual activities for 72 hours after biopsy collection.

- Participants will be instructed to restrict tampon use for 24 hours prior to any clinic visit in which CVF samples are collected.
VR Complaints

- Study product problem may be noted by pharmacy, clinic, and/or participant.
  - May concern dosage form (VR), packaging (overwrap), or other aspect.

- Clinic staff will make thorough record of clinic staff or participant complaint.

- Clinic staff member will email complaint to site pharmacy
  - PTID, Date of observed issue, date issue was reported, date VR was dispensed, did adverse event occur, nature of issue, picture (if possible and applicable), any other necessary details
VR Complaints

- Site pharmacy staff will email all study product complaints to MTN LOC Pharmacy.
- MTN LOC Pharmacy will forward complaints to IPM to be submitted to the IPM Internal Complaint Process.
- If the complaint is concerning an unused VR, then the unused VR should be held in quarantine in the pharmacy.
- If the complaint is concerning a used VR, then the clinic staff should process/store the VR per SSP Section 10.
Contact Information

- If you have any questions, please do not hesitate to contact us:

  Cindy Jacobson  
  (412) 641-8913  
  cjacobson@upmc.edu

  Lindsay Kramzer  
  (412) 641-3865  
  fergusonlm@upmc.edu

Questions? Thank you!