MTN-036/IPM 047
Study Product Considerations

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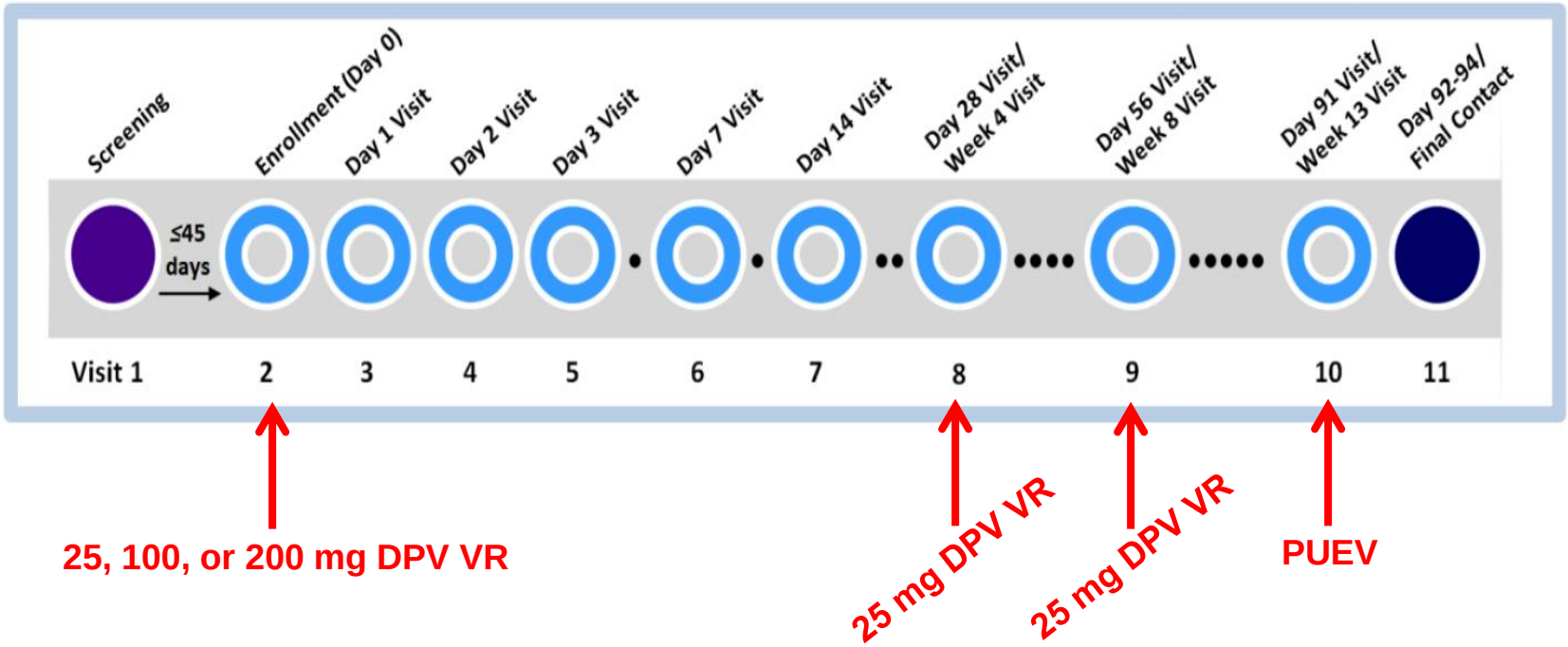
Presentation Overview

- 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

Study Visit Schedule & Regimen



- 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

MTN-036/IPM 047 PRESCRIPTION

Instructions: All entries must be made in dark ink. Press firmly when completing this form. Corrections may be made by drawing a single line through incorrect entries, recording correct information, and initialing and dating the correction.

CRS Name:		CRS ID:	
CRS Location:			

Participant ID: ☐☐☐ – ☐☐☐☐☐☐

Did the participant provide written informed consent for enrollment into MTN-036/IPM 047? YES ☐ NO ☐ Clinic Staff Initials: _____

CHECK ONE:

☐ **25mg dapivirine VR** ☐ **100mg dapivirine VR** ☐ **200mg dapivirine VR**

Sig: Insert one ring into the vagina.

Quantity: One vaginal ring. May be refilled as needed per request by designated clinic staff on MTN-036/IPM 047 Vaginal Ring Request Slip for duration of participation in the study.

Authorized Prescriber Name *(please print)*: _____

Authorized Prescriber Signature: _____

Date: ☐☐ ☐☐☐ ☐☐
dd *MMM* *yy*

Clinic Staff Instructions: Complete all items on this prescription. After initialing and dating below, deliver original white copy (labeled "Pharmacy") to pharmacy. File yellow copy (labeled "Clinic") in participant study notebook.

Clinic Staff Initials: _____ Date: ☐☐ – ☐☐☐ – ☐☐
dd *MMM* *yy*

One prescription for each participant for the entire study

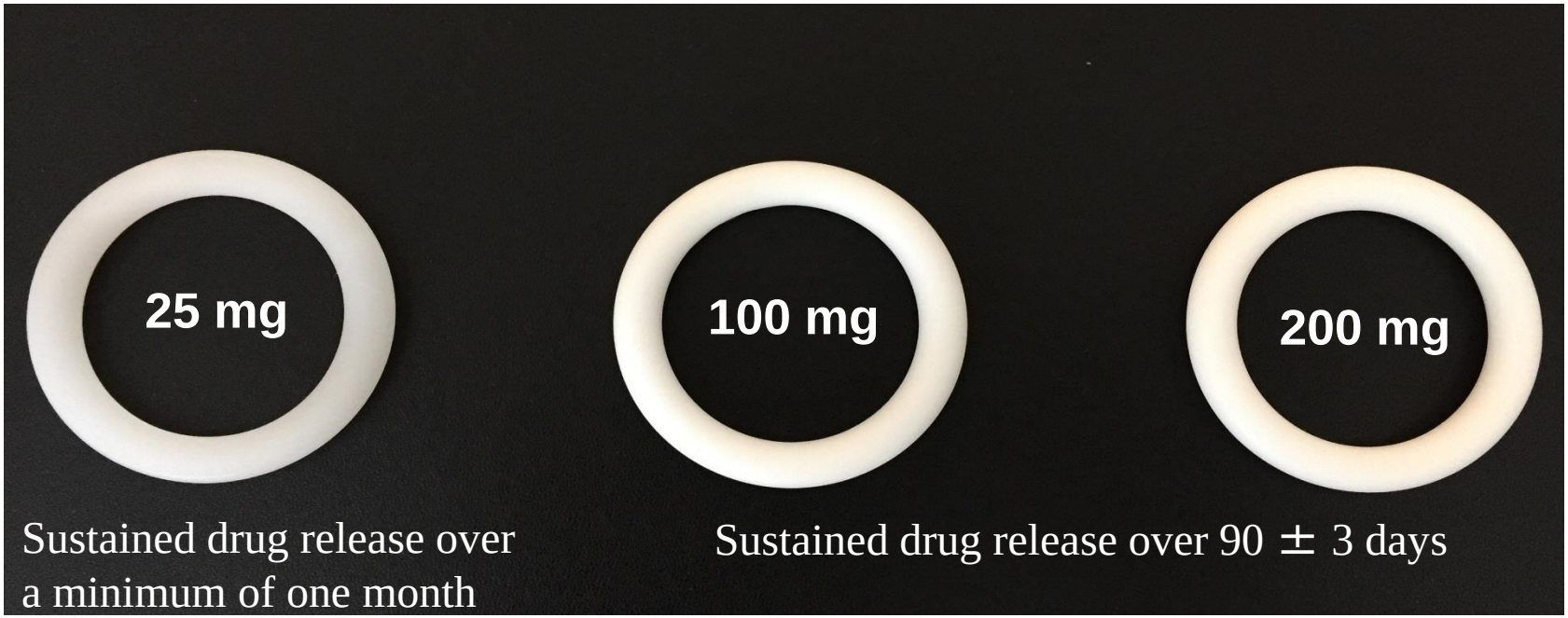
MTN-036/IPM 047 Prescription

- 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

MTN-036/IPM 047 Prescription

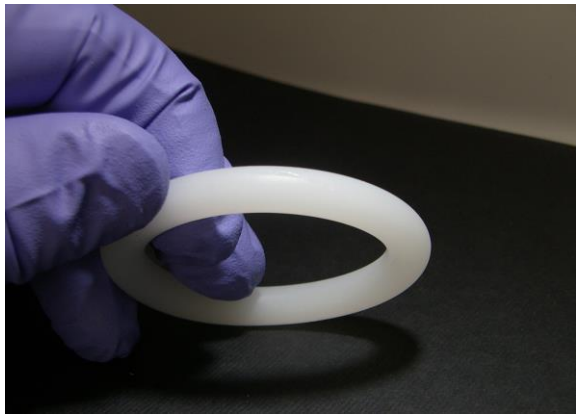
- The pharmacist will review the prescription.
  - Compare to VR indicated on Pharmacy Dispensation CRF
- If an error is noted, the white and yellow copies must be individually corrected by an authorized prescriber with identical information on both copies (correction, initials, date).
- If no problems are noted, the pharmacist will dispense the vaginal ring (VR).

Dapivirine Vaginal Rings

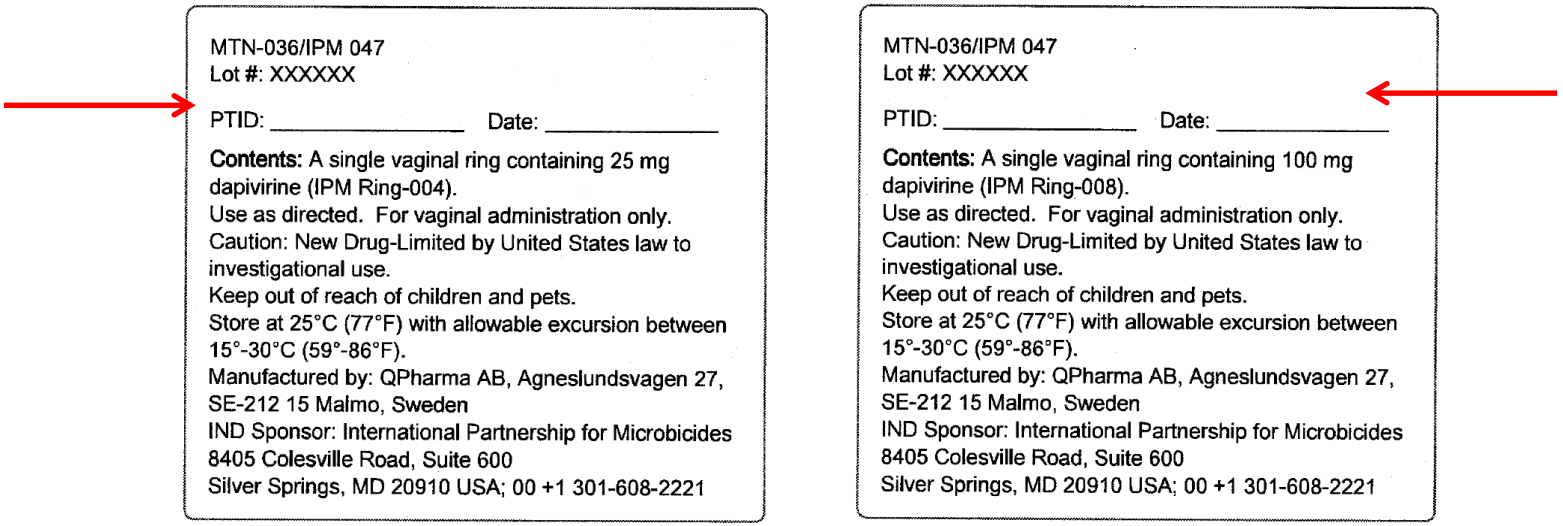


Dapivirine Vaginal Rings

- 56 mm outer diameter and 7.7 mm cross-sectional diameter
- Storage: 20^{o}C-25^{o}C, with allowable excursions between 15^{o}C-30^{o}C



MTN-036/IPM 047 **VR Pouch Label**



MTN-036/IPM 047
Lot #: XXXXXX

PTID: _____ Date: _____

Contents: A single vaginal ring containing 25 mg dapivirine (IPM Ring-004).
Use as directed. For vaginal administration only.
Caution: New Drug-Limited by United States law to investigational use.
Keep out of reach of children and pets.
Store at 25°C (77°F) with allowable excursion between 15°-30°C (59°-86°F).
Manufactured by: QPharma AB, Agneslundsvagen 27, SE-212 15 Malmo, Sweden
IND Sponsor: International Partnership for Microbicides
8405 Colesville Road, Suite 600
Silver Springs, MD 20910 USA; 00 +1 301-608-2221

MTN-036/IPM 047
Lot #: XXXXXX

PTID: _____ Date: _____

Contents: A single vaginal ring containing 100 mg dapivirine (IPM Ring-008).
Use as directed. For vaginal administration only.
Caution: New Drug-Limited by United States law to investigational use.
Keep out of reach of children and pets.
Store at 25°C (77°F) with allowable excursion between 15°-30°C (59°-86°F).
Manufactured by: QPharma AB, Agneslundsvagen 27, SE-212 15 Malmo, Sweden
IND Sponsor: International Partnership for Microbicides
8405 Colesville Road, Suite 600
Silver Springs, MD 20910 USA; 00 +1 301-608-2221

MTN-036/IPM 047
Lot #: XXXXXX

PTID: _____ Date: _____

Contents: A single vaginal ring containing 200 mg dapivirine (IPM Ring-006).
Use as directed. For vaginal administration only.
Caution: New Drug-Limited by United States law to investigational use.
Keep out of reach of children and pets.
Store at 25°C (77°F) with allowable excursion between 15°-30°C (59°-86°F).
Manufactured by: QPharma AB, Agneslundsvagen 27, SE-212 15 Malmo, Sweden
IND Sponsor: International Partnership for Microbicides
8405 Colesville Road, Suite 600
Silver Springs, MD 20910 USA; 00 +1 301-608-2221

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 →

MTN-036/IPM 047 FOR USED RING ONLY

Date Dispensed:_____ PTID #: _____

Contents: 1 used vaginal ring containing up to 200 mg Dapivirine.

Keep out of reach of children and pets
For clinical trial use only
IND Sponsor: International Partnership for Microbicides, Silver Spring, MD USA.
Phone: 00 + 1 301-608-2221

Emergency Contact Name:
_____

Phone Number:
_____

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

CRS Name:	CRS ID:

PHARMACY STAFF					CLINIC STAFF/RUNNER/COURIER		
Date/Time dispensed from pharmacy dd-MMM-yy (hh:mm) 24 hr clock	PTID	No. of VRs Dispensed	25 mg, 100 mg or 200 mg VR	Pharmacist Initials	Date/Time received from pharmacy dd-MMM-yy (hh:mm) 24 hr clock	Clinic Staff/ Runner/Courier Initials	Comments

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

MTN-036/IPM 047 Site-Specific Clinic Study Product Accountability Log

CRS Name		CRS ID	

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.

	PROVIDED				RETURNED			
PTID	Date Provided (dd-MMM-yy)	Visit Code (##.#)	Staff Initials	Comments	Date Returned (dd-MMM-yy)	Visit Code (##.#)	Ring Status	Staff Initials
							☐ 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	
							☐ 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	
							☐ Used ring for destruction: bin # ________ ☐ Used ring for testing: date to lab________ ☐ 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.

Additional VR Dispensation

- 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: ☐☐☐–☐☐☐☐☐☐

CHECK ONE (for RE-SUPPLY and RESUME only):

☐ **25mg dapivirine VR** ☐ **100mg dapivirine VR** ☐ **200mg dapivirine VR**

☐ **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

VR Request Slip – Other Actions

- **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

Condition	Timeframe for Retrieval
Permanent discontinuation or temporary hold due to potential HIV infection or pregnancy	Within 24 hours
Permanent discontinuation for any other reason or IoR discretion	Within 5 working days
Temporary hold for reasons with expected duration of at least 7 days	Within 7 working days

- 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.

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

CRS Name		CRS ID	

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	PROVIDED				RETURNED			
PTID	Date Provided (dd-MMM-yy)	Visit Code (##.#)	Staff Initials	Comments	Date Returned (dd-MMM-yy)	Visit Code (##.#)	Ring Status	Staff Initials
							☐ 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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							☐ 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	

MTN-036/IPM 047 Clinic Study Product Destruction Log

Name of Site:		DAIDS Site Number:	
Protocol Title:	MTN-036/IPM 047: A Phase 1, Randomized Pharmacokinetics and Safety Study of Extended Duration Dapivirine Vaginal Rings		
Site Investigator:		Phone Number:	

Destruction Container Code/Bin #	Date Sent for Destruction	Clinic Staff Initials	Date of Destruction	Clinic Staff Initials	Comments

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

CRS Name:	CRS ID:

CLINIC STAFF/RUNNER/COURIER					PHARMACY STAFF				
Date Returned to Pharmacy (dd-MMM-yy)	PTID	No. of Unused VRs Returned	25 mg, 100 mg or 200 mg VR	Clinic Staff/ Runner/ Courier Initials	Date Received by Pharmacy (dd-MMM-yy)	PTID (verify)	Reason for Return	RPh Initials	QA against Destruction Form Pharmacy Staff Initials

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
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cjacobson@upmc.edu

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Questions?

Thank you!