

**MTN-038**

**Clinic Study Product  
Considerations**

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# Presentation Overview

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

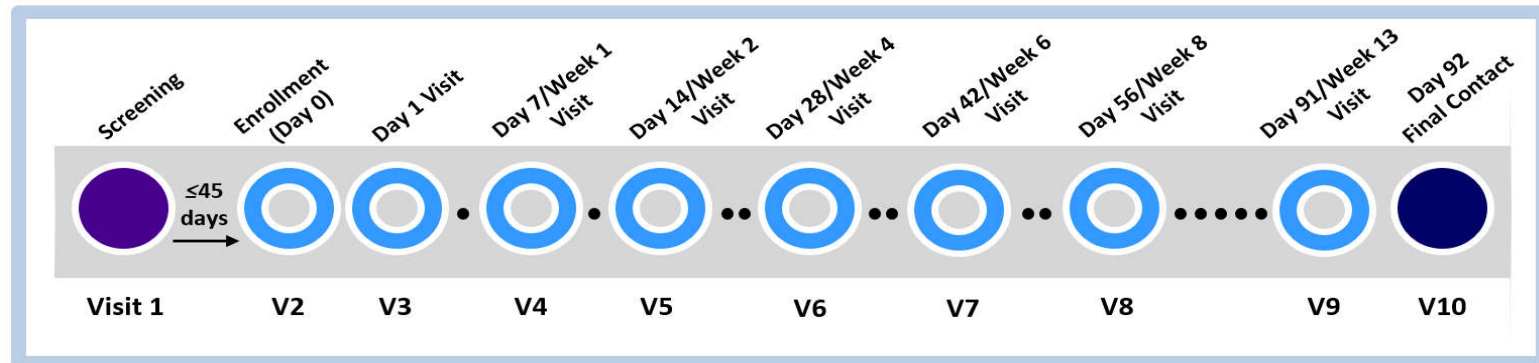


# Reference Materials

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- MTN-038 Protocol, Version 1.0
  - Section 6
- MTN-038 SSP Manual
  - Section 7
- Site-Specific Clinic Study Product Accountability and Destruction SOP (non-pharmacy) for MTN-038

# Study Visit Schedule & Regimen



**Provision of IVR**

**PUEV**

- Participant will self-insert an IVR containing 1.4 g TFV or matching placebo IVR at Visit 2/Day 0: Enrollment. IoR/authorized clinician, if necessary.
- The IVR is inserted once and worn continuously for approximately 91 days.
- The IVR will be removed by the participant (or clinician/designee, if necessary) at the product use end visit (PUEV/Early Termination Visit). Participants will be followed for approximately 1 day following final IVR removal.



# Visit 2/Day 0: Enrollment

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- 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

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- 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-038 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. Deliver original white copy (labeled "Pharmacy") to pharmacy. File yellow copy (labeled "Clinic") in participant study notebook.



CRS Name:		CRS ID:		CRS Location:	
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Participant ID:  -



Did the participant provide written informed consent for enrollment into MTN-038?	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Clinic Staff Initials: _____
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Check one:  1.4 g tenofovir IVR  placebo IVR

**Sig:** Insert one (1) ring into the vagina.

**Quantity:** One vaginal ring. May be refilled as needed per request by designated clinic staff on MTN-038 Vaginal Ring Request Slip for duration of participation in the study.



Authorized Prescriber Name (*please print*): \_\_\_\_\_

Authorized Prescriber Signature: \_\_\_\_\_

Date:  -  -   
*dd MMM yy*



# MTN-038 Prescription

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- 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





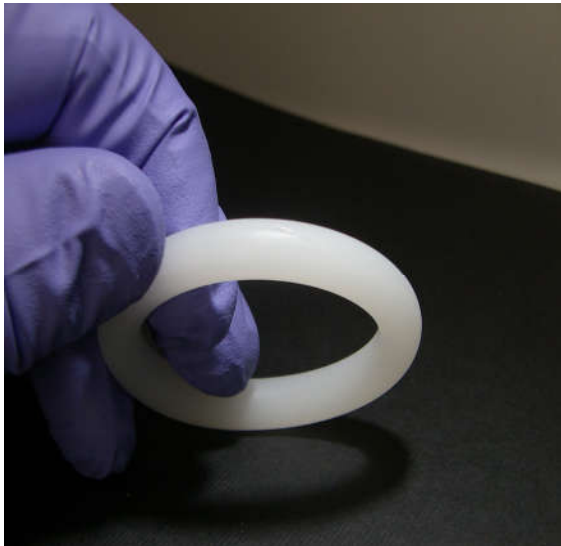
# MTN-038 Prescription

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- The pharmacist will review the prescription.
  - Compare to IVR 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 (IVR).

## □ Dapivirine Ring

- 56 mm outer diameter and 7.7 mm cross-sectional diameter
- The IVR is an off-white, flexible ring containing 25 mg of dispersed in a platinum-catalyzed-cured silicone matrix.
- Dapivirine 25 mg ring is designed to release approximately 4 mg over 30 days



## □ Tenofovir Ring

- 55 mm outer diameter and 5.5 mm cross-sectional diameter
- TFV IVR is comprised of a drug-loaded hydrophilic polyether urethane (HPU) tube (white segment) that is sealed and joined together (transparent joint) to form the shape of a ring
- Designed to release about 10mg per day for 90 days



# MTN-038 IVR Pouch Label

MTN-038 Expiry Date: DDMMYYYY  
Lot #: XXXXXXXXXXXX

PTID: \_\_\_\_\_ Date: \_\_\_\_\_

Contents: A single placebo vaginal ring.  
Use as Directed. For vaginal administration only.  
Keep out of reach of children and pets.  
CAUTION: New Drug- Limited by Federal (or United States) law to investigational use.  
Store at 25°C (77°F) with allowable excursion between 15°-30°C (59°-86°F).  
Sponsor:  
Division of AIDS/NIAID/NIH/DHHS, 5601 Fishers Lane,  
Bethesda, MD 20892-9829, (240) 292-4939

MTN-038 Expiry Date: DDMMYYYY  
Lot #: XXXXXXXXXXXX

PTID: \_\_\_\_\_ Date: \_\_\_\_\_

Contents: A single 1.4 g tenofovir vaginal ring.  
Use as Directed. For vaginal administration only.  
Keep out of reach of children and pets.  
CAUTION: New Drug- Limited by Federal (or United States) law to investigational use.  
Store at 25°C (77°F) with allowable excursion between 15°-30°C (59°-86°F).  
Sponsor:  
Division of AIDS/NIAID/NIH/DHHS, 5601 Fishers Lane,  
Bethesda, MD 20892-9829, (240) 292-4939

PoR to indicate

# MTN-038 Returned Used IVR Label (on white bag)

MTN-038 FOR USED RING ONLY

PoR to indicate →

Date Dispensed: \_\_\_\_\_ PTID #: \_\_\_\_\_

Contents: 1 used vaginal ring containing up to 1.4 g tenofovir.

Keep out of reach of children and pets.

Refer to participant instructions for bag use.

CAUTION: New Drug- Limited by Federal (or United States) law to investigational use.

Sponsor:

Division of AIDS/NIAID/NIH/DHHS, 5601 Fishers Lane,  
Bethesda, MD 20892-9829, (240) 292-4939


Emergency Contact Name:

Clinic Staff to indicate →

\_\_\_\_\_

Phone Number:

\_\_\_\_\_



# Chain Of Custody

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- The IVR 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 IVR.**

## MTN-038 RECORD OF RETURN OF SITE-SPECIFIC UNUSED INTRAVAGINAL RINGS

CRS Name:	CRS ID:
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CLINIC STAFF/RUNNER/COURIER					PHARMACY STAFF				
Date Returned to Pharmacy (dd-MMM-yy)	PTID	No. of Unused IVRs Returned	1.4 g tenofovir or placebo	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

Instructions: Complete one row each time an unused IVR is returned by the participant to non-pharmacy staff for subsequent return to the site pharmacy. 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.

Version \_\_\_\_\_ Page \_\_\_ of \_\_\_\_



# Chain of Custody

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## Clinic Staff Responsibilities

- Control access to the IVRs in clinic staff custody
- Clinic staff must document provision of the IVR to the designated participant on the **Site-Specific Clinic Study Product Accountability Log**

### MTN-038 Site-Specific Clinic Study Product Accountability Log

CRS Name		CRS ID	
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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, 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 for residual drug testing, 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 unused 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
							<input type="checkbox"/> Used ring for testing: date to lab _____ <input type="checkbox"/> Used ring for destruction: bin # _____ <input type="checkbox"/> Unused ring to pharmacy <input type="checkbox"/> Ring not returned	
							<input type="checkbox"/> Used ring for testing: date to lab _____ <input type="checkbox"/> Used ring for destruction: bin # _____ <input type="checkbox"/> Unused ring to pharmacy <input type="checkbox"/> Ring not returned	
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							<input type="checkbox"/> Used ring for testing: date to lab _____ <input type="checkbox"/> Used ring for destruction: bin # _____ <input type="checkbox"/> Unused ring to pharmacy <input type="checkbox"/> Ring not returned	





# Chain of Custody

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## Clinic Staff Responsibilities

- If a IVR 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 IVR** to the **pharmacy** as soon as participant's visit is completed.

# Additional IVR Dispensation

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- A participant should not require more than one IVR during study participation
- Reasons for an additional IVR dispensation at enrollment or a follow-up visit
  - IVR dropped on floor prior to insertion
    - No PSRT consultation required
  - IVR removed or expelled during follow-up and cannot be reinserted
    - Provisions for the dispensation of additional IVRs will be at the discretion of the IoR and in consultation with the PSRT as needed.

## Slide 18

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**RS12**

Highlight is in line with current SSP 7.3 guidance, so will just need to update if that changes during the review process. Looks ok for now.

Rachel Scheckter, 8/29/2018



# Additional IVR Dispensation

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- If an additional IVR dispensation is necessary
  - Clinic staff will request a new IVR from the pharmacy by completing **MTN-038 Vaginal Ring Request Slip**
    - Mark IVR dose and RE-SUPPLY of one (1) IVR
  - 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-038 INTRAVAGINAL RING REQUEST SLIP

Participant ID:  -

**Instructions:** Mark whether this is a study IVR 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.

<input type="checkbox"/> <b>REQUESTED IVR:</b> (if indicated)	<input type="checkbox"/> 1.4 g tenofovir IVR	<input type="checkbox"/> placebo IVR
<input type="checkbox"/> <b>RE-SUPPLY</b>	→ Pharmacy: Dispense one (1) vaginal ring. Check requested IVR box above.	
<input type="checkbox"/> <b>HOLD</b>	→ Reason: _____  Pharmacy: Do not dispense further vaginal rings to the participant until another MTN-038 Intravaginal Ring Request Slip marked "RESUME" is received.	
<input type="checkbox"/> <b>RESUME</b>	→ Pharmacy: Dispense one (1) IVR. Only an authorized prescriber can indicate RESUME. Check requested IVR box above.	
<input type="checkbox"/> <b>PARTICIPANT DECLINE</b>	→ Pharmacy: Do not dispense at this visit - participant is refusing IVR.	
<input type="checkbox"/> <b>PERMANENT DISCONTINUATION</b>	→ Reason: _____  Pharmacy: Do not dispense any further IVRs to the participant.	
<input type="checkbox"/> <b>PRODUCT USE PERIOD COMPLETE</b>	→ Pharmacy: Do not dispense any further IVRs to the participant.	

Clinic Staff Name (please print): \_\_\_\_\_

Clinic Staff Signature: \_\_\_\_\_

Date:  -  -   
*dd MMM yy*



# IVR Request Slip Completion

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- 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



# IVR Request Slip – Other Actions

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## □ HOLD

- Used by clinic staff to communicate to pharmacist that the participant has a temporary IVR hold due to a clinical/safety reason(s)
- Record reason for hold
- Pharmacy will not dispense any IVRs until RESUME



# IVR Request Slip – Other Actions

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## □ 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 IVR dose and pharmacy will dispense one (1) IVR
- Only an authorized prescriber indicated on the FDA 1572 form can initiate a IVR resume





# IVR Request Slip – Other Actions

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## □ PARTICIPANT DECLINE

- If a participant decides that she does not want to use the IVR, 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 IVR dose and pharmacy will dispense one (1) IVR



# IVR Request Slip – Other Actions

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



# IVR Request Slip – Other Actions

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- **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 9)



# Retrieval of IVR

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

# Retrieval of IVR

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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

- IVR must be retrieved within 5 working days of the PUEV/Early Termination Visit.
- If the IVR is not retrieved within the timeframes stated, the MTN-038 PSRT must be informed.
- All attempts to retrieve study product should be documented.



# USED Vaginal Ring Return/Destruction

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- Follow your Site-Specific Clinic Study Product Accountability and Destruction SOP (non-pharmacy) for MTN-038
  - **Site-Specific Clinic Study Product Accountability Log**
  - Clinic Study Product Destruction Log
    - Expect this to be very rare

## MTN-038 Site-Specific Clinic Study Product Accountability Log

<b>CRS Name</b>	<b>CRS ID</b>
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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, 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 for residual drug testing, 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 unused 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
							<input type="checkbox"/> Used ring for testing: date to lab _____ <input type="checkbox"/> Used ring for destruction: bin # _____ <input type="checkbox"/> Unused ring to pharmacy <input type="checkbox"/> Ring not returned	
							<input type="checkbox"/> Used ring for testing: date to lab _____ <input type="checkbox"/> Used ring for destruction: bin # _____ <input type="checkbox"/> Unused ring to pharmacy <input type="checkbox"/> Ring not returned	
							<input type="checkbox"/> Used ring for testing: date to lab _____ <input type="checkbox"/> Used ring for destruction: bin # _____ <input type="checkbox"/> Unused ring to pharmacy <input type="checkbox"/> Ring not returned	
							<input type="checkbox"/> Used ring for testing: date to lab _____ <input type="checkbox"/> Used ring for destruction: bin # _____ <input type="checkbox"/> Unused ring to pharmacy <input type="checkbox"/> Ring not returned	








# Unused Vaginal Ring Return

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- 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 IVR 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

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- If returning unused IVR because damaged or contaminated, record the details on the record
- The pharmacy will document and quarantine any returned unused IVRs

## MTN-038 RECORD OF RETURN OF SITE-SPECIFIC UNUSED INTRAVAGINAL RINGS

<b>CRS Name:</b>	<b>CRS ID:</b>
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CLINIC STAFF/RUNNER/COURIER					PHARMACY STAFF				
Date Returned to Pharmacy (dd-MMM-yy)	PTID	No. of Unused IVRs Returned	1.4 g tenofovir or placebo	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

Instructions: Complete one row each time an unused IVR is returned by the participant to non-pharmacy staff for subsequent return to the site pharmacy. 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.



# Prohibited Medications

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- 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 5 and 8 or 6 and 9).



# IVR Complaints

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- Study product problem may be noted by pharmacy, clinic, and/or participant.
  - May concern dosage form (IVR), 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 IVR was dispensed, did adverse event occur, nature of issue, picture (if possible and applicable), any other necessary details



# IVR Complaints

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- 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 IVR, then the unused IVR should be held in quarantine in the pharmacy.
- If the complaint is concerning a used IVR, then the clinic staff should process/store the IVR per SSP Section 10.



# Contact Information

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- 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!***