MTN Regional Meeting

Pharmacy Break-out Session

October 30, 2013

Day 2

Wednesday October 3rd

12:30 PM to 1:30 PM	**LUNCH (Restaurant Thirty7)**			
1:30 PM to 2:00 PM	**Welcome and Objectives**			
2:00 PM to 2:30 PM	**Product complaint**		Cindy Jacobson	
2:30 PM to 3:00 PM	Used Rings to Lab		Group Discussion	
3:00 PM to 3:30 PM	**BREAK (Old Harbour Lobby)**			
3:30 PM to 4:00 PM	**Dispensing >1 ring** Protocol Deviations		**Group discussion**	
4:00 PM to 4:30 PM	Off-Site visits		**Cindy Jacobson** **Site Presentation**	
4:30 PM to 5:00 PM	Wrap-up		Cindy Jacobson	
5 : 0 0 P M	**Meeting adjourned**			

Product Complaint

- Any written or oral communication that questions the safety, efficacy, identity, quality, durability, reliability or performance of a Clinical Trial Material. Complaints may come from any source (e.g., telephone contact, letter, conversation, e-mail, report from a Clinical Monitor, etc.).

Product Complaint Process

- Report to MTN pharmacist
- Provide detailed summary of the concern
- Include the IoR name, PTID and sub-lot code
- Whenever possible, save the ring associated with the issue

IPM Responsibility

- The information provided to the MTN pharmacist is forwarded to the IPM QA manager
- A Complaint Form is completed and complaint number assigned and logged
- Inform appropriate area of the complaint (i.e. Penn, QPharma)
- Investigation when appropriate and documentation compiled in written report

IPM Responsibility

- IPM will provide the MTN pharmacist a final response to complete the file/investigation
- MTN pharmacist will provide findings to the PoR
- IPM will monitor frequency of complaints and report trends

Product Complaint Summary

Product Complaint Number	Date Received	Site	Investigator	Complaint	Date Closed		
PC12002	07-Nov-12	Isipingo Site	Gita Ramjee	1 open ring received	10-Dec-12		
PC13002	19-Feb-13	Zengeza Clinic	Nyradzo Mgodi	Irregular Ring (bump)	13-Mar-13		
PC13003	08-Mar-13	Spilhaus	Zvavahera Chirenje	Irregular Ring (bump)	13-Mar-13		
PC13004	18-Mar-13	Spilhaus	Zvavahera Chirenje	Irregular Ring (bump)	6-May-13		
PC13005	18-Mar-13	Spilhaus	Zvavahera Chirenje	Irregular Ring (bump)	3-May-13		
PC13006	16-Apr-13	Zengeza Clinic	Nyradzo Mgodi	Irregular Ring (bump)	7-May-13		
PC13007	22-Apr-13	Spilhaus	Zvavahera Chirenje	Irregular Ring (bump)	7-May-13		
PC13008	13-Aug-13	Zengeza Clinic	Nyaradzo Mavis Mgodi	Discoloration of vaginal ring (partial yellow) post use	open		

New Used Ring Process

- Note that with the transition from biofilm to residual drug testing, sites should collect all used rings for laboratory storage and testing.
- Only in the rare event that a used ring needs to be destroyed (instead of saved), would the final status of ‘destruction’ be marked on the Accountability Log.

New Used Ring Process

- Sites will be provided an SOP template (see MTN website) which should be modified to reflect the specific study product accountability processes at the site.

Dispensing > 1 ring

- See SSP section 9.4
- IoRs may authorize dispensation of one additional vaginal ring (two vaginal rings total) if the participant is unable to attend her next scheduled visit or her next scheduled visit is more than 35 days from ring insertion.

Dispensing > 1 ring

- If IoR is not a physician, decisions to dispense more than one vaginal ring must be made in consultation with the medical officer delegated responsibility for medical oversight of study participants.
- Consider reason:

  Travel away from site for work or family

Things to consider

- Can she be contacted while away
- Storage
- Product use history
- Reproductive history (reliable contraception)

Dispensing >2 rings

- If the participant is unable to attend two consecutive visits, two additional rings are required
- Approval must be obtained from the DAIDS Medical Officer
- Communication via email (copy in ppt binder) or telephone (IoR puts written summary in ppt binder within 1 bus. day

Dispensing > 2 rings

- Can be dispensed at time of call prior to documentation complete
- Must be followed up by written documentation
- The IoR or designee should put a note on the MTN-020 Study Product Request Slip documenting date and time of MO approval

Protocol Deviations Summary

- There have been 2 dispensing error PDs to date-

1. A ring was prepared for dispensing for a participant with a permanent discontinuation.

Error was realized when completing the Record of Receipts form.

- The ring never left the pharmacy
- A PD form was completed

Protocol Deviations Summary

2. The second deviation involved the wrong ring (sub-lot) pulled from the shelf and dispensed.

- The incorrect ring was worn by the participant for about a day
- She retuned to the clinic and the correct ring was given
- The error was realized doing a stock check

Protocol Deviations

- Form revised November 2012
- New numbering
- 02 and 04 refer to error by pharmacy staff
- 02 failure to follow trial randomization or blinding procedures: Includes instances where randomization procedures were not followed by site staff, or product blinding procedures were not followed by pharmacy staff.

Protocol Deviations

- 04 study product dispensing error: The wrong study product was dispensed to a participant, or study product was dispensed to a participant on product hold. Do not include any information related to study product assignment (product codes) on this form. Pharmacy staff must follow-up with MTN pharmacist separately.

MTN-024/IPM 031 (203) PDL-1 (495)

Page

Participant ID

Site Number – Participant Number – Chk

Protocol Deviation Log

Form Completion Date

dd MMM yy

1. Site awareness date:	dd MMM yy
2. Deviation date:	dd MMM yy
3. Has or will this deviation be reported to local IRB/EC?	yes ☐ no ☐
4. Has or will this deviation be reported to DAIDS as a critical event?	yes ☐ no ☐
5. Type of deviation:	☐☐ *deviation code (See back of form for code listing.)*
6. Description of deviation:	
7. Plans and/or action taken to address the deviation:	
8. Plans and/or action taken to prevent future occurrences of the deviation:	
9. Deviation reported by:	☐☐☐☐ *staff code*

Protocol Deviation Log (PDL-1)

Purpose: This form documents and reports protocol deviations identified for study participants.

General Information/Instructions:

Complete this form each time a protocol deviation is identified. Consult the MTN Regulatory Team (mtnregulatory@mtnstopshiv.org) and the Study Management Team if you are unsure if an event requires reporting as a deviation.

Item-specific Instructions:

Page: Number pages sequentially for each participant, starting with 01. Do not re-assign page numbers if a form is marked for deletion.

Item 2: Record the date the event occurred (start date).

Item 5: Record the two-digit category code that best describes the type of deviation. Use "99" (other) if none of the listed categories match. Describe the specifics of the deviation in item 6.

Item 6: Briefly describe the specific details of the deviation.

Item 9: Record staff code of the site staff person who completed the form. Sites will need to assign a four-digit staff code to each site staff person who will be completing this form. This list is created, maintained, and kept at the study site.

Code	Description
01	**Inappropriate enrollment:** The participant enrolled and not all eligibility requirements were met.
02	**Failure to follow trial randomization or blinding procedures:** Include instances where randomization procedures were not followed by site staff, or product blinding procedures were not followed by pharmacy staff.
03	**Study product management deviation:** Site staff did not instruct the participant to hold, permanently discontinue, or resume study product use per protocol requirements.
04	**Study product dispensing error:** The wrong study product was dispensed to a participant, or study product was dispensed to a participant on product hold. Do not include any information related to study product assignment (product codes) on this form. Pharmacy staff must follow up with the MTN Pharmacist separately.
05	**Study product non-use deviation:** Participant did not use the study product (including refusals) or used it incorrectly (i.e., not in accordance with protocol requirements).
06	**Study product sharing:** Participant has shared study product with another person or study participant.
07	**Study product not returned:** Study product was not returned by the participant per protocol requirements.
08	**Conduct of non-protocol procedure:** A clinical or administrative procedure was performed that was not specified in the protocol, and was not covered under local standard of care practice.
09	**Improper AE/EAE follow-up:** Use when an AE or EAE is not followed per protocol. For example, a clinical finding/lab result is not re-assessed as outlined in the protocol.
10	**Unreported AE:** Site staff become aware of an AE, but do not report it per protocol requirements.
11	**Unreported EAE:** Site staff become aware of an EAE, but do not report it per protocol and DAIDS EAE Manual requirements.
12	**Breach of confidentiality:** Include potential and actual cases where participant confidentiality is breached. For example, a staff member puts a participant's name on a case report form.

Code	Description
14	**Lab assessment deviation:** Include missed, or incomplete lab specimen collection.
15	**Mishandled lab specimen:** Include errors in the labeling, physical handling, processing, testing, storage, or shipment of collected lab specimens.
16	**Staff performing duties that they are not qualified to perform:** Use for any instance when any study procedure, including clinical and administrative procedures, is completed by a staff member who is not adequately qualified AND delegated to perform the procedure.
17	**Questionnaire administration deviation:** A required questionnaire was not completed according to protocol requirements. Include instances where the wrong questionnaire was completed.
18	**Counseling deviation:** Protocol-required counseling was not done and/or not documented correctly.
19	**Use of non-IRB/EC-approved materials:** Include use of ANY study-related material that requires IRB or EC approval for use per site requirements.
20	**Use of excluded concomitant medications, devices or non-study products**
21	**Informed consent process deviation:** Examples include failure to accurately execute and/or document any part of the informed consent process.
22	**Visit completed outside of window:** Use when visit procedures for a visit are done within the wrong window or not in a designated visit window. For example, use if Visit 3.0 procedures are done in the Visit 4.0 window.
99	**Other**

Pharmacy – Study Product Accountability

- All study VRs received from Penn Pharma, dispensed, or transferred will also be appropriately logged into the Study Accountability Record (see Appendix III). Each sub-lot requires an Accountability Record.
  - Study VRs on hand should match what is recorded on the Study Accountability Record at all times.

Pharmacy – Study Product Accountability

- The PoR or back-up pharmacist will perform accountability audits at the time of study product dispensing.
- If the actual inventory differs from the recorded inventory on the Study Accountability Record, the discrepancy and the reason for discrepancy should be documented on the Study Accountability Record. The discrepancy should also be reported to CORE Pharmacist (MTN).

- Inventory audit for all product should be completed and documented every 30-31 days

ASPIRE STUDY ACCOUNTABILITY RECORD

PRODUCT SUBLOT CODE: _ _ _ BIN CODE:____

MTN-020 ASPIRE PRODUCT ACCOUNTABILITY RECORD
Dapivirine 25mg or Placebo Vaginal Ring

SITE NAME: _____ INVESTIGATOR: _____

No.	Date	Participant ID (PTID)	Randomization Number	Quantity Dispensed(-) or Received(+)*	Balance Forward	Dispensed Or Received* by (RPh) initial	Comments
1.							

*Received from Penn Pharma.

ASPIRE Off-Site Visits

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A Study to Prevent Infection with a Ring for Extended Use

Off Site Visits

- SSP section 6.4.3 Off-site Visit Procedures (overall guidance)
- SSP section 9.10 Study Product Considerations for Off-Site Visits
- Purpose of retention/tracing or collect product
- Will these be conducted by your site?
- Sites need IRB approval and an SOP

Rationale

- *Why make an allowance for off-site visits in the protocol?*

Extended Clinic Hours

Improving Clinic Flow

Counseling

Off-site visits

Tracking Tools

Outreach

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When to Utilize?

- Generally expected that scheduled study visits will be conducted at the study clinic
- Off-site visits are a tool to be used when needed, should not be the standard
- IoR/designee discretion

What situations do you think would warrant?

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Permitted Locations & Visit Types

- Participant Home or other venues
  - Participant and staff both comfortable
  - Safety and confidentiality can be maintained

- All follow-up Visit Types
  - Monthly, Quarterly, Semi-Annual, PUEV/Term
  - Interim Visits

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Minimum Procedures for VR dispensation:

- **AE assessment and reporting** (verbal report of symptoms is acceptable; if symptoms indicate that further evaluation is necessary, this must be conducted prior to dispensing study product)
- **HIV testing and counseling** (including RR counseling) and **pregnancy testing** are required for product dispensation if this has not been done at the research clinic within the past 60 days (i.e. within last 2 scheduled visits)
- Collection of Used Ring (and unused, if applicable), if available
- Adherence Counseling/Product Use Instructions, as needed

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General Considerations

- Verifying Consent
- Safety/Confidentiality
- Staffing
- Managing symptoms/conditions requiring medical attention
- Materials/Supplies Required

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Study Product Considerations

- Requests for VR in advance
- Chain of custody
- Transport conditions/temperature
- Procedures in the event study product is not delivered
- Collection and transport of used/unused VR
- Documentation

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Source Documentation Considerations

- No *completed* CRFs or other source documents should leave clinic
- Blank CRFs and staff notes summarizing source documents may be taken

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Off Site Visits

Pharmacy considerations should include:

- Specifications on product supply procedures for off-site visits. *NOTE: All pharmacy procedures outlined in the MTN-020 off-site visit SOP should be reviewed and approved by the MTN Director of Pharmacy prior to implementation.*

Off Site Visits

- MTN-020 Study Product Request Slip must indicate if product is for off-site visit
- Ensuring proper chain of custody of participant-specific study product from time of receipt from the pharmacy to time of delivery to the participant, including ensuring that participant-specific study product is delivered to the correct participant

Off Site Visits

- Transporting participant-specific study product at appropriate temperatures from time of receipt to time of delivery to the participant
- Document temperature recordings (max/min thermometer)
- Site SOPs should outline steps that will be taken to document that the temperature during transport was maintained at 15º-30º.

Off Site Visits

- Brief temperature excursions between 5º-40º are permissible. If a temperature excursion occurs in this range the ring may be used, however, the site pharmacist and MTN pharmacist must be notified.
- Temperatures experienced during transport must be documented on the Off-site Visit Log.

Off Site Visits

- Handling/returning participant-specific study product when the participant cannot be located or refuses to receive the product dispensed for her
- Handling of used and unused study product, including procedures for collection and transportation back to clinic for disposal
- Unused product to the pharmacy for quarantine

Off Site Visits

- Procedures and timeframes for this process and completing the documentation should be agreed upon by pharmacy and clinic staff and specified in SOPs
- One MTN-020 Off-site visit log should be completed for each trip away from study site to document product delivery/return
- Return log to the pharmacy same day

Off Site Visits

- Documenting all of the above, and appropriately storing all documentation in either the study clinic and/or pharmacy (as per site SOP)

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PHARMACY BREAKOUT SESSION

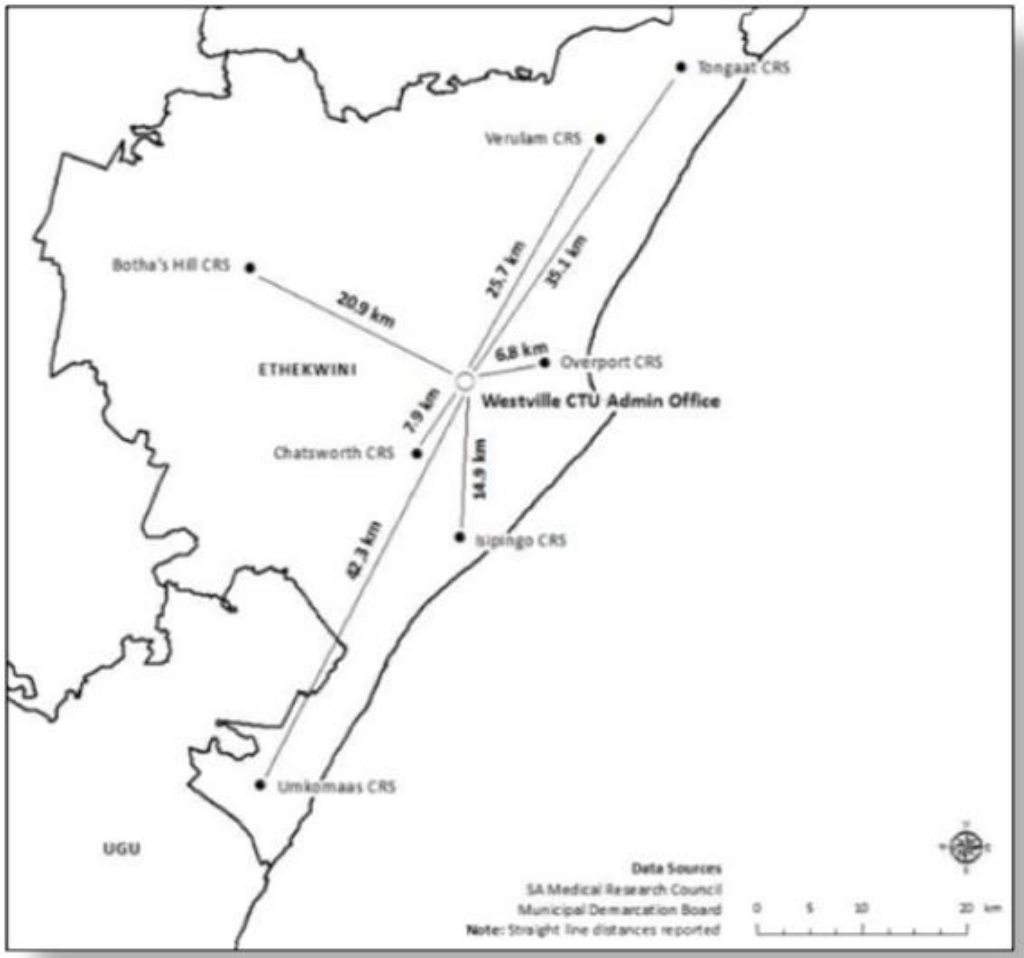
Pharmacy Off Site Visits

Presented by Nivriti Hurbans
Pharmacist – Botha's Hill CRS
HIV Prevention Research Unit
South African Medical Research Council

MTN Regional Meeting
Cape Town
October 2013

Introduction

- Medical Research Council HIV Prevention Research Unit is situated in Westville, Durban
- 6 sites conducting ASPIRE
  - Botha's Hill
  - Chatsworth
  - Isipingo
  - Tongaat
  - Umkomaas
  - Verulam



Off Site Visit Summary

- Off site visits occurred at 2 sites:
  - Verulam – 2
  - Umkomaas - 4

Off Site Visit Summary

Verulam CRS

- Reasons for off site visits:
  - Participant had work commitments
  - Completion of study procedures for a participant who had been discontinued from product and was critically ill with meningitis

- Areas where visits were conducted:
  - Oakford (12 km from site)
  - Lindelani (30 km from site)

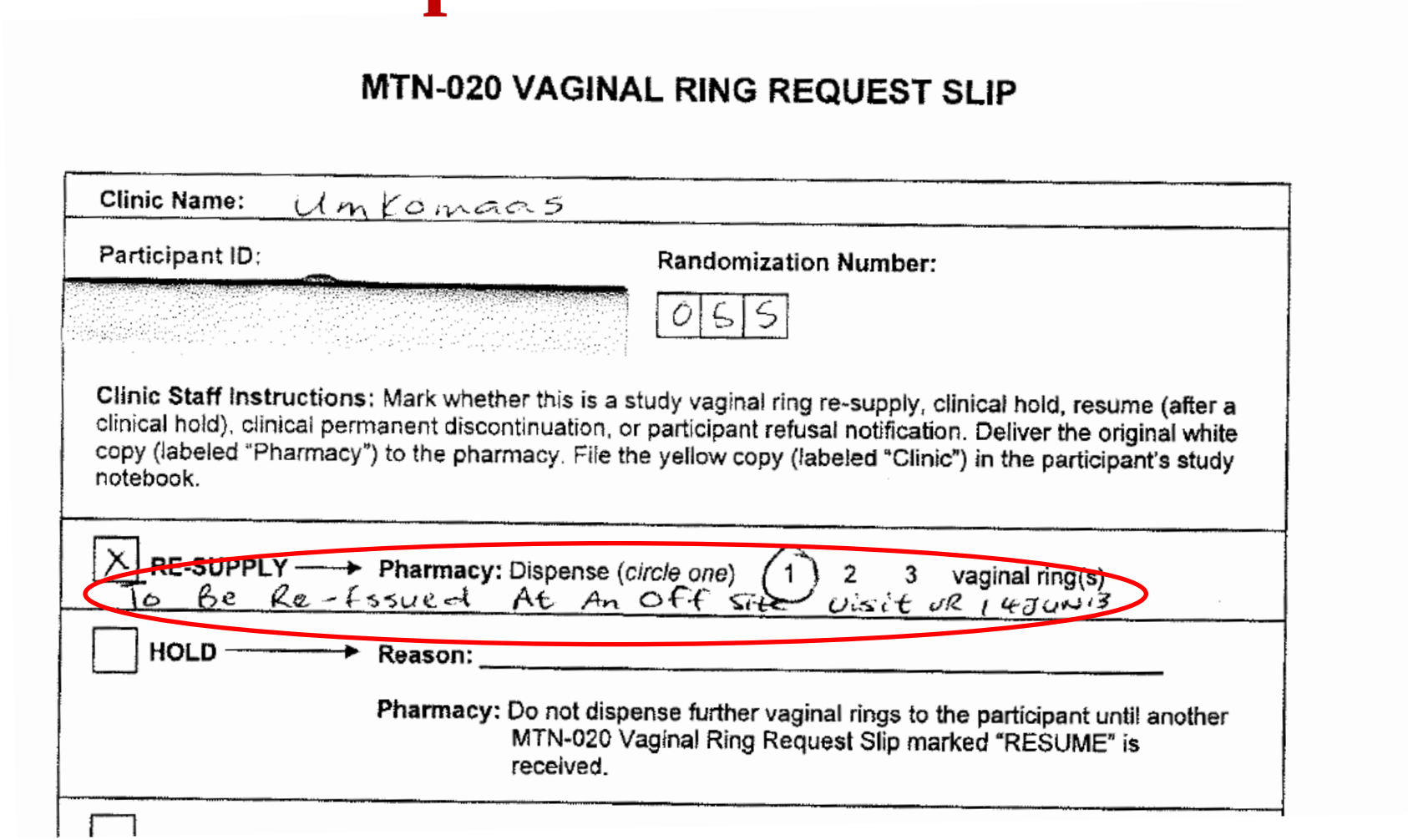
Off Site Visit Summary

Umkomaas CRS

- Reasons for off site visits:
  - Participant relocation (n = 2)
  - Work commitments (n = 1)
  - Family responsibility issues (n = 1)

- Areas where visits were conducted:
  - Durban (50 km from site)
  - Pietermaritzburg (64 km from site)
  - Pinetown (119 km from site)
  - Umthwalume (57 km from site)

Preparation for Off-site Visit



MTN-020 VAGINAL RING REQUEST SLIP

Clinic Name: Umkomaas

Participant ID: [redacted]

Randomization Number: 055

Clinic Staff Instructions: Mark whether this is a study vaginal ring re-supply, clinical hold, resume (after a clinical hold), clinical permanent discontinuation, or participant refusal notification. Deliver the original white copy (labeled "Pharmacy") to the pharmacy. File the yellow copy (labeled "Clinic") in the participant's study notebook.

[X] **RE-SUPPLY** → **Pharmacy:** Dispense (*circle one*) (1) 2 3 vaginal ring(s)
To Be Re-Issued At An Off Site Visit on 14JUN13

[ ] **HOLD** → **Reason:** _____

Pharmacy: Do not dispense further vaginal rings to the participant until another MTN-020 Vaginal Ring Request Slip marked "RESUME" is received.

[ ]

Transporting Study Product

- A ring is dispensed as per SOP
- Polystyrene cooler boxes are used
- The labelled ring is placed into a plastic container and then into the cooler box – to prevent direct contact with ice pack
- Ice packs are placed on either of the plastic container
- Nurses to be trained on the use of the min/max thermometers
- Refresher training on temperature monitoring to be completed prior to the nurse leaving the site
- Nurse to pick VR from pharmacy just prior to leaving for the visit

Transporting Study Product

- Nurse to monitor temperature in the cooler box during transit to ensure that the temperature remains within the range
- If is it a hot day, nurse to ensure that the vehicle air conditioner is turned on and the cooler box is placed out of direct sunlight
- If the temperature drops too low, the nurses are advised to remove an icepack

Documentation of Off-Site Visit

MTN 020 OFF SITE VISIT LOG:

CRS NAME	UMKOMAAS	DATE	14 JUNE 13
DAIDS CRS Number.	31444	PTID	

CLINIC STAFF				PHARMACY	
No. of Rings Received from pharmacy	No. of Rings Left with Participant	No. of Rings Returned to Clinic	Clinic Staff Initials	Rph Initials	Comments
01	01	01 (used ring)	TM1	LP	

Minimum Temp.	15.4	Maximum Temp.	22.7

Conclusion

- Off sites visits for product delivery requires some planning but is relatively simple to undertake with the participants permission.

- Sites should be encouraged to use off -site visits as an opportunity to reduce the number of missed visits and ensure maximum product coverage to study participants

Wrap-up

- What has changed over the past year since the last meeting
- What do we want to change over the next year
- Meeting feedback
- Any questions