HIV PREVENTION RESEARCH UNIT

LESSONS LEARNT FROM MTN 001, MTN 003 & MTN 015

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On behalf of HPRU Laboratory Team &

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MTN REGIONAL MEETING

5 – 6 OCTOBER 2010

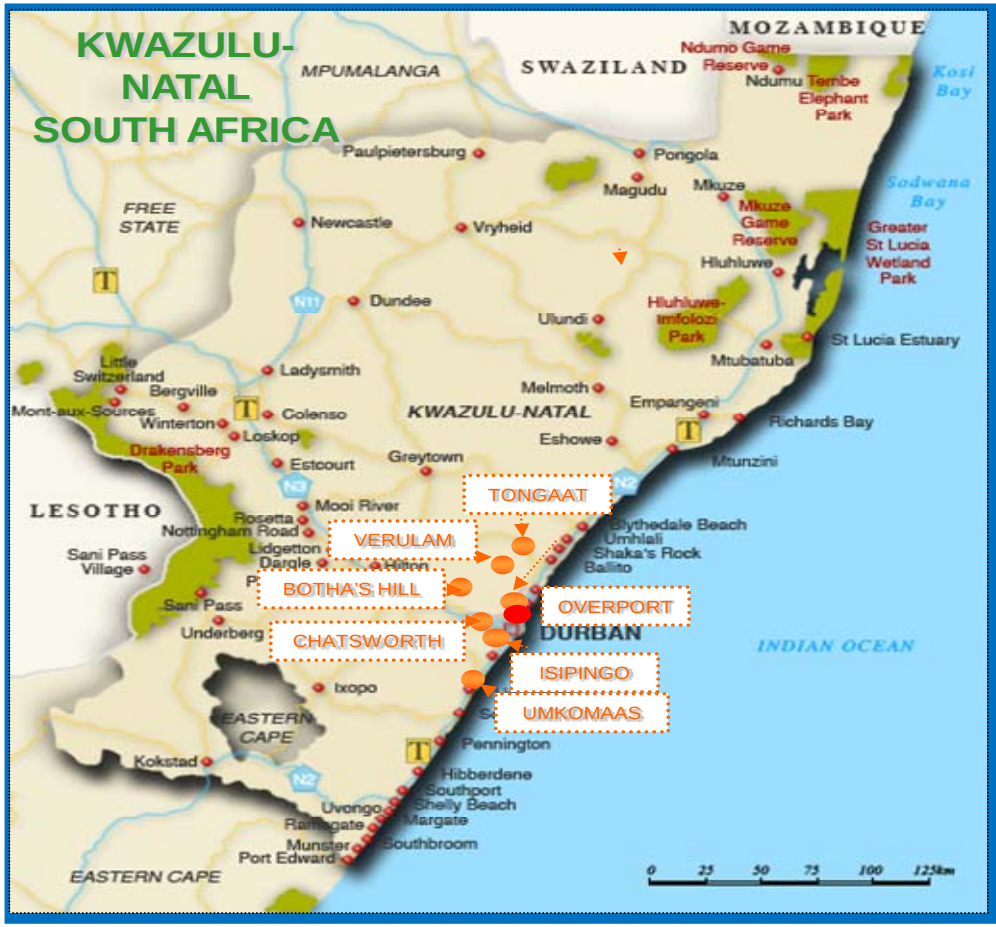
CAPE TOWN

Background

SOUTH AFRICAN MEDICAL RESEARCH COUNCIL

HPRU VOICE CLINICAL TRIAL SITES

Building a healthy nation through research



- BOTHA'S HILL
- CHATSWORTH
- ISIPINGO
- OVERPORT
- TONGAAT
- UMKOMAAS
- VERULAM

LABORATORY MANAGEMENT & COMMUNICATION PLAN

Building a healthy nation through research

32 LAB STAFF

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ANTONIA GWALA
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Verulam
SANDY NAIDOO
THOKOZANI MKHIZE
NATRICIA SUKDEO

Tongaat
LARIN LABUSCHAGNE
BONGEKA ZAMA
KAMANE CHETTY

Umkomaas
BHEKI TEMBE
NOZIPHO CANHAM
JUHINA BHAGAWANDEEN

CRS ON SITE LABORATORIES
2 MED TECHS +1 LAB QA/QC RA

On-Site Laboratories

- Conduct following Rapid Testing:
  - Rapid HIV Abbott Determine HIV ½
  - Rapid HIV Unigold Recombigen
  - Urine Pregnancy: Quick Vue
  - KOH Preparation: For Yeasts and Pseudohyphae
  - Urine Dipstick: Siemens Uristix 4, Multistix 9 and Uristix 2
  - Rapid BV: Gryphus BV Blue Test
  - Rapid TV: Osom Trichomonas Rapid Test

On-Site Laboratories

- Sample Storage Includes: Plasma, serum, cervico vaginal lavages, gram stains and Dacron swabs.
- All HIV Western Blot and GC/CT ProbeTec testing shipped to our in-house HPRU Central Routine Laboratory.
- Remainder testing to an accredited Out-sourced Laboratory.

Lessons Learnt

- **Case 1:** Standardization of Laboratory Documentation (All MTN Studies)
- **Case 2:** MTN Laboratory Result Form (All MTN Studies)
- **Case 3:** MTN 003 / MTN 015 Combined Testing and Specimen Storage workflows
- **Case 4:** Requesting of testing by Clinical team at site (MTN 003 & MTN 015)

Lessons Learnt

- **Case 5:** Creatinine Clearance Calculation (MTN 001 & MTN 003)
- **Case 6:** Seroconvertor Sample 2 (MTN 003)
- **Case 7:** Site Sample collection time and Data Clarification Forms (All MTN Studies)

CASE 1: Standardization of Laboratory Documents across Sites

- With 7 sites across Kwa-Zulu Natal and 4 studies per site with lab components; ensuring standardization can be tricky.

- Standardization of documentation as important as testing procedures.

Recommendations and Lessons Learnt

- Developed several indexes for all on-site documentation with roles and responsibilities.
- Master SOPS/Logs and study specific [note FDA and DAIDS archival regulations].
- All documents are compiled centrally, version controlled and copies distributed to all 7 sites.
- Created timelines for staff to meet local and international deadlines.
- Centralized EQA and Training/Personnel Files.

Recommendations and Lessons Learnt

- Each site has 2 Medical Technologists & one Lab QA/QC RA.
- In event of Med Tech calling in sick, second Med Tech at site to continue with testing.
- Previously one Lab QA/QC RA between 2 sites; posed problems as volume of work per site extremely high.
- Monthly Lab meetings: address training needs, staffing needs, challenges discussed, PPD audit preparations, PPD audit trend analysis and discussions on way forward.
- Adhoc emergency meetings: discuss corrective action - problems that require urgent attention.

Recommendations and Lessons Learnt

- All lab staff trained, assessed for standardized conformance via competency, proficiency and aptitude testing.
- Lab RAs photocopied and mirrored filing as per Unit Lab files thus ensuring all sites are standardized.
- Internal Lab Monitoring of 7 site labs concurrently ensures files are maintained as per Unit Lab with gaps identified and corrective action implemented, re-trains to occur, root cause analysis and standardized messaging.
- Measure QC error rate per staff/lab- healthy internal competition.

CASE 2: MTN Laboratory Result Form

- Due to several MTN studies per site, tedious and time consuming to have several Lab Result Forms for each study. HPRU in-house source document - record all on-site laboratory tests.

- Lab staff entering kit and study names onto Lab Result Forms – time consuming and greater room for error.

Recommendations and Lessons Learnt

- Unit Laboratory created one Lab Result Form for all MTN studies: MTN 003, MTN 015, MTN 003/MTN 015, MTN 009.
- One Lab Result Form saves printing costs, no need for extra storage space for several batches of Lab Result Forms, better version control.
- Test kit names added onto forms – saves lab staff time from writing kit names onto Lab Result Forms and reduces transcription errors.
- Male Partner testing area added on.

MTN LABORATORY RESULT FORM FOR ON SITE TESTS

PTID: ☐☐☐-☐☐☐☐☐-☐

Date of Visit: ☐☐/☐☐☐/☐☐ DD/MMM/YY

Visit Code: ☐☐.☐

Visit: (*Please indicate with a cross=X*) *MTN 003 ONLY* ☐ *MTN 015 ONLY* ☐ *MTN 003/015* ☐ *MTN 009* ☐

Screening (1) ☐ Screening (2) ☐ Enrolment ☐ Month ☐ _____

Quarterly ☐ Semi-Annual ☐ Annual ☐ PUEV ☐

Unscheduled ☐ Termination ☐ Other ☐ _____

Test	Result		QC Initials/Date
	Positive	Negative	
Pregnancy Test - QuickVue			
HIV Rapid Test 1 – Determine HIV1/2			
HIV Rapid Test 2 – Unigold Recombigen HIV			
Back-up HIV Rapid Test Option – OraSure OraQuick			
Rapid TV – OSOM Trichomonas Rapid Test			
Rapid BV – OSOM BV Blue Test			
Wet Mount: *KOH Prep only!*	Symptomatic ☐	Asymptomatic ☐	
Urine Dipstick:	*Values*	*Grading*	
Leukocyte Esterase			
Nitrites			
Protein			
Glucose			
Urine Culture	YES ☐	NO ☐	

Med. Tech. Sign: _____ Date: _____

Clinician Sign: _____ Date: _____

MRC Staff: _____ Date: _____

Partner Test Result [If Applicable]: _____

Comments: _____

CASE 3: MTN 003/MTN 015 Combined Testing & Specimen Storage

- Study staff unsure how to proceed with combined testing and storage for 2 protocols.
- Extensive procedures and high work volume for both studies; gives rise to confusion, missed testing and storage.
- This could jeopardize study end points if correct testing procedures and specimen storage not completed.

Recommendations and Lessons Learnt

- Cheatsheets created:
  - MTN 003 and MTN 015 Storage Cheatsheet
  - MTN 003/MTN 015 Combined Visit Testing Cheatsheet
- Allows Lab staff possible scenarios for testing and storage at combined visits.
- Cheatsheet sent to Network Lab for approval.
- Q & A session to trouble shoot some examples.
- Lab staff trained on use of both cheatsheets; training documented on training log.

MTN 003 and MTN 015 STORAGE

STUDY/VISIT	1x 5ml SST SERUM 3x 0.5ml	1x 10ml EDTA PLASMA / FTC & TDF LEVELS 5x 1ml	1x 10ml + 1x 4ml EDTA GENOTYPE PLASMA 6x 1ml	VAGINAL SWABS x2	VAGINAL SWABS x1	ENDO-CERVICAL SWABS x1	CVL 9x 1ml; minimum 7x 1ml	GRAM STAINS x2 Slides	PBMC's 5x 10ml EDTA @Scr/Enr; 6x 10ml EDTA thereafter
MTN 015									
Screening /Enrollment	X	N/A	X	X	N/A	N/A	X	N/A	X
Month 1 Post Seroconversion	N/A	N/A	N/A	X	N/A	N/A	X	N/A	X
Month 3 Post Seroconversion	N/A	N/A	N/A	X	N/A	N/A	X	N/A	X
Month 6 & Q6 Post Seroconversion	N/A	N/A	N/A	X	N/A	N/A	X	N/A	X
Week 2, Month 1 & Month 3 Post ART	X	N/A	☺	X	N/A	N/A	Month 3 ONLY	N/A	Week 2 /Month 3 ONLY
Month 6 & Q6 Months Visit after ART Initiation	N/A	N/A	☺	X	N/A	N/A	X	N/A	X
Final Visit	X	N/A	N/A	X	N/A	N/A	X	N/A	X
MTN 003									
Monthly	N/A	☺	N/A	N/A	☺	☺	N/A	N/A	N/A
Quarterly	N/A	X	N/A	N/A	☺	☺	N/A	N/A	N/A
Semi-Annual	N/A	X	N/A	N/A	X	X	N/A	X	N/A
Annual-Month 12 & 24	N/A	X	N/A	N/A	X	X	N/A	X	N/A
PUEV	N/A	X	N/A	N/A	X	X	N/A	X	N/A
Termination	N/A	X	N/A	N/A	☺	☺	N/A	N/A	N/A

KEY: YELLOW - ON SITE LAB BLUE – BARC SA/LANCET
X - Protocol–defined procedure;
☺ - Performed as indicated;
N/A – Not Applicable

MTN 003/MTN 015 COMBINED VISIT TESTING

Please note: to use this table - check the test required for that study and visit - if it is a common test - please do one for that visit!

STUDY/VISIT	PREGNANCY	URINE DIPSTICK	KOH	TV	BV	VAGINAL pH	GC/CT	PAP	GRAM	FBC	ALT, AST, ALP, CRE, T BILI, PHOSPHATE	RPR, TPHA	HBsAg & HBsAb	CD4	HIV RNA	HIV-1 GENOTYPE RESISTANCE
MTN 015																
Screening /Enrollment	X	☺	☺	X	☺	X	X	X	N/A	X	X	X	N/A	X	X	X
Month 1 Post Seroconversion	☺	☺	☺	☺	☺	☺	☺	☺	N/A	N/A	N/A	☺	N/A	X	X	N/A
Month 3 Post Seroconversion	☺	☺	☺	☺	☺	☺	☺	☺	N/A	X	X	☺	N/A	X	X	N/A
Month 6 & Q6 Post Seroconversion	☺	☺	☺	☺ *	☺	☺ *	☺ *	☺ *	N/A	X	X	☺ *	N/A	X	X	N/A
Week 2, Month 1 & Month 3 Post ART	☺	☺	☺	☺	☺	☺	☺	☺	N/A	☺	☺	☺	N/A	X	X	☺
Month 6 & Q6 Months Visit after ART Initiation	☺	☺	☺	☺ *	☺	☺ *	☺ *	☺ *	N/A	X	X	☺ *	N/A	X	X	☺
Final Visit	X	☺	☺	X	☺	X	X	☺	N/A	X	X	X	N/A	X	X	N/A
MTN 003																
Monthly	X	Month 1 ONLY	☺	☺	☺	☺	☺	☺	N/A	☺	Month 1 ONLY	☺	☺	N/A	N/A	N/A
Quarterly	X	X	☺	☺	☺	☺	☺	☺	N/A	☺	X	☺	☺	N/A	N/A	N/A
Semi-Annual	X	X	☺	☺	☺	X	☺	☺	X	X	X	☺	☺	N/A	N/A	N/A
Annual-Month 12 & 24	X	X	☺	X	☺	X	X	☺	X	X	X	X	☺	N/A	N/A	N/A
PUEV	X	X	☺	X	☺	X	X	☺	X	X	X	X	HBsAg ONLY	N/A	N/A	N/A
Termination	X	☺	☺	☺	☺	☹	☺	☺	N/A	☺	☺	☺	☺	N/A	N/A	N/A

KEY: YELLOW – ON SITE LAB PURPLE – HPRU CENTRAL LAB BLUE – BARC SA/LANCET

X = Protocol–defined procedure;

☺ = Performed as indicated;

*** = Done annually;**

N/A = Not Applicable

CASE 4: Requesting of Non-Protocol tests at sites

- LFT – Certain clinicians requested out of protocol tests. Instead of AST, ALT, PO4 and Serum Creatinine as per protocol, entire LFT profile requested.

- Wet Mount – At one site the saline preparation wet mount performed instead of KOH preparation only.

Recommendations and Lessons Learnt

- Extremely important to follow Protocol regarding specimen testing on enrolled participants in a study.

- Out of Protocol testing for clinical care and management must be chart noted along with referrals.

Recommendations and Lessons Learnt

- Clinically indicated testing (out of Protocol testing) can be performed however Unit Laboratory should be informed.

- Helps prevent Protocol violations – as per IC participants consented to Protocol defined testing .

CASE 5: Creatinine Clearance Calculation (MTN 001 and MTN 003)

- Towards end of MTN 001 and early stages of MTN 003, many queries generated from SCHARP regarding inconsistent Calculated Creatinine Clearance results.

- There were two calculators on the web site namely 'Convert' and 'No Convert ' - both calculations gave conflicting results.

Recommendations and Lessons Learnt

- Unit lab completed several examples and found the calculators on the website were faulty at the base formula.
- An additional event – age range for MTN 001 was 18-44, so you couldn't enter any age from 43 and 1 months onwards.
- Weight range for 003 was 35-130kg
- Reported to Network Laboratory and SCHARP.

Recommendations and Lessons Learnt

- Problem resolved by providing examples to SCHARP: going forward it was decided that the 'No Convert' calculator be utilized by the sites for both protocols.
- A lab note to file prepared and filed to cover the manual calculations.
- SOP /Log on Manual calculations from study start – used during web downtime or power loss

CASE 6: MTN 003 Seroconvertor Sample 2

- 2 Seroconvertors missed CD4 count and viral load testing when sample 2 was collected.
- This poses problems as all tests should be performed at specified time points as per Protocol.
- This was picked up early enough to call the participant for a blood draw the following day.
- Network Laboratory contacted and informed of missed testing.

Recommendations and Lessons Learnt

- The importance of referencing SOPs, SSP Manuals and the Protocol reiterated to study staff to ensure consistency and accuracy of data and study procedures.

- Laboratory staff re-trained, reassessed and re-evaluated on handling of seroconvertors for MTN 003.

- Meetings held in real time, bimonthly and monthly to discuss corrective actions.

Recommendations and Lessons Learnt

- Standardization of messaging to all on-site labs to prevent re-occurrence.

- A brightly colored A3 cheat sheet created by the Laboratory Manager, laminated and mounted on wall in several parts of the clinic sites for easy access.

Recommendations and Lessons Learnt

- Site laboratories requested to communicate queries directly with MRC HPRU Unit Laboratory.

- **Positive Note: No sample archive lost at time points.**

CASE 7: Site Sample Collection Time and Data Clarification Forms

- PPD Audit Finding: Urine collection time on urine container serves as source document. This poses a problem as this source document is discarded after testing.

- Off-site Laboratory audit by Unit Laboratory - noted that the PAP collection time only recorded on the requisition form and slide but not recorded on the participant file.

Site Sample Collection Time and Data Clarification Forms cont….

- High rate of errors on requisition forms noted by out-sourced laboratories.
- Data Clarification Forms create unnecessary delays in result reports which impacts on screening and enrolment procedures.
- Errors increase PPD audit findings which adversely affects the reputation of the CRS.

Recommendations and Lessons Learnt

- All site Research Assistants document urine collection time on Visit Tracking Log in the participant file.
- Site Clinicians requested to document PAP collection time on Visit Tracking log and chart notes.
- Unit Lab notified and a Note to file prepared and filed.

Recommendations and Lessons Learnt

- Nurses and Clinicians currently QC and sign the requisition forms prior to forwarding to the laboratory.
- Laboratory staff QC requisition forms prior to shipping to Outsourced laboratory.
- Helps track staff member requiring retrain.
- DCF's discussed at laboratory meeting and good communication encouraged in order to reduce the number of DCF's generated.

Acknowledgments

- Site Laboratory Staff
- HPRU Core Laboratory Group
- Network Lab and Protocol Team
- MRC - HPRU

THANK YOU