LESSONS LEARNT FROM
MTN 001, MTN 003 & MTN 015

Presented by:
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Resha Boodhram (MRC–HPRU Unit Laboratory)

On behalf of HPRU Laboratory Team &
Professor Gita Ramjee

MTN REGIONAL MEETING
5 – 6 OCTOBER 2010
CAPE TOWN
Background

HPRU VOICE CLINICAL TRIAL SITES

KWAZULU-NATAL SOUTH AFRICA

- BOTHA’S HILL
- CHATSWORTH
- ISIPINGO
- OVERPORT
- TONGAAT
- UMKOMAAS
- VERULAM
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 □ ______________

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>QC Initials/Date</th>
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<tbody>
<tr>
<td>Pregnancy Test - QuickVue</td>
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<td>HIV Rapid Test 1 – Determine HIV1/2</td>
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<td>HIV Rapid Test 2 – Unigold Recombigen HIV</td>
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<td>Back-up HIV Rapid Test Option – OraSure OraQuick</td>
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<td>Rapid TV – OSOM Trichomonas Rapid Test</td>
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<td>Rapid BV – OSOM BV Blue Test</td>
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<td>Wet Mount: KOH Prep only!</td>
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<td>Urine Dipstick:</td>
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<td>Leukocyte Esterase</td>
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<td>Nitrites</td>
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<td>Urine Culture</td>
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Med. Tech. Sign: ___________________________ Date: ___________________________
Clinician Sign: ___________________________ Date: ___________________________
MRC Staff: ___________________________ Date: ___________________________
Partner Test Result [If Applicable]: ______________
Comments: __________________________________________

MTN  Lab Result Form V2.0
30 August 2010
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

<table>
<thead>
<tr>
<th>STUDY/VISIT</th>
<th>1x 5ml SST SERUM 3x 0.5ml</th>
<th>1x 10ml EDTA PLASMA / FTC &amp; TDF LEVELS 5x 1ml</th>
<th>1x 10ml + 1x 4ml EDTA GENOTYPE PLASMA 6x 1ml</th>
<th>VAGINAL SWABS x2</th>
<th>VAGINAL SWABS x1</th>
<th>ENDOCERVICAL SWABS x1</th>
<th>CVL 9x 1ml; minimum 7x 1ml</th>
<th>GRAM STAINS x2 Slides</th>
<th>PBMC’s 5x 10ml EDTA @Scr/Enr; 6x 10ml EDTA thereafter</th>
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<tbody>
<tr>
<td>Screening /Enrollment</td>
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<td>Month 3 Post Seroconversion</td>
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<tr>
<td>Month 6 &amp; Q6 Post Seroconversion</td>
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<td>Week 2, Month 1 &amp; Month 3 Post ART</td>
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<td>Week 2 /Month 3 ONLY</td>
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## MTN 003

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<td>Annual-Month 12 &amp; 24</td>
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## 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!*

<table>
<thead>
<tr>
<th>STUDY/visit</th>
<th>PREGNANCY</th>
<th>URINE DIPSTICK</th>
<th>KOH</th>
<th>TV</th>
<th>BV</th>
<th>VAGINAL pH</th>
<th>GC/CT</th>
<th>PAP</th>
<th>GRAM</th>
<th>FBC</th>
<th>ALT, AST, ALP, CRE.</th>
<th>TBIL, PHOSPHATE</th>
<th>RPR, TPHA</th>
<th>HBsAg &amp; HBsAb</th>
<th>CD4</th>
<th>HIV RNA</th>
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### MTN 003

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**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

MTN 003/MTN 015 Combined Visit Testing, V1.0  07 July 2010
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.
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.**
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 outsourced 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