MTN 015 SPECIMEN REVIEW

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Review of MTN 015 Study

• MTN 015 is a multi-site observational cohort study whose study population are women who sero-converted during the HPTN 035 Microbicide Study. There are no investigational products.

• Primary Objective-
  To compare the plasma HIV-1 RNA level twelve months after HIV-1 sero-conversion among ART naïve participants assigned to an active microbicidal agent as compared to the control participants.
MTN 015 Specimen Collection

- Specimen collection from study participants is usually necessary to achieve the objectives of the study.
- All specimen collection, handling, testing, storage and shipment is conducted adhering to GCLP, MTN 015 SSP Manual, HPTN-MTN Lab Manual and the site SOPs.
- Specimen containers must be labeled with SCHARP provided participant ID labels. Specimen collection dates are handwritten in indelible ink.
Specimen Collection

• All specimens collected from MTN 015 participants in the clinic are documented on the site Lab Request Form.
• Specimens requiring storage are documented on the LDMS Tracking Sheet.
• Proper chain of custody is followed from sample collection, transportation, delivery, processing, testing, result reporting and sample storage.
UNC Project Lab Request Form

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>TEST DESCRIPTION</th>
<th>CODE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Blood Cells (Blood)</td>
<td>B210</td>
</tr>
<tr>
<td>2</td>
<td>C-reactive Protein (CRP)</td>
<td>CRP2</td>
</tr>
<tr>
<td>3</td>
<td>Electrolytes (Electrolyte Panel)</td>
<td>ELE2</td>
</tr>
<tr>
<td>4</td>
<td>Hemoglobin (Hgb)</td>
<td>HGB2</td>
</tr>
<tr>
<td>5</td>
<td>Markers (Sialic Acid)</td>
<td>SIA2</td>
</tr>
<tr>
<td>6</td>
<td>Red Blood Cells (RBC)</td>
<td>RBC2</td>
</tr>
<tr>
<td>7</td>
<td>Urea (Urea)</td>
<td>URE2</td>
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</tbody>
</table>

**COMMENTS:**

**LIS ACCESSION NUMBER:**

**SPECIMEN COLLECTED BY:**

<table>
<thead>
<tr>
<th>ID</th>
<th>DATE</th>
<th>TIME</th>
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</table>

**RECEIVING TECH:**

<table>
<thead>
<tr>
<th>ID</th>
<th>DATE</th>
<th>TIME</th>
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</table>
MTN 015 LDMS Tracking Sheet

<table>
<thead>
<tr>
<th>Participant ID</th>
<th>Visit Code</th>
<th>Specimen Collection Date</th>
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</tbody>
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### Notes for Lab
- Blood (BLUE)
- Whole Blood
- Plasma
- Serum
- Cell Culture
- Hematology
- Flow Cytometry
- Immunohistochemistry
- Western Blot
- Mass Spectrometry
- Next Generation Sequencing

### Comments
- Site: [Site Name]
- Date: [Date]

**Initials**: [Initials]
**LDMS Date Entry Date**: [Date]
**Version**: 2.0, 14 OCT 08
Specimen Transmission Form

<table>
<thead>
<tr>
<th>TIME OF COLLECTION</th>
<th>REPO OF COLLECTION</th>
<th>STUDY</th>
<th>SPECIMEN ID NUMBER</th>
<th>VISIT CODE</th>
<th>SENDING TECHNICIAN</th>
<th>NATURE OF SPECIMEN</th>
<th>COMMENTS</th>
<th>TRANSMISSION DRIVER</th>
<th>RECEIVING TECHNICIAN</th>
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</table>

DATE AND TIME SPECIMENS RECEIVED

SPECIMEN TRANSFER FORM - 17-03-02, WD Updated 08-04-2009.
MTN 015 Specimens

- Three Types of Specimens are collected from MTN 015 participants.
  - Urine
  - Blood
  - Pelvic Samples
Urine Samples

- **Collection** - 15-60mls is collected in a sterile plastic urine cup labeled with PTID label. Urine should not be mid-stream and participant should not have urinated 1 hour prior to collection.

- **Testing** - pregnancy test and chlamydia and gonorrhea. At visits when both tests are required, 5-10ml of urine is aliquoted to a secondary container for pregnancy testing (in the clinic) the rest is sent to lab for GC/CT testing.

- **Storage** - for sites without a validated SDA test.
Blood Samples

• **Collection**-Different blood volumes are collected in EDTA or plain tubes depending on test/storage requirement at each visit.

• **Testing**-
  EDTA blood – HIV RNA, CD4 T cell ct, CBC, PBMC processing.
  Plain tube blood – Syphilis, liver (ALT, AST, ALP, T.Bili) and kidney (creatinine) function tests.
Blood Samples

- **Storage-**
  - Serum- for HIV-1 ELISA and WB confirmation at MTN NL.
  - Plasma – for genotypic resistant testing, PCR for drug resistant codons at NL and HSV2 at regional Lab.
  - PBMC- testing for markers of cell mediated immunity at the HVTN lab.
Pelvic Samples

• **Collection** - pelvic samples are collected per the site’s clinic SOPs.
• **Testing** - vaginal pH testing (in clinic), wet mount testing (in lab), pap smears at selected sites.
• **Storage**
  Vaginal swabs – for vaginal flora proteomics and markers of inflammation at NL.
  Cervical/vaginal lavage - for HIV-1 viral load, HIV-1 genotypic resistant shedding and molecular analysis of vaginal flora.
Storage of MTN 015 Specimens

Plasma, serum, PBMCs, Vaginal Swabs, CVL and urine samples must be entered into the LDMS and labeled with the LDMS generated labels before storage.

Weekly, the MTN designated technician reconciles LDMS stored samples against the clinic MTN 015 sample collection log. The study coordinator and lab manager are notified of any discrepancies.
Shipment of Stored Samples

Samples are shipped to MTN NL when the site is notified.

All personnel handling the shipments must participate in IATA training every two years and must have IATA certification on file.
## Test Methodology

<table>
<thead>
<tr>
<th>Test</th>
<th>Location</th>
<th>Kit/Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy</td>
<td>Clinic</td>
<td>Quidel QuickVue</td>
</tr>
<tr>
<td>GC/CT</td>
<td>Site Lab</td>
<td>BD ProbeTec</td>
</tr>
<tr>
<td>WB</td>
<td>Site Lab</td>
<td>FDA approved test</td>
</tr>
<tr>
<td>HIV-1 RNA</td>
<td>Site Lab</td>
<td>Roche Amplicor</td>
</tr>
<tr>
<td>HIV-1 Resistant</td>
<td>NL</td>
<td>Genotyp. Characterization</td>
</tr>
<tr>
<td>CD4+ Cell</td>
<td>Site Lab</td>
<td>Not specified</td>
</tr>
<tr>
<td>CBC</td>
<td>Site Lab</td>
<td>Not specified</td>
</tr>
<tr>
<td>Liver function</td>
<td>Site Lab</td>
<td>Not specified</td>
</tr>
<tr>
<td>PBMC</td>
<td>Site Lab</td>
<td>HANC CN SOP</td>
</tr>
</tbody>
</table>
Test Methodology

• It’s important to adhere to the test methodology approved by the MTN NL for the duration of the study; however if it’s necessary to switch to an alternate method or kit after study initiation, the site must inform the MTN NL and perform a validation study.
EQA Testing

- **CAP**
  Hematology, chemistry, hCG, syphilis, SDA GC/CT
- **UKNEQAS**
  CD4+ T Cell Count
- **VQA**
  HIV-1 RNA PCR
- **DUKE IQA**
  PBMC
- **MTN NL**
  Wet Mount
Challenges in MTN 015 Study

- Clinic Problems
- Incorrect documentation on requisition forms - e.g. forget to mark Alk phos test.
- Insufficient blood collection.
- Missed sample collection e.g. vaginal swabs
- Mismatch of information on sample container against the Lab Request Form.
Challenges in MTN 015 Study

- Lab-
- Samples forgotten at 2 – 8°C until following day.
- Samples lost in the lab-missed storage.
- Hemolyzed sample for PBMCs are not reported to the clinic immediately for recollection.
- Missed test requisition in LIS.
- Clerical errors when logging samples in LDMS/LIS.
Resolutions to Challenges

- Retraining of nurses in blood collection procedures and filing of Lab Request Forms.
- Checklist in reception area – used at end of shift.
- Hired a lab QC assistant to double check the LIS/LDMS entries.
- Weekly reconciliation of LDMS storage samples.
Specimen collection in Clinic
Specimen Receipt in Lab
Test Requisition in LIS
Labeling Specimen with Accession #
Processing of Specimens
Specimen Testing
Specimen entry into LDMS
Specimen Storage
 QUESTIONS???