ENHANCING LAB PERFORMANCE

HPTN Regional Meeting
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Introduction

- HPTN Lab QA/QC Core
- PALs
- CAPAs
- Lessons Learned
  - Network evaluation
  - New Shipping Requirements
  - Sample Completeness
  - LDMS Reconciliations
Laboratory Center (LC)
Susan Eshleman (PI)
Mark Marzinke (Co-PI)
Estelle Piwowar-Manning
(Deputy Director)

Protocol Specialists
Vanessa Cummings
Denni Lennon
Paul Richardson
Phil Sullivan

Regulatory Compliance
Barbara Debevec

Sample Management and Testing
Michelle Xing
Stephanie Veater
Tammy Walsky

International Coordinators
Yaw Agyei
Lebah Lugalia
Danielle Heyl
Special strengths of the QA/QC Core

**QA/QC Core**

- Certified Clinical Laboratory Scientists, each with between 10 to 40 years of experience in regulated laboratories
- Expertise in Hematology, Chemistry, Immunology, Flow Cytometry, Serology, Virology, HIV diagnostics, Blood Banking, Molecular Pathology, Microbiology
- Over 20 years of involvement in laboratory QA/QC activities at US and non-US CTU / CRS laboratories for HIV prevention trials
- Estelle managed two international laboratories for 5 years
• Protocol team members - development, SSP, HIV algorithm, training
• Site support
• QA/QC testing
• Specialized HIV testing
• Specializing in lab specimen management, freezer management, international shipping
• Production of training videos in laboratory practices
# PAL – Protocol Analyte List

<table>
<thead>
<tr>
<th>Assay</th>
<th>Primary Instrument</th>
<th>Primary Method/Reagent Kit</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chemistry</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALT</td>
<td>COBAS ROCHE C311</td>
<td>ALT W/out pyridoxal phosphate activation ROCHE 20764907322 Yes</td>
</tr>
<tr>
<td>AST</td>
<td>COBAS ROCHE C311</td>
<td>AST W/out pyridoxal phosphate activation ROCHE 20764949322 Yes 20-Jul-15</td>
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<tr>
<td>ALP</td>
<td>ROCHE C311</td>
<td>ALP IFCC LIQUID ROCHE 31185132216 Yes 20-Jul-15</td>
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<tr>
<td>Creatinine</td>
<td>ROCHE C311</td>
<td>Creatinine Jaffe' Method ROCHE 11489291216 Yes 20-Jul-15</td>
</tr>
<tr>
<td>BUN/Urea</td>
<td>ROCHE C311</td>
<td>Dichlorophenyl diazonium salt (DPD) ROCHE 11489364215 Yes 20-Jul-15</td>
</tr>
<tr>
<td>CK</td>
<td>ROCHE C311</td>
<td>Creatinine Kinase liquid acc to IFCCMethod ROCHE 12132524 Yes 20-Jul-15</td>
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<tr>
<td>Total Bilirubin</td>
<td>ROCHE C311</td>
<td>Dihydroporphyrin diazonium salt (DPD) ROCHE 11489194216 Yes 20-Jul-15</td>
</tr>
<tr>
<td>Phosphorous</td>
<td>ROCHE C311</td>
<td>Phosphomolybdate ROCHE PHOS 11127993216 Yes 20-Jul-15</td>
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<tr>
<td>Glucose</td>
<td>ROCHE C311</td>
<td>Glucose Oxidase- Peroxidase Method ROCHE 11448668216 Yes 20-Jul-15</td>
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<tr>
<td>Amylase</td>
<td>ROCHE C311</td>
<td>Enzymatic colorimetric ROCHE 3183742122 Yes 20-Jul-15</td>
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<tr>
<td>Lipase</td>
<td>ROCHE C311</td>
<td>Enzymatic colorimetric ROCHE 3029590322 Yes 20-Jul-15</td>
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<tr>
<td>Calcium</td>
<td>ROCHE C311</td>
<td>Enzymatic colorimetric ROCHE 3039773190 Yes 20-Jul-15</td>
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<tr>
<td>Total Cholesterol</td>
<td>ROCHE C311</td>
<td>Enzymatic colorimetric ROCHE 4399803190 Yes 20-Jul-15</td>
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<tr>
<td>HDL Cholesterol</td>
<td>ROCHE C311</td>
<td>Enzymatic colorimetric ROCHE 20767107322 Yes 20-Jul-15</td>
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<tr>
<td>Triglyceride</td>
<td>ROCHE C311</td>
<td>Enzymatic colorimetric ROCHE 20765960190 Yes 20-Jul-15</td>
</tr>
</tbody>
</table>
PAL Completion

• PALs must
  – Reflect all assays defined in the protocol.
  – Reflect FDA approval of assays.
  – Reflect current primary and secondary labs/methods.
  – Reflect EQA enrolment.

• Changes in PAL information or reference intervals must be communicated to HPTN LC immediately.

• Provides an overview of testing methodologies for LC and safety / CMC reference
EXAMPLE FLOW CHART FOR COC

**St Mary’s Clinic**
- Specimen Collection
- Pregnancy test
- Urine Dipstick
- Rapid Trichomomas Test
- Rapid HIV test

**UZCRC On-site laboratory**
- Specimen Collection
- Pregnancy test
- Urine Dipstick
- Rapid Trichomomas Test
- Rapid HIV test

**Spillhaus Onsite laboratory**
- Specimen Collection
- Pregnancy test
- Urine Dipstick
- Rapid Trichomomas Test
- Rapid HIV test

**Zengeza On-site laboratory**
- Specimen Collection
- Pregnancy test
- Urine Dipstick
- Rapid Trichomomas Test
- Rapid HIV test

**UZCHS-CTU Central Lab**
- Accessioning
- Plasma separation
- Plasma storage
- Serology, HIV, Syphilis, Hep B,C
- CD4 counts
- Molecular, CTNG, Viral Load
- Chemistry tests
- Haematology, FBC
Corrective Action / Preventive Action

• Tools to improve site lab performance
  – Timely completion of CAPAs for EQA failures, referred to as Investigation Reports
  – Submission of corrective actions for DAIDS audit findings.
  – Submission of corrective actions for HPTN LC visit findings
## Network Evaluation – Laboratory Component

### NEW!! NEW!! NEW!!

<table>
<thead>
<tr>
<th>Monitor</th>
<th>Description</th>
<th>Requirement</th>
<th>Data Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality of specimen handling/shipment</td>
<td>Number of shipments received within the specified timeframe</td>
<td>90% received within timeframe</td>
<td>LC reports</td>
</tr>
<tr>
<td>Specimen storage completeness</td>
<td>Number of aliquots stored/number of aliquots anticipated per specimen type per visit per protocol</td>
<td>95% storage completeness</td>
<td>SDMC report to LC for interpretation</td>
</tr>
</tbody>
</table>
Shipping Requirements – 083/084

Samples to be shipped quarterly.

- Plasma- starting from enrollment store (-01) aliquots in a box marked “To be shipped”.
- Shipment quarterly
Sample Completeness

- Ensure all study required samples are collected.
  - Collect volumes indicated in the SSP
  - Enter exact volumes in LDMS (insert volumes collected).
Sample Completeness cont.

- Process and store aliquots as per SSP
- Inform HPTN LC of any short storage
  - Less than 3 aliquots of plasma (e.g. HPTN 084)

![Image of test tubes with volumes 1.8 mL, 1.0 mL, and 0.0 mL (0.01 mL, QNS)
LDMS Reconciliation

Stored specimens are key!

- Minimize problems with LDMS
- Ensure that all samples are appropriately collected, labeled and stored

The Laboratory Manager, QA/QC coordinator or designee, and clinic/site personnel must review on a weekly basis:

LDMS tracking sheets vs.
LDMS entry vs.
Clinic collection and CRFs
HPTN LC are available for lab consultations.

- Keep PAL updated
- Collaborate with HPTN LC on EQA performance
- Meet with clinic on LDMS issues and blood volumes
- Track shipments
The HIV Prevention Trials Network is funded by the National Institute of Allergy and Infectious Diseases (UM1AI068619, UM1AI068613, UM1AI1068617), with co-funding from the National Institute of Mental Health, and the National Institute on Drug Abuse, all components of the U.S. National Institutes of Health.