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ENHANCING LAB PERFORMANCE

HPTN Regional Meeting

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Introduction

- HPTN Lab QA/QC Core
- PALs
- CAPAs
- Network evaluation (083 specific)
  - New Shipping Requirements
  - Sample Completeness
  - LDMS Reconciliations
- Lab specific differences between HPTN 083 and AMP

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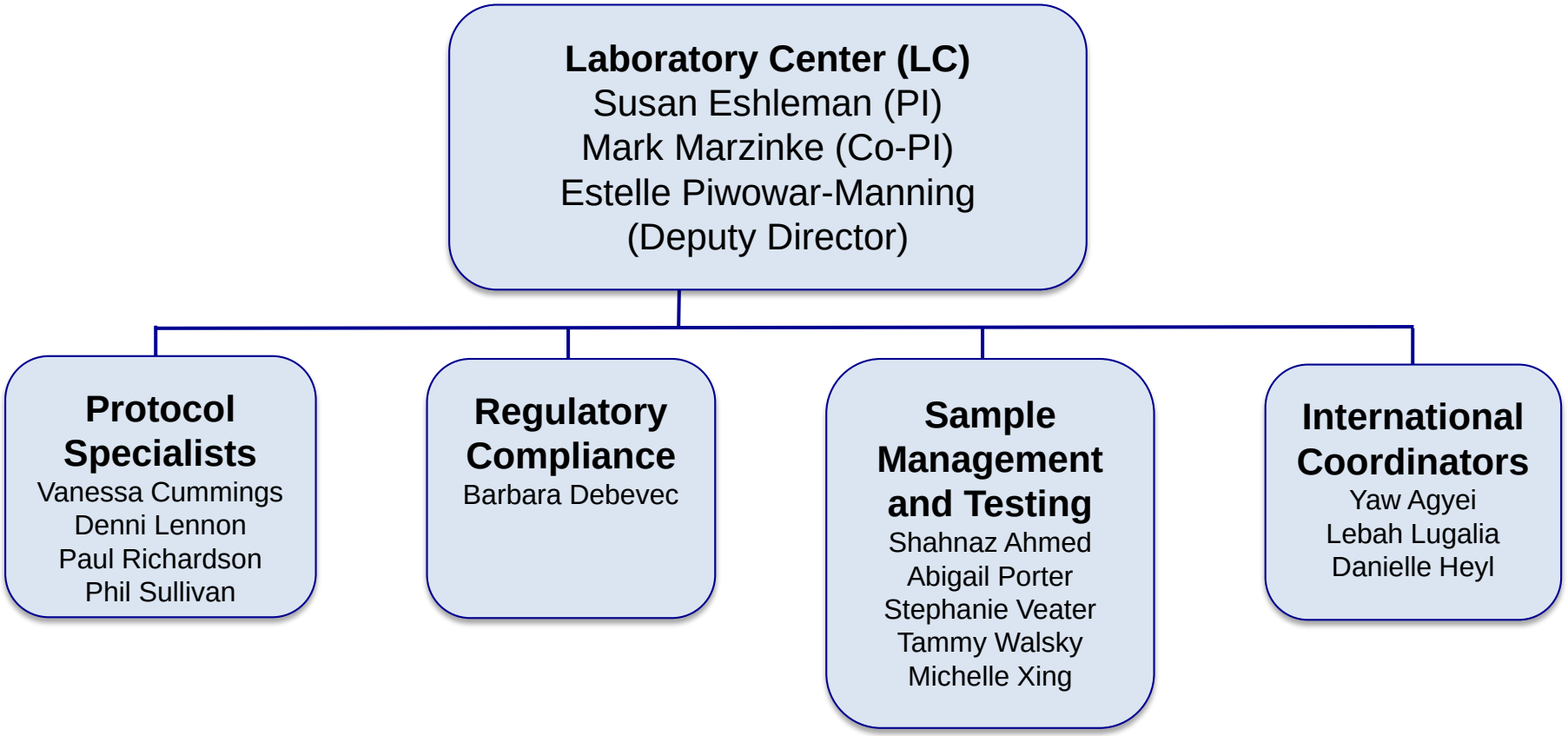

Special strengths of the QA/QC Core

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

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- 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

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PAL – Protocol Analyte List

CRS Number:	**30320, 30294, 30304, 30313, 30303**
Protocol:	**HPTN 084**
LDMS Number	**306**
HPTN LC contact	**Estelle Piwowar-Manning**
	Yaw Agyei

Completed By:	Allen Matubu
Date Completed:	6-Mar-17
Reviewed By:	
Date Reviewed:	
Revision	Allen Matubu
Updated date:	7-Sep-17
Date Reviewed:	

CKD: Sam Ghanta, 10 March 2017

Please fill in as much detailed information as you can provide. Please add any assays that are missing.

Assay		Primary Instrument				Primary Method/Reagent Kit				
	Primary Lab	Instrument Name	Instrument Manufacturer	Instrument Model Number	FDA Approved (Yes/No/Don't Know)	Method/Kit Name	Method/Kit Manufacturer	Method/Kit Product Number or Product Code	FDA Approval (Yes/No)	Validated (Date or No)
Chemistry										
ALT	UZCHS-CTU	COBAS	ROCHE	C311	YES	ALT W/out pyridoxal phosphate activation	ROCHE	20764957 322	Yes	
AST	UZCHS-CTU	COBAS	ROCHE	C311	YES	AST W/out pyridoxal phosphate activation	ROCHE	20764949 322	Yes	20-Jul-15
ALP	UZCHS-CTU	COBAS	ROCHE	C311	YES	ALP IFCC LIQUID	ROCHE	10851132216	Yes	20-Jul-15
Creatinine	UZCHS-CTU	COBAS	ROCHE	C311	YES	Creatinine Jaffe' Method	ROCHE	11489291	Yes	20-Jul-15
BUN/Urea	UZCHS-CTU	COBAS	ROCHE	C311	YES	Dichlorophenyl diazonium salt (DPD)	ROCHE	11489364215	Yes	20-Jul-15
CPK	UZCHS-CTU	COBAS	ROCHE	C311	YES	Creatinine Kinase liquid acc to IFCCMethod	ROCHE	12132524	Yes	20-Jul-15
Total Bilirubin	UZCHS-CTU	COBAS	ROCHE	C311	YES	Dichlorophenyl diazonium salt (DPD)	ROCHE	11489194 216	Yes	20-Jul-15
Phosphorous	UZCHS-CTU	COBAS	ROCHE	C311	YES	Phosphomolybdate	ROCHE	PHOS 11127993 216	Yes	20-Jul-15
Glucose		COBAS	ROCHE	C311	YES	Glucose Oxidase- Peroxidase Method	ROCHE	11448668216	Yes	20-Jul-15
Amylase	UZCHS-CTU	COBAS	ROCHE	C311	YES	Enzymatic colorimetric	ROCHE	3183742122	Yes	20-Jul-15
Lipase	UZCHS-CTU	COBAS	ROCHE	C311	YES	Enzymatic colorimetric	ROCHE	3029590322	Yes	20-Jul-15
Calcium	UZCHS-CTU	COBAS	ROCHE	C311	YES	Colorimetric End point Assay	ROCHE	5061482190	Yes	20-Jul-15
Total Cholesterol	UZCHS-CTU	COBAS	ROCHE	C311	YES	Enzymatic colorimetric	ROCHE	3039773190	Yes	20-Jul-15
HDL Cholesterol	UZCHS-CTU	COBAS	ROCHE	C311	YES	Enzymatic colorimetric	ROCHE	4399803190	Yes	20-Jul-15
Triglyceride	UZCHS-CTU	COBAS	ROCHE	C311	YES	Enzymatic colorimetric	ROCHE	20767107322	Yes	20-Jul-15

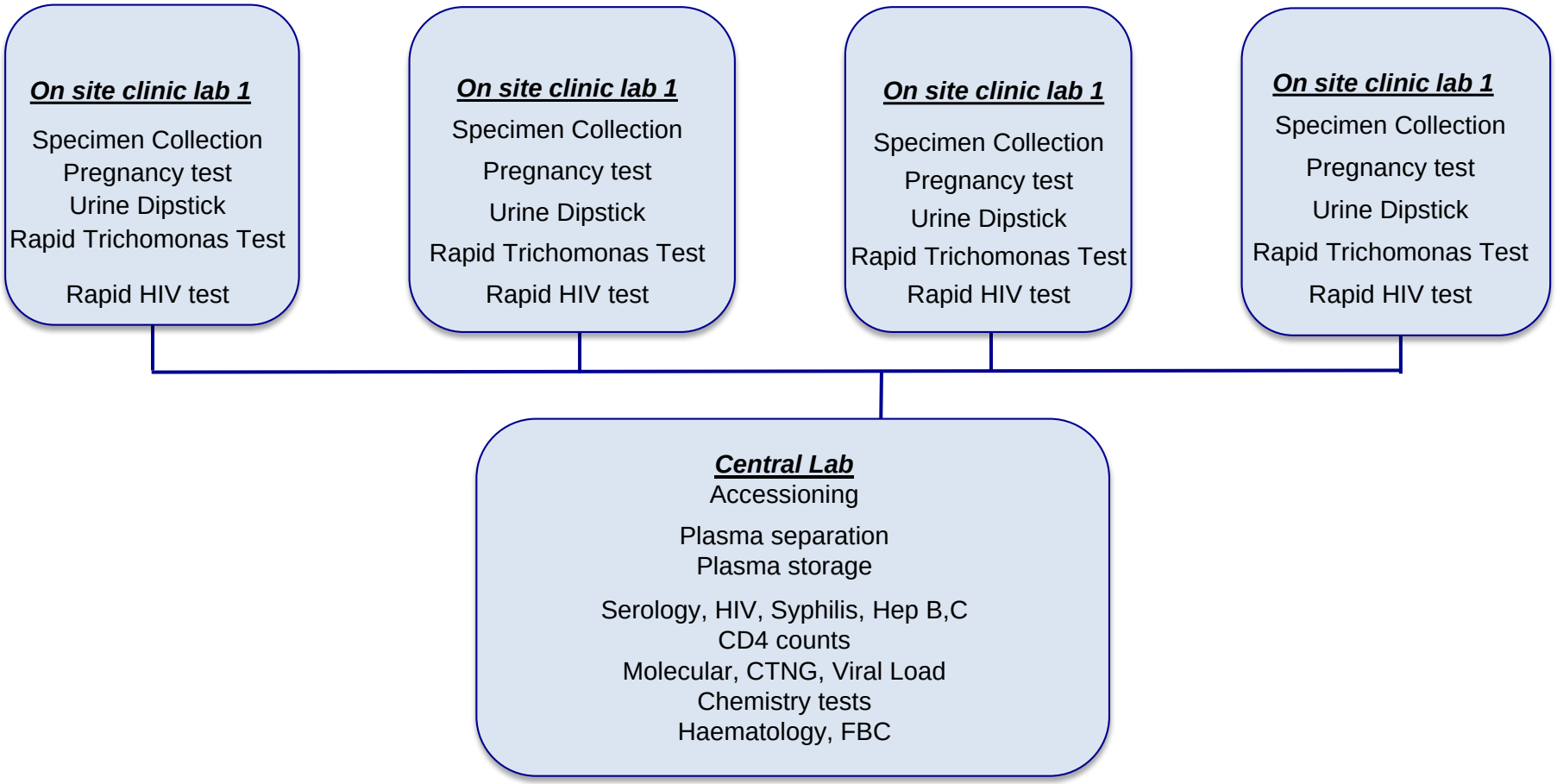
PAL Completion

- 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



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
  - Training available on the DAIDS Learning portal

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Network Evaluation – Laboratory Component

NEW!! NEW!! NEW!!

Monitor	Description	Requirement	Data Source
Quality of specimen handling/ shipment	Number of shipments received within the specified timeframe	90% received within timeframe	LC reports
Specimen storage completeness	Number of aliquots stored/ number of aliquots anticipated per specimen type per visit per protocol	95% storage completeness	SDMC report to LC for interpretation
LDMS Reconciliation	Number of LDMS reports	90% response received within 1 week	LC reports

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HPTN 083

- Storage and Shipping
- Sample completeness
- LDMS reconciliations

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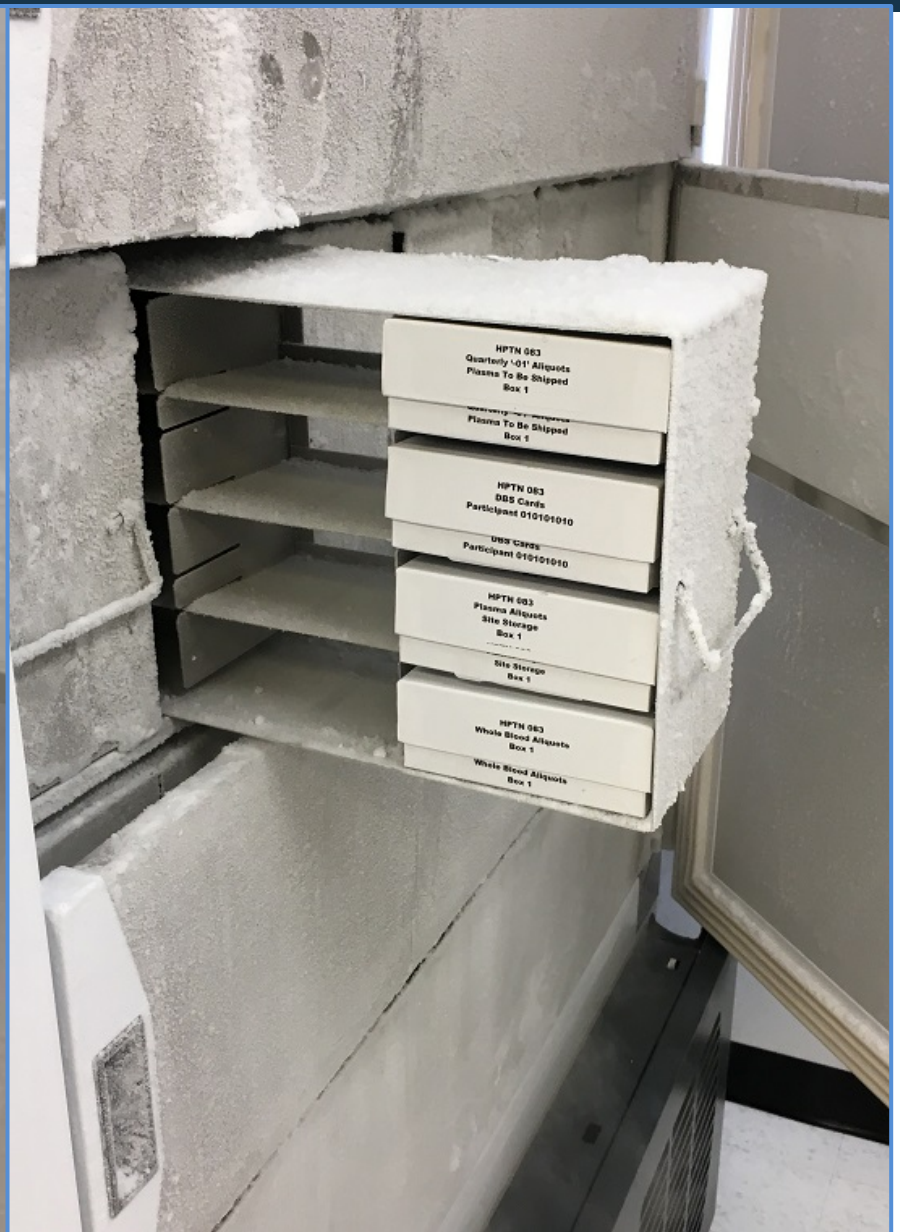
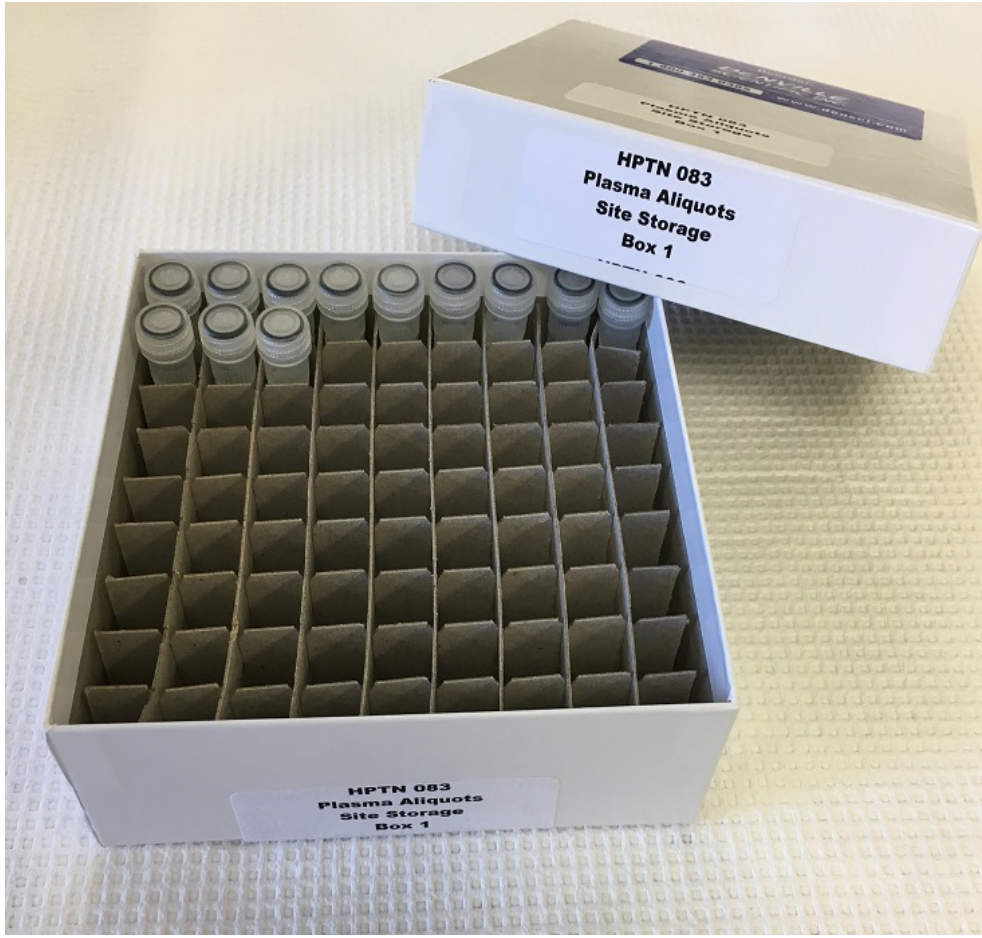


Shipping Requirements – HPTN 083

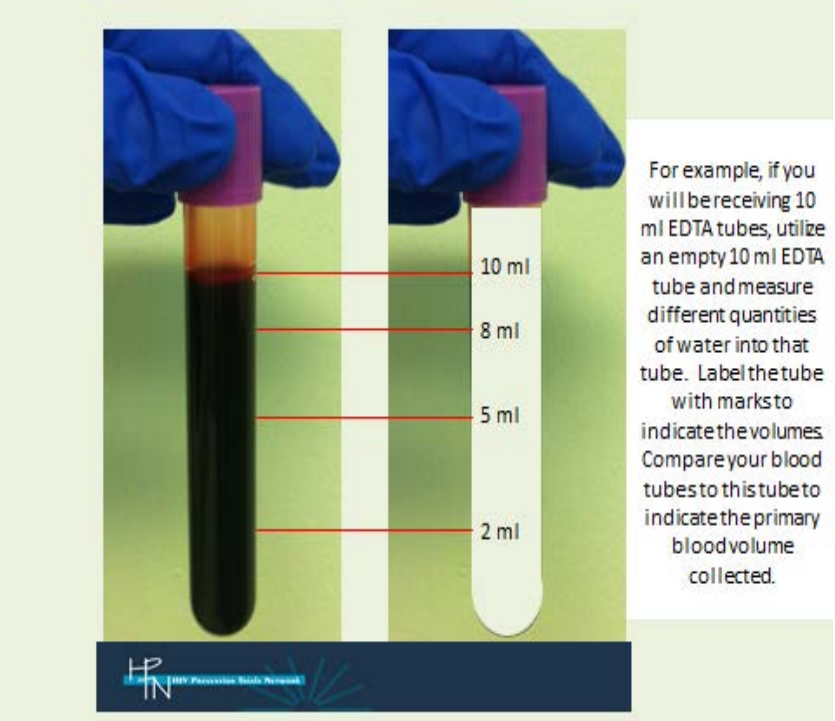
Samples to be shipped quarterly.

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



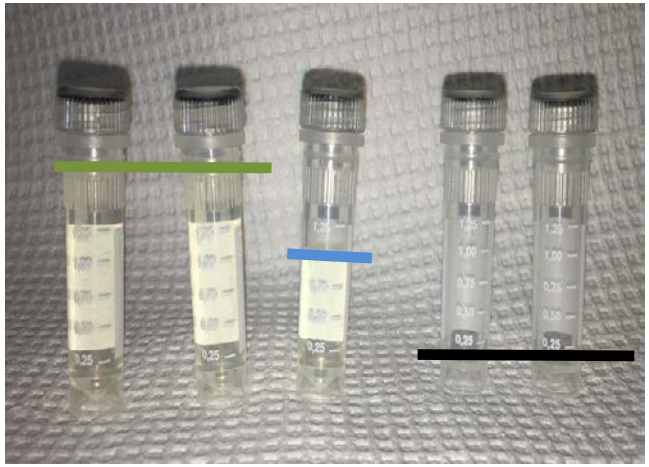
Sample Completeness

- 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 (HPTN 083 – PL2)
- Inform HPTN LC of any short storage
  - 3 or less aliquots of plasma (e.g. HPTN 083)



1.8 mL **1.0 mL** **0.0 mL** (0.01mL, QNS)

Number of aliquots stored/ number of aliquots anticipated per specimen type per visit per protocol

LDMS Reconciliation

Stored specimens and LDMS exportation are key!

- Minimize problems with LDMS
- Ensure that all samples are appropriately collected, labeled and stored
- Discrepancies, errors, and missing storage information must be investigated and responded to within 1 week

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

Lab requisition (LDMS tracking sheet) vs.
LDMS entry (Spec Log/Storage Reports) vs.
Clinic collection and eCRFs

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Differences between HPTN 083 and HVTN704/HPTN085 - AMP

- HIV Diagnostics
- Storage
- Shipping
- LDMS Reconciliation versus SDQC

HIV testing

- AMP – samples go to a regional testing lab for HIV diagnostics
- HPTN 083 – testing is done at the local sites using the HIV algorithm in the protocol:
  - Rapid HIV test(s), FDA cleared
  - 4th or 5th Gen EIA or CMIA
  - RNA at screening within 14 days of enrollment

Storage

- AMP – PL1 (single spun plasma)

  All samples stored -80°C until shipped minimum weekly/biweekly

- HPTN 083 – PL2 (double spun plasma)

  Samples stored on site at -80°C until requested/quarterly

Shipping

- AMP - Samples shipped a minimum of biweekly to a repository and weekly to HIV regional testing lab
  - ✓ Repository disperses samples to testing labs
- 083 - Samples stored on site until requested
  - ✓ 1 aliquot per visit per participant shipped quarterly to LC
  - ✓ DBS shipped quarterly on a request basis
  - ✓ Testing contained within the LC

LDMS reconciliations versus SDQC

- AMP utilizes on-line tool for both clinic and lab, need reliable internet
- HPTN 083 utilizes excel sheets for tracking of clinic LDMS lab related issues, required response within 1 week

Summary

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

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Acknowledgements

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