

## Section 11. Laboratory and Specimen Management Procedures

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## 11.1 Overview of Section 11

This section contains information on the laboratory procedures performed in HPTN 084.

Laboratory procedures will be performed in a variety of settings, including:

1. Clinics
2. Local laboratories
3. The HPTN Laboratory Center (LC, Baltimore, MD, USA)
4. Other laboratories designated by the HPTN LC

Tables in this document list the time points, testing location(s), and specimen requirements for each test. In all settings, laboratory procedures will be performed according to the guidelines included in this section of the SSP and in addition study site Standard Operating Procedures (SOPs) that have been reviewed and approved by the LC. In addition, package insert instructions must be followed.

Ideally, one method, test kit, and/or combination of test kits will be used for each test throughout the duration of the study. **If for any reason a new or alternative method, kit, or test must be used after study initiation, site laboratory staff must inform the HPTN LC to determine if any test kit validation is required.**

Regardless of whether tests are performed in clinic or laboratory settings, study staff that perform the tests must be trained in proper testing and associated quality control (QC) procedures before performing the tests for study purposes; documentation of training should be available for inspection at any time.

As transmission of HIV and other infectious agents can occur through contact with contaminated needles, blood, blood products, and vaginal secretions, all study staff must take appropriate precautions when collecting and handling biological specimens. Guidance on universal precautions is available from the US Centers for Disease Control and Prevention at:

<https://www.cdc.gov/niosh/topics/healthcare/default.html> and  
<https://www.cdc.gov/niosh/topics/bbp/>

Additional reference information can be requested from the HPTN LC. The information provided below is intended to standardize laboratory procedures for HPTN 084 across the study sites. Adherence to the specifications detailed in this section is essential to ensure that primary, secondary and exploratory endpoint data derived from laboratory testing will be considered acceptable to regulatory authorities.

## 11.2 Specimen Labeling

All containers into which specimens are initially collected (e.g., blood collection tubes) will be appropriately labeled according to local practices. Participant Identification (PTID) labels will be provided by the HPTN Statistical and Data Management Center (SDMC, SCHARP) if required

for this function. Laboratory Data Management System (LDMS) Tracking Forms will also be provided for use if required although sites may use their own specimen transport documentation. The staff member who collects the samples will ensure the visit code, specimen collection date and time as well as their initials or code is documented.

More detailed information about the labeling procedures must be provided in the site's Chain of Custody SOP.

When specimens are tested at the laboratories, any additional labeling required for in-country specimen management or chain of custody will be performed in accordance with site-specific SOPs. Stored specimens will be entered into the LDMS and labeled with LDMS-generated labels.

### **11.2.1 Local Specimen Processing and Storage**

For samples that are processed and stored locally, each sample will be entered into the LDMS and labeled with the LDMS generated labels. If needed, any temporary labels (e.g. during plasma processing) for samples will include at least the full PTID, in addition to any other information required by lab SOPs.

### **11.2.2 Local Specimen Testing**

Sites will follow local testing arrangements for the collection and testing of samples, this will be described in the site SOPs. All lab results must be recorded following local guidelines.

### **11.2.3 Remote Specimen Testing**

Samples that will be sent to the HPTN LC will be entered into the LDMS and labeled with the LDMS generated labels.

### **11.2.4 Use of the LDMS**

LDMS must be used at all sites to track specimens that will be tested, stored, or shipped off-site for testing. Detailed instructions for use of LDMS are available in the LDMS User Manual:

<https://www.ldms.org/resources/manuals/>

Web (Cloud-Based) <https://www.ldms.org/resources/ldms/web/>

All sites are responsible for ensuring they are using the most recent version of LDMS. All sites must use the *HPTN barcode* label format in order to ensure that both the specimen ID and the global specimen ID assigned to each specimen are printed on LDMS-generated labels.

An example of a two-dimensional LDMS-generated barcode label is below:

## Windows



500V08000009  
FEQ0043F-01  
999515640 057  
03/Jan/2005 08:00  
BLD EDT PL2 N/A  
1.00 ML 0 Scr

- Row 1: LDMS Specimen ID
- Row 2: Global Specimen ID
- Row 3: Patient Identifier (ID1) and Study/Protocol Identifier (ID2)
- Row 4: Specimen Date or Harvest Date and Specimen Collection Time
- Row 5: Primary Type, Additive Type, Derivative Type, and Sub Additive/Derivative Type
- Row 6: Volume/Volume Unit and Visit/Visit Unit (VID)
- Row 7: Other Specimen ID (if applicable)

## Web



0500-001RDD00-001  
999515640 057.0  
07/Jul/2017 08:30  
BLD EDT PL2 N/A  
1.00 ML 0 Scr

- Row 1: Global Specimen ID
- Row 2: Patient Identifier (ID1) and Study/Protocol Identifier (ID2)
- Row 3: Specimen Date or Harvest Date and Specimen Collection Time
- Row 4: Primary Type, Additive Type, Derivative Type, and Sub Additive/Derivative Type
- Row 5: Volume/Volume Unit and Visit/Visit Unit (VID)

Row 6: Other Specimen ID (if applicable)

Questions related to use of LDMS for HPTN 084 should be directed to Yaw Agyei (yagyei1@jhmi.edu).

Technical support for the general use of LDMS is available from Frontier Science. (www.LDMS.org)

**LDMS User Support at Frontier Science**

Regular Hours: 24-hour coverage 7 days a week with the exception of Select US Holidays – Thanksgiving Day, Christmas Day, New Year’s Day, Memorial Day, Independence Day. See below for contact details.

<https://www.ldms.org/contact/>

Phone: +1 (716) 834-0900, extension 7311

Email: [ldmshelp@fstrf.org](mailto:ldmshelp@fstrf.org)

Fax: +1 (716) 832-8448 (should be used to fax Installation Reports only)

When you contact LDMS user support, there are certain pieces of information that you can provide to help them better respond to your question. Please provide the following information in your email support:

**1. Your name**

**2. Your laboratory’s LDMS ID number**

This is a 3-digit number assigned by Frontier Science to uniquely identify your laboratory. It appears when you start LDMS, and can also be found in the bottom-right corner of the screen.

**3. A full explanation of the issue**

Your explanation should include any error messages or error numbers that appeared, what you were doing in LDMS at the time the issue occurred, and steps needed to reproduce the issue. The more details that you can provide, the faster LDMS User Support can help you.

**4. How you want to be contacted**

If you want LDMS user support to call a specific telephone number, please provide that number and extension.

**5. (If applicable) The license code or challenge code being generated by LDMS**

Note: If you are contacting user support about a license or challenge code, do not close the window with the code. Doing so will cause LDMS to generate a new code.

Below are a few other details that can also be helpful to include in your email:

1. Have there been any recent changes to the computer with LDMS, such as new hardware installed, a firewall upgrade, a network name change, or another change?
2. Are you or another user able to repeat the issue?
3. If you have LDMS installed on multiple computers, does the issue occur on all of them or does it only occur on a specific computer?

Each site using the windows version of LDMS must export its LDMS data to Frontier Science (FSTRF) on a minimum weekly basis or whenever changes or additions are made to the LDMS database.

Exported data are used by the HPTN SDMC to generate daily Specimen Data Quality Check (SDQC) reports comparing the data from the LDMS with that entered onto the CRFs/Medidata Rave. Any discrepancies identified are included in the SDQC for each site. The HPTN SDMC reviews the discrepancy reports for critical samples (e.g., plasma needed for confirmatory HIV testing) that appear to be missing and works with the LC and site staff to undertake appropriate corrective action. All corrective action should be documented in paper-based clinic and/or laboratory records per site standards (CAPA or NTF) as appropriate and entered in the details section of LDMS. Any corrections to the LDMS need to be made following guidelines provided by FSTRF on behalf of the HPTN LC.

#### 11.2.5 LDMS Reconciliation

All sites must follow the HPTN LC approved site-specific SOP for regular reconciliation and verification of specimens that are stored; these independent SOPs or detailed Chain of Custody procedures must be followed throughout the study. All sites must also create a monthly Primary Specimen report to submit to the HPTN LC for review. See section 11.12 for directions on how to make a primary specimen report. The report will provide the HPTN LC with the primary blood draw information for each participant logged into the LDMS. **In addition, all sites must create a Specimen Log report to submit weekly to the HPTN LC for review.** See section 11.12 for directions on how to make a specimen log report. The report will provide the HPTN LC with the participant, primary, and aliquot information for each of the specimens logged into the site LDMS during the week. The report also provides the condition codes, comments, and shipping information (if available) for the given specimens. In the event that the required volume or number of sample aliquots based on Sections 11.3 and 11.4 is not obtained at any time point, designated site clinic and lab staff must immediately inform the HPTN LC. The LC will liaise with the LOC, and HPTN SDMC and will provide guidance on how to respond to the problem. In addition to following this guidance, designated site and lab staff will work together to document the problem, take appropriate corrective and preventive action, and document all action taken. Reconciliation must be performed for all specimen types that are received by the laboratory and stored in the LDMS. It is the originating processing LDMS laboratory responsibility to notify subsequent laboratories with changes, corrections, and modification to LDMS entries of shipped samples e.g. DBS cards, Plasma aliquots.

### 11.3 Protocol related testing and sample collection

Samples will be collected and processed at the screening, enrollment, and follow up visits as indicated in tables 11-1, 11-2, 11-3.

Participants who have received at least one injection and refuse further injections or discontinue due to an AE will enter Step 3 and be followed on open-label TDF/FTC according to Step 3 as indicated in table 11-3.

Participants who are unable to receive the first injection for any reason will be terminated from the study. If the reason is due to HIV infection, those participants will be referred for care and will be terminated from the study.

Collect specimens and label tubes according to manufacturer recommendations and local regulations as well as the Blood Collection, Breast milk, Cord blood, and Urine Collection SOPs. Blood collection tubes must be filled to the appropriate fill level as indicated by the tube manufacturer. After collection:

- EDTA tubes should be gently inverted at least 8 times (or as specified by manufacturer) after specimen collection, to prevent clotting.
- EDTA collections must be performed after samples collected for serum chemistry testing.
- For plasma storage, 20 mL of whole blood should be collected into spray dried EDTA tubes, e.g. BD 366643 or other, to yield 5 x 1.8mL plasma aliquots.
- For Pharmacogenomic testing, a minimum of 1mL of whole blood should be collected in an EDTA tube.
- For Cord blood, collect in a 5mL K2EDTA tube, to yield 2 X 1.0ml plasma aliquots
- For infant collections, collect 750uL to 1ml K2EDTA to yield 300uL of plasma.
- Breast milk will be collected in sufficient quantity to store a minimum of 3 mL of whole breast milk.



**Table 11-1: Schedule of Study Visits and Specimen Collection –Step 1. Screening, Enrollment, Week 2 and 4.**

	Screening	Step 1		
		Day 0 Enrollment	Week 2	Week 4
HIV testing <sup>1</sup>	X	X	X	X
Pregnancy testing <sup>2</sup>	X	X	X	X
HBV and HCV testing <sup>3</sup>	X	X		
CBC with Differential	X	X	X	X
Chemistry testing (BUN/urea, creatinine, CPK, calcium, phosphorous, glucose, amylase and lipase)	Creatinine only	X	X	X
Liver Function Test (AST, ALT, total bilirubin, alkaline phosphatase)	ALT and Total Bilirubin only	X		X
Fasting Lipid Profile <sup>4</sup>		X		
Syphilis serological testing		X		
GC/CT and TV testing <sup>5</sup>		X		
Urinalysis (protein and glucose) <sup>6</sup>		X		
Plasma Storage <sup>7</sup>	X	X	X	X
DBS storage <sup>7</sup>				X
Whole blood storage <sup>7</sup>		X		
Additional sample storage for participants enrolled in the Injectable Contraception Sub-Study <sup>7</sup>		X		

<sup>1</sup> Following the HIV algorithms described in SSP figures 11.1 to 11.3, section 11.3. RNA testing for acute HIV must be negative and must be performed within 14 days of enrolling the participant. At least one HIV test must be available the same day as sample collection and before product is administered. HIV testing does not need to be performed after confirmation of HIV infection (based on results from samples collected on two separate dates).

<sup>2</sup> Pregnancy testing may be performed in the clinic or the laboratory. Results must be available the same day as sample collection and before product is administered. Testing may be performed using a urine, plasma, or serum sample. The assay used for pregnancy testing must have a limit of detection of 25 mIU/mL or lower. Pregnancy testing is not required at subsequent visits if a positive result is obtained and the participant is still pregnant.

<sup>3</sup> At Screening: HBsAg and HCV antibody testing. At Enrollment: HBsAb and HBcAb total testing. Note: These tests can all be done at Screening at the discretion of the IOR

<sup>4</sup> The fasting lipid profile includes total cholesterol, HDL, triglycerides, and LDL (either calculated or measured). Participants should have fasted for at least 8 hours, preferably 12 hours, prior to sample collection. If participants are not fasting, do not order the lipid testing. Participants may return for testing or it can be performed at next visit.

<sup>5</sup> GC/CT NAAT testing may be performed using urine or a vaginal swab; TV testing is performed using a vaginal swab.

<sup>6</sup> Urinalysis may be performed in the clinic or the laboratory. Results from urinalysis are not needed prior to enrollment.

<sup>7</sup> See section 11.4 for plasma processing and storage instructions; section 11.6 for DBS processing and storage instructions; section 11.7 for whole blood storage instructions; section 11.5 for Injectable Contraception sub-study storage instructions. **Blood must be collected prior to study product administration during the visit. Also, record the date that the participant's LARC was last injected/inserted).** Whole blood collection and storage is only required for participants who consent to genetic testing.

**Table 11-2: Schedule of Study Visits and Specimen Collection – Step 2. Blinded Injections and Daily Oral Pills**

	Week 5	Week 6	Week 9	Week 13	Week 17	Week 21	Week 25	Week 33	Week 41	Week 42	Week 49	Week 57
HIV testing <sup>1</sup>	X	X	X	X	X	X	X	X	X	X	X	X
Pregnancy testing <sup>2</sup>	X	X	X	X	X	X	X	X	X	X	X	X
HCV antibody testing												X
CBC with Differential	X	X	X	X	X	X	X	X	X	X	X	X
Chemistry testing (BUN/urea, creatinine, CPK, calcium, phosphorous, glucose, amylase and lipase)	X	X	X	X	X	X	X	X	X	X	X	X
LFT (AST, ALT, total bilirubin, alkaline phosphatase)	X	X	X	X	X	X	X	X	X	X	X	X
Fasting Lipid Profile <sup>3</sup> (Total Cholesterol, HDL, LDL, Triglycerides)												X
Syphilis serological testing								X				X
Urine GC/CT and TV testing <sup>4</sup>								X				X
Urinalysis (protein and glucose)												X
Plasma Storage <sup>5</sup>	X	X	X	X	X	X	X	X	X	X	X	X
DBS storage <sup>5</sup>								X				X
Additional sample storage for participants enrolled in the injectable Contraception Sub-study <sup>5</sup>			X	X	X	X	X					

<sup>1</sup> Following the HIV algorithms described in SSP figures 11.1 to 11.3, section 11.3.1. At least one HIV test must be available the same day as sample collection and before product is administered. HIV testing does not need to be performed after confirmation of HIV infection (based on results from samples collected on two separate dates). Additional HIV testing may be requested by the 084HIV alias.

<sup>2</sup> Pregnancy testing may be performed in the clinic or the laboratory. Results must be available the same day as sample collection and before product is administered. Testing may be performed using a urine, plasma, or serum sample. The assay used for pregnancy testing must have a limit of detection of 25 mIU/mL or lower. Pregnancy testing is not required at subsequent visits if a positive result is obtained and the participant is still pregnant.

<sup>3</sup> Participants should have fasted for at least 8 hours, preferably 12 hours, prior to sample collection. If participants are not fasting, do not order the lipid testing. Participants may return for testing or it can be performed at next visit.

<sup>4</sup> GC/CT NAAT testing may be performed using urine or a vaginal swab; TV testing is performed using a vaginal swab.

<sup>5</sup> See section 11.4 for plasma processing and storage instructions; section 11.6 for DBS processing and storage instructions; section 11.5 for Injectable Contraception sub-study storage instructions. Whole blood collection and storage is only required for participants who consent to genetic testing.

**Table 11-2 (Cont'd): Schedule of Study Visits and Specimen Collection – Step 2. Blinded Injections and Daily Oral Pills**

	Week 65	Week 73	Week 81	Week 89	Week 97	Week 105
HIV testing <sup>1</sup>	X	X	X	X	X	X
Pregnancy testing <sup>2</sup>	X	X	X	X	X	X
HCV antibody testing						X
CBC with Differential	X	X	X	X	X	X
Chemistry testing (BUN/urea, creatinine, CPK, calcium, phosphorous, glucose, amylase and lipase)	X	X	X	X	X	X
LFT (AST, ALT, total bilirubin, alkaline phosphatase)	X	X	X	X	X	X
Fasting Lipid Profile <sup>3</sup> (Total Cholesterol, HDL, LDL, Triglycerides)						X
Syphilis serological testing			X			X
Urine GC/CT testing and TV testing <sup>4</sup>			X			X
Urinalysis (protein and glucose)						X
Plasma Storage <sup>5</sup>	X	X	X	X	X	X
DBS storage <sup>5</sup>			X			X
Additional sample storage for participants enrolled in the injectable Contraception Sub-study <sup>5</sup>						

<sup>1</sup> Following the HIV algorithms described in SSP figures 11.1 to 11.3, section 11.3.1. At least one HIV test must be available the same day as sample collection and before product is administered. HIV testing does not need to be performed after confirmation of HIV infection (based on results from samples collected on two separate dates). Additional HIV testing may be requested by the 084HIV alias.

<sup>2</sup> Pregnancy testing may be performed in the clinic or the laboratory. Results must be available the same day as sample collection and before product is administered. Testing may be performed using a urine, plasma, or serum sample. The assay used for pregnancy testing must have a limit of detection of 25 mIU/mL or lower. Pregnancy testing is not required at subsequent visits if a positive result is obtained and the participant is still pregnant.

<sup>3</sup> Participants should have fasted for at least 8 hours, preferably 12 hours, prior to sample collection. If participants are not fasting, do not order the lipid testing. Participants may return for testing or it can be performed at next visit.

<sup>4</sup> GC/CT NAAT testing may be performed using urine or a vaginal swab; TV testing is performed using a vaginal swab.

<sup>5</sup> See section 11.4 for plasma processing and storage instructions; section 11.6 for DBS processing and storage instructions; section 11.5 for Injectable Contraception sub-study storage instructions. Whole blood collection and storage is only required for participants who consent to genetic testing.

**Table 11-2 (Cont'd): Schedule of Study Visits and Specimen Collection – Step 2. Blinded Injections and Daily Oral Pills**

	Week 113	Week 121	Week 129	Week 137	Week 145	Week 153
HIV testing <sup>1</sup>	X	X	X	X	X	X
Pregnancy testing <sup>2</sup>	X	X	X	X	X	X
HCV antibody testing						X
CBC with Differential	X	X	X	X	X	X
Chemistry testing (BUN/urea, creatinine, CPK, calcium, phosphorous, glucose, amylase and lipase)	X	X	X	X	X	X
LFT (AST, ALT, total bilirubin, alkaline phosphatase)	X	X	X	X	X	X
Fasting Lipid Profile <sup>3</sup> (Total Cholesterol, HDL, LDL, Triglycerides)						
Syphilis serological testing			X			X
Urine GC/CT testing and TV testing <sup>4</sup>			X			X
Urinalysis (protein and glucose)						X
Plasma Storage <sup>5</sup>	X	X	X	X	X	X
DBS storage <sup>5</sup>			X			X

<sup>1</sup> Following the HIV algorithms described in SSP figures 11.1 to 11.3, section 11.3.1. At least one HIV test must be available the same day as sample collection and before product is administered. HIV testing does not need to be performed after confirmation of HIV infection (based on results from samples collected on two separate dates). Additional HIV testing may be requested by the 084HIV alias.

<sup>2</sup> Pregnancy testing may be performed in the clinic or the laboratory. Results must be available the same day as sample collection and before product is administered. Testing may be performed using a urine, plasma, or serum sample. The assay used for pregnancy testing must have a limit of detection of 25 mIU/mL or lower. Pregnancy testing is not required at subsequent visits if a positive result is obtained and the participant is still pregnant.

<sup>3</sup> Participants should have fasted for at least 8 hours, preferably 12 hours, prior to sample collection. If participants are not fasting, do not order the lipid testing. Participants may return for testing or it can be performed at next visit.

<sup>4</sup> GC/CT NAAT testing may be performed using urine or a vaginal swab; TV testing is performed using a vaginal swab.

<sup>5</sup> See section 11.4 for plasma processing and storage instructions; section 11.6 for DBS processing and storage instructions.

**Table 11-2 (Cont'd): Schedule of Study Visits and Specimen Collection – Step 2. Blinded Injections and Daily Oral Pill**

	Week 161	Week 169	Week 177	Week 185
HIV testing <sup>1</sup>	X	X	X	X
Pregnancy testing <sup>2</sup>	X	X	X	X
HCV antibody testing				
CBC with Differential	X	X	X	X
Chemistry testing (BUN/urea, creatinine, CPK, calcium, phosphorous, glucose, amylase and lipase)	X	X	X	X
LFT (AST, ALT, total bilirubin, alkaline phosphatase)	X	X	X	X
Fasting Lipid Profile <sup>3</sup> (Total Cholesterol, HDL, LDL, Triglycerides)				
Syphilis serological testing			X	
Urine GC/CT testing and TV testing <sup>4</sup>			X	
Urinalysis (protein and glucose)				
Plasma Storage <sup>5</sup>	X	X	X	X
DBS storage <sup>5</sup>			X	

<sup>1</sup> Following the HIV algorithms described in SSP figures 11.1 to 11.3, section 11.3.1 HIV testing does not need to be performed after confirmation of HIV infection (based on results from samples collected on two separate dates). Additional HIV testing may be requested by the 084HIV alias.

<sup>2</sup> Pregnancy testing may be performed in the clinic or the laboratory. Results must be available the same day as sample collection and before product is administered. Testing may be performed using a urine, plasma, or serum sample. The assay used for pregnancy testing must have a limit of detection of 25 mIU/mL or lower. Pregnancy testing is not required at subsequent visits if a positive result is obtained and the participant is still pregnant.

<sup>3</sup> Participants should have fasted for at least 8 hours, preferably 12 hours, prior to sample collection. If participants are not fasting, do not order the lipid testing. Participants may return for testing or it can be performed at next visit.

<sup>4</sup> GC/CT NAAT testing may be performed using urine or a vaginal swab; TV testing is performed using a vaginal swab.

<sup>5</sup> See section 11.4 for plasma processing and storage instructions; section 11.6 for DBS processing and storage instructions.

**Table 11-3: Schedule of Study Visits and Specimen Collection – Step 3. Open Label TDF/FTC Daily Oral (Post-Last Injection)**

	Step 3 Day 0*	Step 3 Week 12	Step 3 Week 24	Step 3 Week 36	Step 3 Week 48
HIV testing <sup>1</sup>	X	X	X	X	X
Pregnancy testing <sup>2</sup>	X	X	X	X	X
Chemistry testing <sup>3</sup>			X		X
Liver function testing <sup>4</sup>			X		X
Syphilis testing	X <sup>5</sup>		X		X
GC/CT and TV testing <sup>6</sup>	X <sup>5</sup>		X		X
Plasma storage <sup>7</sup>	X	X	X	X	X
DBS storage <sup>7</sup>			X		X

<sup>1</sup> Following the HIV algorithms described in SSP figures 11.1 to 11.3, section 11.3.1. At least one HIV test must be available the same day as sample collection and before product is administered. HIV testing does not need to be performed after confirmation of HIV infection (based on results from samples collected on two separate dates). Additional HIV testing may be requested by the 084HIV alias.

<sup>2</sup> Pregnancy testing may be performed in the clinic or the laboratory. Results must be available the same day as sample collection and before product is administered. Testing may be performed using a urine, plasma, or serum sample. The assay used for pregnancy testing must have a limit of detection of 25 mIU/mL or lower. Pregnancy testing is not required at subsequent visits if a positive result is obtained and the participant is still pregnant.

<sup>3</sup> Chemistry testing includes: BUN/Urea, creatinine, CPK, calcium, phosphorous, glucose, amylase, and lipase.

<sup>4</sup> Liver function testing includes: AST, ALT, TBili, and alkaline phosphatase.

<sup>5</sup> Skip Day 0 if testing has occurred within the last 3 months of Day 0 and do only at Weeks 24 and 48.

<sup>6</sup> GC/CT NAAT testing may be performed using urine or a vaginal swab; TV testing is performed using a vaginal swab.

<sup>7</sup> See section 11.4 for plasma processing and storage instructions; section 11.6 for DBS processing and storage instructions.

**Table 11-4: Additional Procedures: Participants who have a Reactive or Positive HIV test at any time after Enrollment**

	HIV Confirmation visit	Post HIV + Week 12	Post HIV + Week 24	Post HIV + Week 36	Post HIV + Week 48 <sup>1</sup>
HIV testing <sup>2</sup>	X				
CD4 cell count.	X		X		X
HIV viral load testing	X		X		X
HIV resistance testing <sup>3</sup>	X				
Chemistry testing (BUN/Urea, creatinine, CPK, calcium, phosphorous, glucose, amylase, lipase)		X	X	X	X
LFT (AST, ALT, total bilirubin, alkaline phosphatase)		X	X	X	X
Plasma Storage <sup>4,5</sup>	X	X	X	X	X
DBS storage <sup>5</sup>	X				

<sup>1</sup>The week 48 visit should be timed as closely as possible to 52 weeks after the participant received their last injection.

<sup>2</sup> The HIV confirmatory visit must be held on a different day from the visit where the participant had their initial reactive/positive HIV test. The testing algorithm for the HIV Confirmation Visit is provided in the SSP Manual. If HIV rapid testing is included in the HIV testing algorithm, this testing may be performed in the clinic or the laboratory. Additional HIV testing may be requested by the 084HIV alias.

<sup>3</sup> Sites may collect specimens for resistance testing at a local laboratory to assist with clinical management; results from resistance testing performed at local laboratories will not be reported to the SDMC. Stored plasma may not be used real-time/local resistance testing; additional samples must be collected for this testing.

<sup>4</sup> Stored plasma will be used for Quality Assurance testing and other assessments at the HPTN LC (see Section 9). Assessments will be performed retrospectively; results will not be returned to study sites or participants, except as noted in Section 9.0.

<sup>5</sup>See section 11.4 for plasma processing and storage instructions; section 11.6 for DBS processing and storage instructions.

The Seroconversion Committee (084HIV@hptn.org) must be notified immediately and study drug should be discontinued if one or more reactive HIV test results are obtained on the Laboratory based test at enrollment or at any follow up visit after enrollment. The procedures listed for Weeks 12, 24, 36, and 48 apply only to participants with confirmed HIV infection during Step 2 of the study. Participants with confirmed HIV infection in Step 3 of the study may undergo similar procedures and will be determined by the members of the 084HIV@hptn.org. Note that participants who acquire HIV infection during Step 1 will permanently discontinue study product, will be terminated from the study, and referred for HIV related care. The additional blood draw for HIV testing and plasma storage at the HIV confirmation visit should be performed on a different date than the blood draw that gave the initial reactive or positive HIV test.

**Table 11-5: Schedule of Study Visits and Specimen Collection: For Pregnant Participants**

<b>WEEKS in Study</b>	<b>4 weeks after first positive pregnancy test</b>	<b>Quarterly Visit 1 (12 weeks since first positive pregnancy test)</b>	<b>Quarterly Visit 2 (24 weeks since first positive pregnancy test)</b>	<b>Quarterly Visit 3 (36 weeks since first positive pregnancy test)</b>
<b>LOCAL LABORATORY EVALUATIONS &amp; PROCEDURES</b>				
<b>HIV testing<sup>1</sup></b>	X	X	X	X
<b>Pregnancy testing<sup>2</sup></b>	X			
<b>Chemistry testing<sup>4</sup></b>			X	
<b>Liver function testing<sup>5</sup></b>			X	
<b>Syphilis testing</b>	X <sup>7</sup>		X	
<b>Vaginal GC/CT and TV Testing<sup>3</sup></b>	X <sup>7</sup>		X	
<b>Plasma storage<sup>6</sup></b>	X	X	X	X
<b>DBS storage</b>	X	X	X	X

<sup>1</sup> The HIV testing algorithm is provided in the SSP Manual. If HIV rapid testing is indicated, this testing may be performed in the clinic or the laboratory. At least one HIV test must be available the same day as sample collection and before product is administered.

<sup>2</sup> Pregnancy testing may be performed in the clinic or the laboratory. Results must be available the same day as sample collection and before product is administered. Testing may be performed using a urine, plasma, or serum sample. The assay used for pregnancy testing must have a limit of detection of 25 mIU/mL or lower. Pregnancy testing is not required at subsequent visits if a positive result is obtained and the participant is still pregnant. If the confirmatory pregnancy test is positive, the participant is referred for an Ultrasound and evaluation by an obstetric specialist at about 12-14 weeks gestational age, for other testing, counseling, and management. Further biochemical blood testing may be done as indicated. All findings and outcomes will be collected and reported.

<sup>3</sup> GC/CT NAAT testing may be performed using urine or a vaginal swab; TV testing is performed using a vaginal swab.

<sup>4</sup> BUN/urea, creatinine, CPK, calcium, phosphorous, glucose, amylase, and lipase.

<sup>5</sup> AST, ALT, TBili, and alkaline phosphatase.

<sup>6</sup> Stored plasma will be used for Quality Assurance testing and other assessments at the HPTN LC (see Section 9). Assessments will be performed retrospectively; results will not be returned to study sites or participants, except as noted in Section 9.0.

<sup>7</sup> If not done within 4 weeks of initial positive pregnancy test



**Table 11-6: Schedule of Evaluations - Step 2, Injectable Contraceptive Substudy ONLY**

Weeks in study	Enrollment	5	6	9	13	17	21	25	33	41	42	49	57	65	73	81	89	97	105	113	121	129	137	145	153	161	169	177	185	
Plasma storage <sup>1,2</sup>	X							X				X			X															
DBS <sup>1,2</sup>	X							X				X			X															

<sup>1</sup> Additional stored plasma will be used for PK evaluations and DMPA, NET-EN, Etongestrel

<sup>2</sup> Blood must be collected prior to study product administration during the visit. Also, record the date that the participant's LARC was last injected/inserted.

### 11.3.1 Open Label (OL) Cabotegravir samples.

**Table 11-7: Schedule of Evaluations - Step 4a, Participants initially randomized to TDF/FTC who elect to move to OL CAB LA with optional Oral Lead-In First.**

	<b>DAY 0/ of Step 4a</b>
<b>HIV testing<sup>2</sup></b>	X
<b>HIV viral load testing<sup>3</sup></b>	X
<b>Pregnancy testing<sup>1</sup></b>	X
<b>CBC with differential,</b>	X
<b>Chemistry testing<sup>4</sup></b>	X
<b>Liver function tests<sup>5</sup></b>	X
<b>Fasting lipid profile,</b>	X
<b>Plasma storage<sup>7,8</sup></b>	X
<b>DBS storage<sup>8</sup></b>	X

<sup>1</sup> Pregnancy testing may be performed in the clinic or the laboratory. Results must be available the same day as sample collection and before product is administered. Testing may be performed using a urine, plasma, or serum sample. The assay used for pregnancy testing must have a limit of detection of 25 mIU/mL or lower. Pregnancy testing is not required at subsequent visits if a positive result is obtained and the participant is still pregnant.

<sup>2</sup> HIV rapid testing may be performed in the clinic or the laboratory. At least one HIV test must be available the same day as sample collection and before product is administered.

<sup>3</sup> This testing will be performed for all study participants, regardless of HIV status or the results of other HIV tests. This testing must be performed with an assay with a lower limit of quantification of 50 copies/mL or lower.

<sup>4</sup> Albumin, BUN/urea, creatinine. Additional testing may be required if abnormalities of clinical significance are detected.

<sup>5</sup> AST, ALT, total bilirubin.

<sup>6</sup> Total cholesterol, HDL, triglycerides, and LDL (either calculated or measured). Participants should have fasted for at least 8 hours, preferably 12 hours, prior to sample collection. If participants are not fasting, do not order the lipid testing. Participants may return for testing or it can be performed at next visit

<sup>7</sup> Stored plasma may be used for Quality Assurance testing, possible HSV-2 testing and other assessments at the HPTN LC.

<sup>8</sup> Assessments on stored samples will be performed retrospectively; results will not be returned to study sites or participants, except as noted in the SSP.

**Table 11-8: Schedule of Evaluations - Step 4b, Participants initiating or re-starting CAB LA without the optional Oral Lead-In; the initial Dose Visit.**

	<b>DAY 0/ of Step 4b</b>
<b>HIV testing<sup>2</sup></b>	X
<b>HIV viral load testing<sup>3</sup></b>	X
<b>Pregnancy testing<sup>1</sup></b>	X
<b>CBC with differential, if not done in Step 4a</b>	X
<b>Chemistry testing<sup>4</sup></b>	X
<b>Liver function tests<sup>5</sup></b>	X
<b>Fasting lipid profile, if not done in Step 4a<sup>6</sup></b>	X
<b>Plasma storage<sup>7,8</sup></b>	X
<b>DBS storage<sup>8</sup></b>	X

<sup>1</sup> Pregnancy testing may be performed in the clinic or the laboratory. Results must be available the same day as sample collection and before product is administered. Testing may be performed using a urine, plasma, or serum sample. The assay used for pregnancy testing must have a limit of detection of 25 mIU/mL or lower. Pregnancy testing is not required at subsequent visits if a positive result is obtained and the participant is still pregnant.

<sup>2</sup> HIV rapid testing may be performed in the clinic or the laboratory. At least one HIV test must be available the same day as sample collection and before product is administered.

<sup>3</sup> This testing will be performed for all study participants, regardless of HIV status or the results of other HIV tests. This testing must be performed with an assay with a lower limit of quantification of 50 copies/mL or lower.

<sup>4</sup> Albumin, BUN/urea, creatinine. Additional testing may be required if abnormalities of clinical significance are detected.

<sup>5</sup> AST, ALT, total bilirubin.

<sup>6</sup> Total cholesterol, HDL, triglycerides, and LDL (either calculated or measured). Participants should have fasted for at least 8 hours, preferably 12 hours, prior to sample collection. If participants are not fasting, do not order the lipid testing. Participants may return for testing or it can be performed at next visit

<sup>7</sup> Stored plasma may be used for Quality Assurance testing, possible HSV-2 testing and other assessments at the HPTN LC.

<sup>8</sup> Assessments on stored samples will be performed retrospectively; results will not be returned to study sites or participants, except as noted in the SSP.

**Table 11-9: Schedule of Evaluations - Step 4c, Participants on maintenance Dose of CAB LA or TDF/FTC**

Time on OL Study Product	Week 0 of Step 4c <sup>±</sup>	Week 8	Week 16	Week 24	Week 32	Week 40	Week 48
HIV testing <sup>2</sup>	X	X	X	X	X	X	X
HIV viral load testing <sup>3</sup>	X	X	X	X	X	X	X
Pregnancy testing <sup>1</sup>	X	X	X	X	X	X	X
CBC with differential, if not done in Step 4a or 4b	X <sup>5</sup>			X			X
Chemistry testing, <sup>4</sup>	X <sup>5</sup>			X			X
Liver function testing <sup>6</sup>	X			X			X
Fasting lipid profile <sup>7</sup>							X
Syphilis testing	X			X			X
Vaginal GC/CT and TV testing <sup>8</sup>	X			X			X
Urinalysis (protein, glucose)	X			X			X
Plasma storage <sup>8,9,10</sup>	X	X	X	X	X	X	X
DBS storage <sup>9</sup>	X	X	X	X	X	X	X

<sup>1</sup> Pregnancy testing may be performed in the clinic or the laboratory. Results must be available the same day as sample collection and before product is administered. Testing may be performed using a urine, plasma, or serum sample. The assay used for pregnancy testing must have a limit of detection of 25 mIU/mL or lower. Pregnancy testing is not required at subsequent visits if a positive result is obtained and the participant is still pregnant.

<sup>2</sup> HIV rapid testing may be performed in the clinic or the laboratory. At least one HIV test must be available the same day as sample collection and before product is administered.

<sup>3</sup> This testing will be performed for all study participants, regardless of HIV status or the results of other HIV tests. This testing must be performed with an assay with a lower limit of quantification of 50 copies/mL or lower.

<sup>4</sup> Albumin, BUN/urea, creatinine. Additional testing may be required if abnormalities of clinical significance are detected.

<sup>5</sup> Only for those who did not have this collected in steps 4a and 4b

<sup>6</sup> AST, ALT, total bilirubin.

<sup>7</sup> Total cholesterol, HDL, triglycerides, and LDL (either calculated or measured). Participants should have fasted for at least 8 hours, preferably 12 hours, prior to sample collection. If participants are not fasting, do not order the lipid testing. Participants may return for testing or it can be performed at next visit

<sup>8</sup> GC/CT and TV testing to be done only if not performed in the past 3 months. GC/CT NAAT testing may be performed using urine or a vaginal swab; TV testing is performed using a vaginal swab. If a woman is menstruating, the swab may be collected at a later visit and all testing using the swab may be performed at that later visit

<sup>9</sup> Stored plasma may be used for Quality Assurance testing, possible HSV-2 testing and other assessments at the HPTN LC.

<sup>10</sup> Assessments on stored samples will be performed retrospectively; results will not be returned to study sites or participants, except as noted in the SSP.

**Table 11-10: Schedule of Evaluations - Step 4d, Participants who become pregnant during step 4 and who received at least one CAB LA injection.**

Time on Pregnancy and Infant Sub-study	Week 0	Week 4	Week 8	Week 12	Week 16	Week 20	Week 24	Week 28	Week 32	Week 36	Week 40	Delivery	Week 2, pp	Week 4, pp	Week 8, pp	Week 16 pp	Week 24, pp	Week 32, pp	Week 40, pp	Week 48, pp	
HIV testing <sup>1</sup>	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
HIV viral load testing <sup>2</sup>	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Pregnancy testing <sup>3</sup>															X	X	X	X	X	X	X
CBC with differential	X						X			X					X						X
Chemistry testing <sup>4</sup>	X						X			X					X						X
Liver function testing <sup>5</sup>	X						X			X					X						X
Syphilis testing	X						X								X						X
Vaginal GC/CT and TV testing <sup>6</sup>	X						X								X						X
Urinalysis (protein, glucose)	X						X			X					X						X

<b>Time on Pregnancy and Infant Sub-study</b>	<b>Week 0</b>	<b>Week 4</b>	<b>Week 8</b>	<b>Week 12</b>	<b>Week 16</b>	<b>Week 20</b>	<b>Week 24</b>	<b>Week 28</b>	<b>Week 32</b>	<b>Week 36</b>	<b>Week 40</b>		<b>Delivery</b>	<b>Week 2, pp</b>	<b>Week 4, pp</b>	<b>Week 8, pp</b>	<b>Week 16 pp</b>	<b>Week 24, pp</b>	<b>Week 32, pp</b>	<b>Week 40, pp</b>	<b>Week 48, pp</b>
<b>Plasma storage<sup>7,8</sup></b>	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X
<b>Breastmilk storage<sup>8,9</sup></b>														X	X	X	X				
<b>DBS storage for women on TDF/FTC only<sup>8,10</sup></b>	X	X	X	X	X	X	X	X	X	X	X		X		X	X	X	X			
<b>Infant assessment</b>	<b>Week 0</b>	<b>Week 4</b>	<b>Week 8</b>	<b>Week 12</b>	<b>Week 16</b>	<b>Week 20</b>	<b>Week 24</b>	<b>Week 28</b>	<b>Week 32</b>	<b>Week 36</b>	<b>Week 40</b>		<b>Delivery</b>	<b>Week 2, pp</b>	<b>Week 4, pp</b>	<b>Week 8, pp</b>	<b>Week 16 pp</b>	<b>Week 24, pp</b>	<b>Week 32, pp</b>	<b>Week 40, pp</b>	<b>Week 48, pp</b>
<b>Infant HIV testing, if the mother has one or more reactive/positive HIV test result<sup>11</sup></b>													X	X	X	X	X	X	X	X	X
<b>Cord blood storage<sup>8,12</sup></b>													X								
<b>Dried Blood spot storage<sup>8,12</sup></b>													X	X	X	X	X	X	X	X	X

Time on Pregnancy and Infant Sub-study	Week 0	Week 4	Week 8	Week 12	Week 16	Week 20	Week 24	Week 28	Week 32	Week 36	Week 40		Delivery	Week 2, pp	Week 4, pp	Week 8, pp	Week 16 pp	Week 24, pp	Week 32, pp	Week 40, pp	Week 48, pp
Infant plasma storage <sup>8,12</sup>													X	X	X	X	X	X	X	X	X

**NOTE: PK analysis will be performed on cord blood and infant plasma samples at an offsite laboratory.**

<sup>1</sup> HIV rapid testing may be performed in the clinic or the laboratory. At least one HIV test must be available the same day as sample collection and before product is administered.

<sup>2</sup> This testing will be performed for all study participants, regardless of HIV status or the results of other HIV tests. This testing must be performed with an assay with a lower limit of quantification of 50 copies/mL or lower.

<sup>3</sup> Pregnancy testing may be done if indicated. Pregnancy testing may be performed in the clinic or the laboratory. Testing may be performed using a urine, plasma, or serum sample. The assay used for pregnancy testing must have a limit of detection of 25 mIU/mL or lower. Pregnancy testing is not required at subsequent visits if a positive result is obtained and the participant is still pregnant.

<sup>4</sup> Albumin, BUN/urea, creatinine. Additional testing may be required if abnormalities of clinical significance are detected.

<sup>5</sup> AST, ALT, total bilirubin.

<sup>6</sup> GC/CT NAAT testing may be performed using urine or a vaginal swab; TV testing is performed using a vaginal swab. If a woman is menstruating, the swab may be collected at a later visit and all testing using the swab may be performed at that later visit.

<sup>7</sup> Stored plasma may be used for Quality Assurance testing, possible HSV-2 testing and other assessments at the HPTN LC.

<sup>8</sup> Assessments on stored samples will be performed retrospectively; results will not be returned to study sites or participants, except as noted in the SSP.

<sup>9</sup> Breastmilk collection does not need to be performed if the mother is not breastfeeding or producing milk.

<sup>10</sup> DBS will be stored for participants who elect to receive TDF/FTC. Processing and storage procedures will be described in detail in the SSP. Assessments will be performed retrospectively; results will not be returned to study sites or participants.

<sup>11</sup> Perform infant HIV testing at this visit and all subsequent study visits using local infant testing algorithms if the mother has one or more reactive/positive tests, even if HIV infection in the mother is not confirmed. If HIV testing indicates that an infant has HIV infection, a second confirmatory visit should be conducted to confirm HIV infection in the infant. If infant infection is confirmed, resistance testing should be performed locally using a separate (additional) infant sample collected for this purpose.

<sup>12</sup> Stored cord blood, DBS, and plasma samples will be used for PK analysis and may be used for other assessments, including virology testing. Results from this testing will not be returned to the study sites or participants.



**Table 11-11: Schedule of Evaluations - Step 5, Participants taking OL TDF/FTC for 48 weeks after premature CAB LA discontinuation.**

Time in Step 5	Step 5, Day 0*	Step 5, Week 12	Step 5, Week 24	Step 5, Week 36	Step 5, Week 48
HIV testing <sup>1</sup>	X	X	X	X	X
HIV viral load testing <sup>2</sup>	X	X	X	X	X
Pregnancy testing <sup>3</sup>	X	X	X	X	X
Chemistry testing <sup>4</sup>	X		X		X
Liver function testing <sup>5</sup>	X				X
Syphilis testing	X <sup>7</sup>		X		X
GC/CT and TV testing <sup>6</sup>	X <sup>7</sup>		X		X
Plasma storage <sup>7,8</sup>	X	X	X	X	X
DBS storage <sup>8</sup>	X	X	X	X	X

<sup>1</sup> HIV rapid testing may be performed in the clinic or the laboratory. At least one HIV test must be available the same day as sample collection and before product is administered.

<sup>2</sup> This testing will be performed for all study participants, regardless of HIV status or the results of other HIV tests. This testing must be performed with an assay with a lower limit of quantification of 50 copies/mL or lower.

<sup>3</sup> Pregnancy testing may be done if indicated. Pregnancy testing may be performed in the clinic or the laboratory. Testing may be performed using a urine, plasma, or serum sample. The assay used for pregnancy testing must have a limit of detection of 25 mIU/mL or lower. Pregnancy testing is not required at subsequent visits if a positive result is obtained and the participant is still pregnant.

<sup>4</sup> Albumin, BUN/urea, creatinine. Additional testing may be required if abnormalities of clinical significance are detected.

<sup>5</sup> AST, ALT, total bilirubin.

<sup>6</sup> GC/CT NAAT testing may be performed using urine or a vaginal swab; TV testing is performed using a vaginal swab. If a woman is menstruating, the swab may be collected at a later visit and all testing using the swab may be performed at that later visit.

<sup>7</sup> Stored plasma may be used for Quality Assurance testing, possible HSV-2 testing and other assessments at the HPTN LC.

<sup>8</sup> Assessments on stored samples will be performed retrospectively; results will not be returned to study sites or participants, except as noted in the SSP.

**Table 11-12: Schedule of Evaluations – Participants with Reactive/Positive HIV tests during OL portion of the trial**

<b>Participants who acquire HIV infection</b>	
	<b>HIV Confirmation Visit</b>
HIV testing <sup>1</sup>	X
CD4 cell count	X
HIV viral load testing <sup>2</sup>	X
HIV resistance testing <sup>3</sup>	X
Chemistry testing <sup>4</sup>	X
Liver function testing <sup>5</sup>	X
Plasma storage <sup>6,7</sup>	X
DBS Storage <sup>7</sup>	X

<sup>1</sup> The HIV confirmatory visit must be held on a different day from the visit where the participant had their initial reactive/positive HIV test. The testing algorithm for the HIV Confirmation Visit is provided in the SSP Manual. If HIV rapid testing is included in the HIV testing algorithm, this testing may be performed in the clinic or the laboratory. Additional HIV testing may be requested by the 084HIV alias committee.

<sup>2</sup> This testing must be performed with an assay with a lower limit of quantification of 50 copies/mL or lower.

<sup>3</sup> Sites may collect specimens for resistance testing at a local laboratory to assist with clinical management; results from resistance testing performed at local laboratories will not be reported to the SDMC. Stored plasma may not be used for real-time/local resistance testing; additional samples must be collected for this testing.

<sup>4</sup> Required chemistry testing: Albumin, BUN/urea, creatinine

<sup>5</sup> Required LFTs: AST, ALT, total bilirubin

<sup>6</sup> Stored plasma will be used for Quality Assurance testing and other assessments at the HPTN LC.

<sup>7</sup> Assessments on stored samples will be performed retrospectively; results will not be returned to study sites or participants, except as noted in the SSP. Additional HIV testing may be requested by the 084 HIV alias committee.

### 11.3.2 HIV Testing

All HIV test results from previous visits, and at least one HIV test result from the current visit, must be available and reviewed prior to administration of study products. If any of these tests is reactive/positive, study drug should not be administered. **HIV rapid testing must be performed the same day and prior to administration of study drug.**

HIV testing will be performed using blood collected by phlebotomy (**no finger-stick or oral fluid testing**) at participant visits in accordance with the testing algorithms described in Figures 11.1 through 11.3.

For further help on implementing the HIV testing algorithm prior to study start, seek guidance from the HPTN LC.

Whole blood will be collected according to site-specific procedures.

Participants with one or more reactive HIV test results at the screening visit (Figure 11.1) or enrollment visit (see notes associated with Figure 11.2 regarding result review) will not be eligible for enrollment, regardless of subsequent test results.

RNA testing for acute HIV infection, must be collected and performed within the 14 days prior to the Enrollment visit.

RNA testing must be collected and performed at all visits after enrollment.

**Every time a blood specimen is drawn for HIV testing, additional blood must be drawn for plasma storage if it does not exceed the visit blood draw limits stated in your local consent forms. This includes split visits, interim visits, and all visits for repeat HIV testing and confirmatory testing. The amount of blood drawn if not limited by consent forms should be sufficient to yield 5 x 1.8mL (approximately) plasma aliquots.**

The Seroconversion Committee (084HIV@hptn.org) must be notified immediately if one or more HIV test results are reported as reactive (or if rapid HIV results are not able to be reported during a visit) at any follow-up visit after enrollment. In certain circumstances as outlined in Appendix I Discordant-Discrepant Testing Management, the Seroconversion committee may request further testing and additional sample collections on a case by case basis. Per Appendix I, participants may be placed on product hold and the additional testing results need to be communicated to the Seroconversion Committee promptly upon receipt. In addition, select samples will be requested for further testing at the HPTN LC in order to assist with the HIV diagnosis. These samples should be shipped as soon as possible per the instructions from the Seroconversion Committee. **Do not contact HPTN LC protocol team members or the CMC.**

Additional HIV testing may be performed at any time at the discretion of the site investigator/clinician.

All tests and associated QC procedures must be documented on local laboratory log sheets or other laboratory source documents. Kit lot numbers and expiry dates must also be documented. Note that US FDA-cleared HIV rapid tests are required.

*All staff* involved in HIV testing and verification of HIV test results should be aware of the testing time frame for the HIV test, so that all tests are performed, read, and confirmed within the specified time frame of testing. Place appropriate timekeeping devices in all test settings to ensure that each test is read and verified at appropriate time points. Documentation is required for the testing start and stop times, as well as, result confirmation and verification times (second trained staff member confirms initial reading). These must be recorded on testing log sheets.

If a participant has a reactive or positive HIV test, the participant will not receive additional doses of study products pending further direction regarding testing and continued participation in the study from designated study team members.

If a participant has a reactive or positive HIV test at any time after enrollment, additional blood draw and testing is required as detailed in Table 11-4.

HIV infection must be confirmed using two independent samples collected on different days. Plasma storage is required at every visit at which HIV testing is performed.

For split visits, excluding confirmation visits (held specifically to perform further HIV testing), the laboratory-based HIV EIA (4<sup>th</sup> Gen/5<sup>th</sup> Gen) assay does not need to be repeated if the split visit (i.e. x.1) occurs less than seven days from the initial visit (i.e. x.0). If the split visit is seven or more days from the initial visit, the HIV lab assay must be repeated. This also applies to DBS samples if regularly scheduled for that visit (i.e. if repeating HIV testing at seven or more days, repeat DBS collection and storage with that days visit). Keep all samples from all visits unless specifically directed to handle stored samples differently by the HPTN LC.

Participants with confirmed HIV infection during Step 1, prior to receipt of their first injection will have oral study product permanently discontinued and will be transitioned to local HIV-related care and terminated from the study.

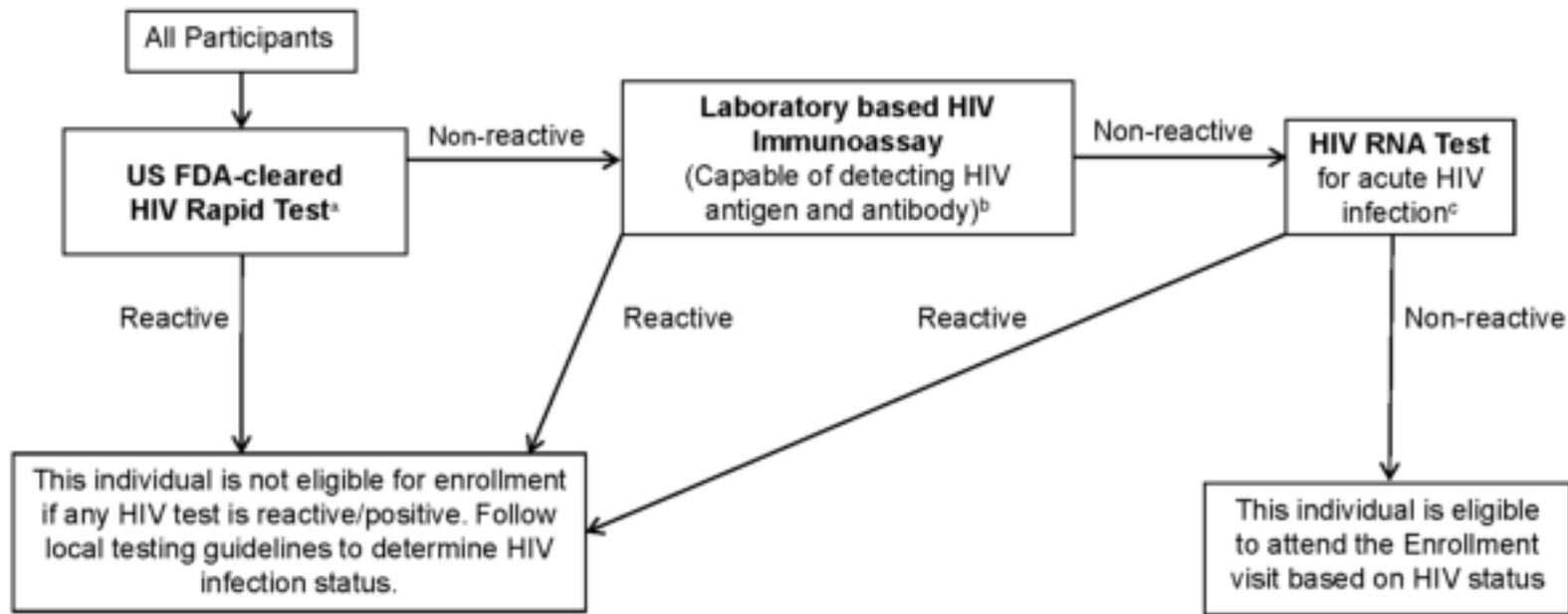
Participants with confirmed HIV infection during Step 2 will not receive additional injections or oral study product and will be followed per the Schedule of Evaluations and Procedures in Appendix II of the protocol for approximately 48 weeks.

Participants with confirmed HIV infection during Step 3 will be followed quarterly, at least for the duration of Step 3, with possible additional assessments and follow-up to be determined by the members of CMC [084HIV@hptn.org](mailto:084HIV@hptn.org).

Additional samples from participants with confirmed HIV infection may be sent to a local laboratory for resistance testing to assist with clinical management (results from resistance testing performed in local laboratories should not be reported to the HPTN SDMC or the HPTN LC).

Figure 11.1 HIV Testing Algorithm at the Screening Visit

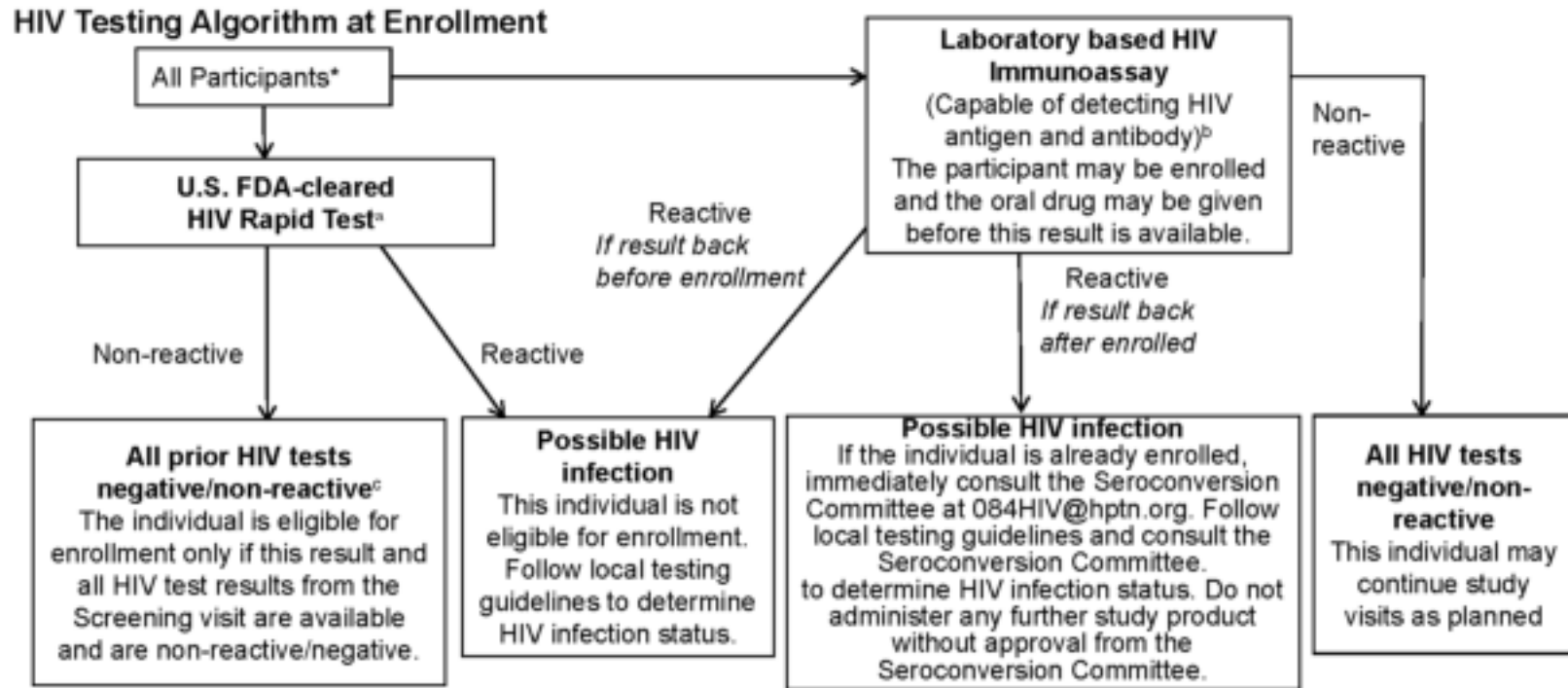
HIV Testing Algorithm at Screening\*



**NOTES:**

- \* Site-specific HIV testing plans must be approved by the HPTN LC before the study opens.
- <sup>a</sup> Sites that are not able to obtain HIV rapid test kits that are cleared by the US FDA may seek approval from the HPTN LC to use an alternate kit.
- <sup>b</sup> This testing must be performed using a laboratory based, non-rapid HIV immunoassay that detects both HIV antigen and HIV antibody (either a 4<sup>th</sup> generation or 5<sup>th</sup> generation assay).
- <sup>c</sup> Screening for acute infection should be performed using an RNA test that, in the opinion of the site investigator, is able to detect early HIV infection. If possible, the site should use an assay that is FDA-cleared for this testing, such as the APTIMA HIV-1 RNA Qualitative Assay. RNA test results must be obtained from a specimen collected within 14 days prior to enrollment.

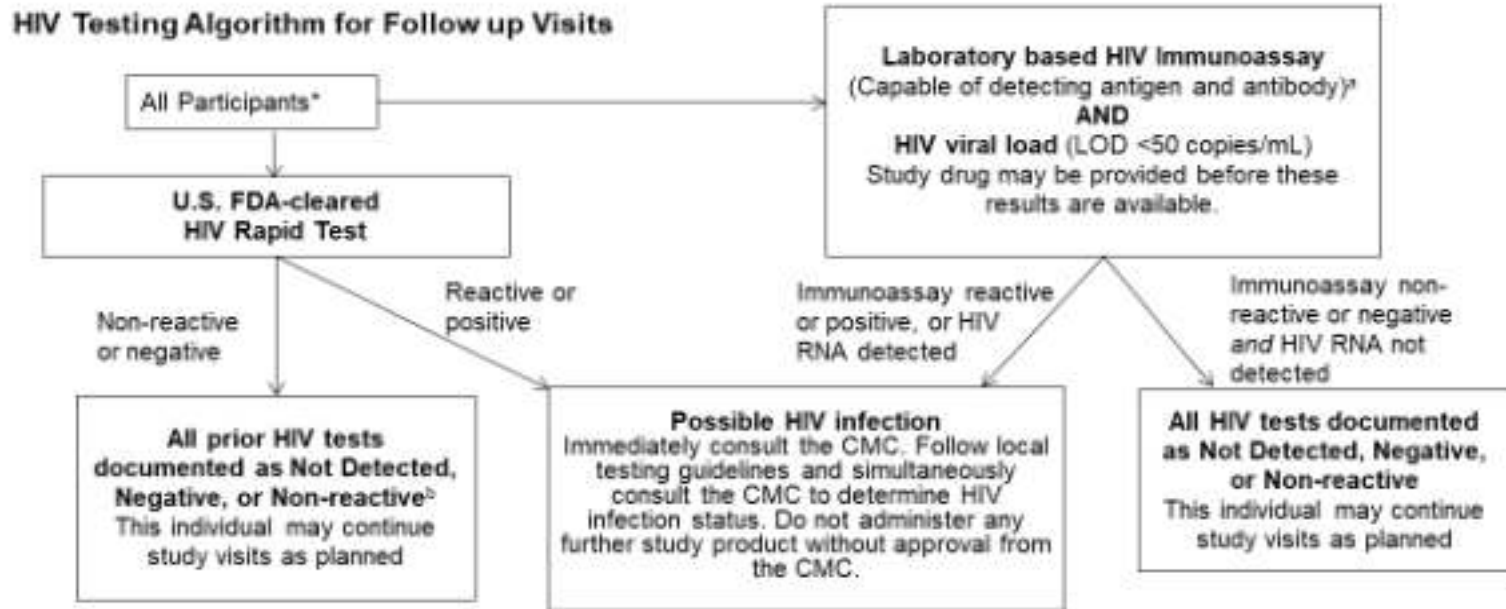
Figure 11.2 HIV Testing Algorithm at the Enrollment Visit



**NOTES:**

- \* If acute HIV infection is suspected, do not enroll the participant or administer study product at this time. In addition to following the algorithm above, the site should send a sample for an RNA test that, in the opinion of the site investigator, is able to detect early HIV infection. If possible, the site should use an assay that is FDA-cleared for early HIV diagnosis, such as the APTIMA HIV-1 RNA Qualitative Assay. The site should contact the Seroconversion Committee (084HIV@hptn.org) for additional guidance once all of the test results from this visit (including the HIV RNA test) are available.
- <sup>a</sup> Sites that are not able to obtain HIV rapid test kits that are cleared by the US FDA may seek approval from the HPTN LC to use an alternate kit.
- <sup>b</sup> This testing must be performed using a laboratory based, non-rapid HIV immunoassay that detects both HIV antigen and HIV antibody (either a 4<sup>th</sup> generation or 5<sup>th</sup> generation assay).
- <sup>c</sup> Before providing study drug, the site must ensure that the HIV rapid test from the Enrollment visit, and all HIV results from the Screening visit are available and are negative or non-reactive.

Figure 11.3 HIV Testing Algorithm at the Follow up Visits



**NOTES**

If acute HIV infection is suspected, do not administer any further study product. Immediately consult the CMC. In addition to following the algorithm above, the site should send a sample for an RNA test that, in the opinion of the site investigator, is able to detect early HIV infection. If possible, the site should use an assay that is FDA-cleared for early HIV diagnosis, such as the APTIMA HIV-1 RNA Qualitative Assay. The site should contact the Seroconversion Committee ( [D04HIV@hptn.org](mailto:D04HIV@hptn.org) ) for additional guidance once all of the test results from this visit (including the HIV RNA test) are available.

\* This testing must be performed using a laboratory based, non-rapid HIV immunoassay that detects both HIV antigen and HIV antibody (commonly referred to previously as either a 4<sup>th</sup> generation or 5<sup>th</sup> generation assay).

² At any visit where study product will be given, the site must ensure that the HIV rapid test from this visit, and all HIV results from prior study visits are negative or non-reactive or not detected.

### 11.3.3 Hepatitis Testing

Testing for HBV (HBsAb, HBsAg, HBcAb total) and HCV will be performed at screening, enrollment, and other time points as dictated by tables 11-1 and 11-2. Sites will follow local testing arrangements for the collection and testing of samples, this will be described in the site SOPs.

Test results are required for the enrollment visit.

Persons with a positive HBsAg and/or HCV antibody test will be excluded from the study.

### 11.3.4 Safety Testing

CBC, Chemistry, and LFTs will be performed at various time points throughout the study. Sites will follow local testing arrangements for the collection and testing of samples, this will be described in the site SOPs. Participants do not have to be fasting before having blood drawn for glucose.

Test results from the screening visit are required prior to enrollment.

Same day test results are not required prior to the issue of study product.

**Note: Please inform the HPTN LC and SDMC before using your back-up laboratory. Use of your back up lab may result in different reference ranges used and reported via Medidata/Rave.**

### 11.3.5 Creatinine Clearance

The calculated creatinine clearance will be performed at all visits where creatinine testing is performed, using the Cockcroft-Gault formula.

$eCcr$  (female in mL/min =  $[(140 - \text{age in years}) \times (\text{actual body weight in kg})] / (72 \times \text{serum creatinine in mg/dL}) \times 0.85$ .

For participants who join from the HPTN 084-01 protocol, the calculated creatinine clearance (estimated Glomerular Filtration Rate *eGFR*) will be performed using the Modified Bedside Schwartz Equation (2009). HPTN 084 leadership requested that sites continue to use this equation. This equation is validated only for individuals <18yrs of age.

$eGFR = (0.413 \times \text{height}) / (\text{serum creatinine})$

*eGFR* units are mLs/minute per 1.73m<sup>2</sup>, when height is by cm and serum creatinine as mg/dL

### 11.3.6 Fasting Lipid Profile

A fasting lipid profile (total cholesterol, HDL, triglycerides, LDL – calculated or measured) will be collected at the enrollment, week 57, and week 105 visits. Participants should be fasting for at



least 8 [preferably 12] hours prior to sample collection. If participants are not fasting, do not order the lipid testing. Participants may return for testing or it can be performed at next visit.

Sites will follow local testing arrangements for the collection and testing of the lipid profile. This will be described in the site SOPs.

Results from the lipid profile at the enrollment visit are NOT required prior to the issue of study product.

### **11.3.7 Urinalysis Testing**

Sites will follow local testing arrangements for the collection and testing of urine for urinalysis (only for protein and glucose). This will be described in the site SOPs.

Urinalysis results from the enrollment visit are not required prior to enrollment.

### **11.3.8 Pregnancy Testing**

Sites will follow local testing arrangements for the collection and testing of urine, plasma, or serum for beta human chorionic gonadotropin ( $\beta$ HCG) pregnancy test (sensitivity of  $\leq 25$  mIU/mL) performed and results known the same day and before initiating the protocol-specified study product(s) at Enrollment. Pregnancy test must be confirmed to be negative PRIOR to injection/dispensing of study products. This is a requirement at all visits at which study product is to be administered or continued. Pregnancy testing is not required at subsequent visits if a woman had a positive pregnancy test at a previous visit and this has been confirmed 4 weeks after the first test, and the participant is still pregnant.

This will be described in the site SOPs.

### **11.3.9 Syphilis Testing**

Sites will follow local testing arrangements for the collection and testing of serum or plasma for syphilis testing. This will be described in the site SOPs.

### **11.3.10 Urine or Vaginal Sample for GC/CT Testing**

Sites will follow local testing arrangements for the collection and testing of urine/vaginal swab sample for GC/CT nucleic acid testing. This will be described in the site SOPs. GC/CT results from the enrollment visit are not required prior to enrollment.

### **11.3.11 Vaginal Sample for Trichomonas vaginalis (TV) Testing**

Sites will follow local testing arrangements for the collection and testing of Vaginal swabs for TV (Rapid test) or Wet mount. This will be described in the site specific SOPs.

## **11.4 Plasma Processing for Storage Main Study**

Approximately 20 mL of EDTA whole blood should be drawn into spray dried EDTA tubes for plasma storage at each time point at which HIV testing is performed as indicated in Tables 11-1 to 11-3. Sites are requested to store 5 x 1.8 mL aliquots of plasma if possible. HPTN LC should be informed at any time that three or fewer aliquots of 1.8mL or less are stored via a NTF (see Section 11.2.4)

An additional 20 mL (approximately) of EDTA whole blood will be drawn for plasma storage for participants with a reactive or positive HIV test at any time after enrollment as indicated in Table 11-4. This additional plasma will be stored in the same way.

Sites will follow the instructions below or may follow site specific SOPs for plasma processing which will include the following:

- Collect blood into lavender top blood collection tubes (EDTA) labeled with a SCHARP-provided PTID label. The sizes of tubes will be reviewed by the HPTN LC to ensure blood draws will yield the required number of aliquots for storage. An alternate, site-specific labeling process may be used if an SOP is in place, and HPTN LC approved, but still must use the PTID with other identifiers. Size and number of collection tubes may vary depending on local lab requirements.
- Deliver the samples to the local LDMS laboratory along with the LDMS Specimen Tracking Sheet or site-specific requisition that contains the required information.
- Using the LDMS Specimen Tracking Sheet or site-specific requisition, log the sample into LDMS (specimen type = BLD) and generate the appropriate number of LDMS cryovial labels. The lab should store plasma in labeled cryovials. Cryovial size must be 2.0 mL. We require the use of Sarstedt tube (#72.694.006) 2 mL cryovials, or cryovials of the same dimension. Reminder: Do not add more than 1.8 mL due to expansion of plasma during freezing. Other cryovial types may only be used if specifically approved by the HPTN LC
- Blood processing and plasma storage should be performed within 6 hours of sample collection.
- Centrifuge tube at 800 - 1000 x g for 10 minutes to separate cells and plasma.
- Carefully remove plasma and avoid disturbing the cell layer. Transfer the plasma to an appropriately labelled sterile centrifuge tube.
- Centrifuge plasma again at 800 - 1000 x g for 10 minutes to remove any contaminating debris, cells, or platelets.
- Log samples into LDMS and generate LDMS labels (PL2). Each aliquot will have its own individual identification number (Global Specimen ID).
- Store plasma in aliquot number order. For example, if there is only 3 mL of plasma for storage: store 1.8 mL in aliquot 1, then store the remaining 1.2 mL of plasma in aliquot 2 and adjust the aliquot volume in LDMS to indicate 1.2 mL. The remaining aliquots (3, 4, and 5) should be entered as QNS.
- Store the aliquots in the freezer locations assigned in LDMS in an ultra-low minus 70°C to minus 90°C freezer. Aliquots may be requested as needed

Plasma for storage will be stored on site until all protocol-related testing is complete. Note that some testing will be performed after study visits have been completed. Study sites should plan to store specimens until all of the protocol specified testing (including assessments at the HPTN LC) has been completed and the primary research paper has been published.

**LDMS Entry:**

PL2 aliquots from the 20mL EDTA draw as follows:

- Several possible tube combinations equaling at least 20mL (per individual site chain of custody)
- A single primary container of EDTA whole blood is created
- 5 PL2 aliquots of 1.8mL are created (adjusted to approximate aliquot volume as needed during storage)
  - Primary container and aliquot entries should have the “SHV” (short volume) condition code used as needed when incomplete volumes are obtained. Change condition code to SAT or SHV only if you store < 5 aliquots for primary tubes, and SHV for any aliquots < 1.8 mL.
  - Please remember to contact the HPTN LC when using condition codes not listed in the SSP.
- No other aliquots are created from this primary container
- See figures 11.4 and 11.5

**LDMS Specimen Code for Plasma Storage**

<b>Test</b>	<b>Primary LDMS Code</b>	<b>Additive</b>	<b>Derivative</b>	<b>Sub Add/Deriv</b>
<b>Plasma Storage</b>	<b>BLD</b>	<b>DPE</b>	<b>PL2</b>	<b>N/A</b>

**Codes used in table:**

- BLD**                      **Blood**
- DPE**                      **Spray Dried EDTA**
- PL2**                      **Plasma, Double Spun**
- N/A**                      **Not Applicable**
- Other Spec ID:**        **Not Applicable**

- All plasma vials are stored electronically in the LDMS and physically in an ultra-low minus 70°C to minus 90°C freezer. Selected aliquots will be shipped to HPTN Laboratory Center (LC) when requested.

All enrolled study participants must consent to collection and storage of their plasma for the duration of their study participation and until all protocol-specified testing has been completed. Participants are asked to consent separately to indefinite storage and possible future research testing of their plasma after the study is completed. Participants may refuse to consent to indefinite storage and possible future research testing and still enroll in the study. After all protocol-specified testing has been completed; the stored plasma of participants who do not consent to indefinite storage and possible future research testing must be destroyed. After all protocol-specified testing has been completed, the HPTN SDMC will provide each site with a list of participants who did not consent to indefinite storage and possible future research testing and the HPTN LC will provide detailed instructions for specimen destruction and documentation thereof.

**Figure 11.4 Example LDMS Entry of Plasma (Windows LDMS)**

The screenshot shows the 'Entry' window in the Windows LDMS software. At the top, it says 'Example Visit 2.0 (Enrollment) LDMS entry' and '2 primary containers for a 24ml EDTA collection'. The main area contains a table with the following columns: Specimen #, Blood Spec ID, Ptsent, Add, Dst, Sub Add On, Volume, Units, Spec Date, Time, Time Unit, Cont, Other Spec ID, and Details. The table has 6 rows, with the first row highlighted in blue. Below the table, there are several input fields and buttons. The 'Specimen #' field contains '100017080022'. The 'Blood Spec ID' field contains 'BLD'. The 'Pntent' field contains 'DPE'. The 'Add' field contains 'PL2'. The 'Dst' field contains 'N/A'. The 'Sub Add On' field contains 'N/A'. The 'Volume' field contains '1.00 ML'. The 'Units' field contains 'SAT'. The 'Spec Date' field contains '11/10'. The 'Time' field contains '11:45'. The 'Time Unit' field contains 'H'. The 'Cont' field contains 'SAT'. The 'Other Spec ID' field is empty. There are buttons for 'Reserve', 'Inquired', 'Input date', 'Enter Specimen ID', and 'Culture Derivative'. At the bottom, there are buttons for 'Add', 'Delete', 'Modify', and 'Clear'.

Find SPD:  Load **Figure 2 - Example Visit 4.0 (follow-up) LDMS entry** 2 primary containers for a 24mL EDTA collection

Specimen	Global Spec ID	Process	Add	Site	Sub-Add/Date	Volume	Units	Spec Time	Time	Time List	Card	Other Spec ID	Spec ID	Details
1	500V1700005	BLD	DPE	PL2	N/A	1.00 ML	ML	11:00			GAT	HPTN000.0	000	Details
2	500V1700005	BLD	DPE	PL2	N/A	1.00 ML	ML	11:00			GAT	HPTN000.0	000	Details
3	500V1700005	BLD	DPE	PL2	N/A	1.00 ML	ML	11:00			GAT	HPTN000.0	000	Details
4	500V1700005	BLD	DPE	PL2	N/A	1.00 ML	ML	11:00			GAT	HPTN000.0	000	Details
5	500V1700005	BLD	DPE	PL2	N/A	1.00 ML	ML	11:00			GAT	HPTN000.0	000	Details
6	500V1700007	BLD	DPE	080	N/A	25.00 UL	UL	11:00			GAT	HPTN000.0	000	Details
7	500V1700007	BLD	DPE	080	N/A	25.00 UL	UL	11:00			GAT	HPTN000.0	000	Details
8	500V1700007	BLD	DPE	080	N/A	25.00 UL	UL	11:00			GAT	HPTN000.0	000	Details
9	500V1700007	BLD	DPE	080	N/A	25.00 UL	UL	11:00			GAT	HPTN000.0	000	Details
10	500V1700007	BLD	DPE	080	N/A	25.00 UL	UL	11:00			GAT	HPTN000.0	000	Details

Find SPD:  Load **Figure 3 - Example Visit 5.0 (follow-up) LDMS entry** 1 primary container for a 24mL EDTA collection

Specimen	Global Spec ID	Process	Add	Site	Sub-Add/Date	Volume	Units	Spec Time	Time	Time List	Card	Other Spec ID	Spec ID	Details
1	500V1700009	BLD	DPE	PL2	N/A	1.00 ML	ML	11:00			GAT	HPTN000.0	000	Details
2	500V1700009	BLD	DPE	PL2	N/A	1.00 ML	ML	11:00			GAT	HPTN000.0	000	Details
3	500V1700009	BLD	DPE	PL2	N/A	1.00 ML	ML	11:00			GAT	HPTN000.0	000	Details
4	500V1700009	BLD	DPE	PL2	N/A	1.00 ML	ML	11:00			GAT	HPTN000.0	000	Details
5	500V1700009	BLD	DPE	PL2	N/A	1.00 ML	ML	11:00			GAT	HPTN000.0	000	Details

Figure 11.5 Example LDMS Entry of Plasma (Web LDMS)

QUIT ADD

Template Comments:

---

Participant Information

Project: HPTN  
 PID: 00011646  
 OPDs:

Figure 4 - Web LDMS - Example Visit 2.0 (Enrollment)  
 24mL EDTA collection for 2 primary containers

Enrollment Information

PROTOCOL: 06L11

Visit Information

ID:   
 Class:   
 Collection Date: 17/24/2017  
 Visit Value: 2.00  
 Visit Units: VET

Primary Information

#	Primary Type	Additive Type	Condition	Collection Time	Received Date	Received Time	Volume	Volume Unit
1	BLD	DP2	SAT	08:00	17/24/2017	08:23	28	ML
2	BLD	DP2	SAT	08:00	17/24/2017	08:28	4	ML

Aspects for Primary #1

Total Aspects	Derivative Type	Sub A-D Type	Condition	Volume	Volume Units	Other Specimen ID
1	BL2	N/A	SAT	1.0	ML	

---

Aspects for Primary #2

Total Aspects	Derivative Type	Sub A-D Type	Condition	Volume	Volume Units	Other Specimen ID
1	BLD	N/A	SAT	1	ML	PODV

## 11.5 Plasma Processing for IC Storage

Approximately 10 mL of EDTA whole blood should be drawn into spray dried EDTA tubes for plasma storage at each time point at which IC testing is performed as indicated in Tables 11-6. Sites are requested to store 3-4 x 1.0 mL aliquots of plasma if possible. HPTN LC should be informed at any time that three or fewer aliquots of 1.0 mL or less are stored via a NTF (see Section 11.2.4)

Sites will follow the instructions below or may follow site specific SOPs for plasma processing which will include the following:

- Collect blood into lavender top blood collection tubes (EDTA) labeled with a SCHARP-provided PTID label. The sizes of tubes will be reviewed by the HPTN LC to ensure blood draws will yield the required number of aliquots for storage. An alternate, site-specific labeling process may be used if an SOP is in place, and HPTN LC approved, but still must use the PTID with other identifiers. Size and number of collection tubes may vary depending on local lab requirements.
  - Deliver the samples to the local LDMS laboratory along with the LDMS Specimen Tracking Sheet or site specific requisition that contains the required information.
  - Using the LDMS Specimen Tracking Sheet or site specific requisition, log the sample into LDMS (specimen type = BLD) and generate the appropriate number of LDMS cryovial labels. The lab should store plasma in labeled cryovials. Cryovial size must be 2.0 mL. We require the use of Sarstedt tube (#72.694.006 ) 2 mL cryovials, or cryovials of the same dimension. Other cryovial types may only be used if specifically approved by the HPTN LC
  - Blood processing and plasma storage should be performed within 6 hours of sample collection.
  - Centrifuge tube at **1300** x g for 10 minutes to separate cells and plasma.
  - Carefully remove plasma and avoid disturbing the cell layer.
  - Log samples into LDMS and generate LDMS labels (PL1). Each aliquot will have its own individual identification number (Global Specimen ID).
  - Store plasma in aliquot number order. For example, if there is only 2.5 mL of plasma for storage: store 2 x 1.0 mL in aliquot 1 and 2, then store the remaining 0.5 mL of plasma in aliquot 3 and adjust the aliquot volume in LDMS to indicate 0.5 mL.
  - Store the aliquots in the freezer locations assigned in LDMS in an ultra-low minus 70°C to minus 90°C freezer. Starting at visit 2 (enrollment visit), and until the end of the study, all plasma aliquots for IC sub study should be stored in a separate “to be shipped” box. The LC will notify sites when to ship these aliquots.

Plasma for storage will be stored on site until all protocol-related testing

is complete. Note that some testing will be performed after study visits have been completed. Study sites should plan to store specimens until all of the protocol specified testing (including assessments at the HPTN LC) has been completed and the primary research paper has been published.

**LDMS Entry:**

PL1 aliquots from the 10mL EDTA draw as follows:

- Several possible tube combinations equaling at least 10mL (per individual site chain of custody)
- A single primary container of EDTA whole blood is created
- 3 to 4 PL1 aliquots of 1.0 mL are created (adjusted to approximate aliquot volume as needed during storage)
  - Primary container and aliquot entries should have the “SHV” (short volume) condition code used as needed when incomplete volumes are obtained. Change condition code to SAT or SHV only if you store < 3 aliquots for primary tubes, and SHV for any aliquots < 1.0 mL.
  - Please remember to contact the HPTN LC when using condition codes not listed in the SSP.
- No other aliquots are created from this primary container
- See figures 11.4 and 11.5

**LDMS Specimen Code for Plasma Storage**

<b>Test</b>	<b>Primary LDMS Code</b>	<b>Additive</b>	<b>Derivative</b>	<b>Sub Add/Deriv</b>
<b>Plasma Storage</b>	<b>BLD</b>	<b>DPE</b>	<b>PL1</b>	<b>N/A</b>

**Codes used in table:**

- BLD**                      **Blood**
- DPE**                      **Spray Dried EDTA**
- PL1**                      **Plasma, Single Spun**
- N/A**                      **Not Applicable**
- Other Spec ID:**        **IC**

All plasma vials are stored electronically in the LDMS and physically in an ultra-low minus 70°C to minus 90°C freezer. Selected aliquots will be shipped to HPTN Laboratory Center (LC) when requested.



## 11.6 Dried Blood Spots (DBS)

### 11.6.1 Supplies:

Possible vendors for DBS supplies: Thermo Fisher Scientific, VWR, Sigma Aldrich, and Market Lab. Some Whatman items may be listed as GE Healthcare Life Sciences. The following supplies may be used. Contact HPTN LC if alternate supplies are to be used.

- EDTA spray dried Blood Collection Tubes
- Whatman Protein Saver Card #903 (Whatman 10534612 or Fisher Scientific # 05-715-121). Please handle with gloves and do not touch spot areas.
- Whatman Plastic Sample Bags (Whatman 10548232 or Fisher Scientific # 09-800-16) or Whatman Foil-Barrier Sample Bags (Whatman 10534321 or Sigma Aldrich # WHA10534321).
- Desiccant pack (GE Healthcare Life Sciences (Whatman)10548234, or P/N WB100003 or Fisher Scientific # 09-800-17).
- Humidity indicator Cards (Manufacturer # MS200032 or MS200033; ADCOA # MS20003-2 or MS20003-3; Fisher Scientific # NC9511648, or NC0281067). Or similar products with similar indicator levels, suitable for storage bag size.
- Whatman card drying rack (VWR # 89015-592 or Sigma Aldrich # WHA10539521) or other suitable drying rack.
- Gloves, preferably powder free.
- Water proof marker (Fisher Scientific# 50853571 or VWR # 95042-566)
- LDMS labels.
- A fixed 25 $\mu$ L, variable 10-100 $\mu$ L, or 20-200 $\mu$ L micropipette with appropriate filtered pipette tips. Sites should check with local suppliers for appropriate tips for their micropipettes.

### 11.6.2 DBS Preparation and Storage

Sites will follow the instructions below or may follow site specific SOPs for DBS processing and storage which will include the following:

DBS will be prepared and stored at Week 4 (not week 5 injection), multiple injection follow-up visits, and HIV positive confirmation visits. See Tables 11-1 to 11-4 for complete schedules.

DBS should be prepared from an EDTA blood tube received in the laboratory. For HPTN 084 it is acceptable to use one of the tubes received for plasma storage before it is processed for plasma storage or a sample received for HIV rapid testing after testing has been performed.

The EDTA tube should be well mixed before preparing the DBS. Pipette 25  $\mu$ L of whole blood directly onto the center of each spot on the filter paper so that it is contained within the circle (Figure 11.11).

- There will be a total of 5 blood spots created
- Whole blood for DBS should be stored at room temperature (approximately 15°C to 25°C) until spots have been created.
- Samples should be processed within 6 hours of the time of collection; the actual time of collection should be recorded on the Case Report Form, and DBS creation time in LDMS.
- Ensure that both hands are gloved before handling the Protein Saver (DBS) card; Do not

touch the areas where the blood spots will be placed (the filter paper portion).

- Label each Protein Saver Card with study protocol number, PID#, Study date and time of sample collection. Use a waterproof pen or a non-removable label.
- Create an LDMS label and enter specimen information into LDMS. See Figures 11.6 to 11.8.
- Assure the blood tube has been inverted 8 times and well mixed. Remove the cap from the EDTA tube and spot 25µl of blood, using a pipette, onto the center of the designated circles on the Protein Saver Cards (see Figures 11.11 to 11.13 below). Return the cap to the tube and process for other lab tests (i.e. plasma processing).
  - Pipette tip should be held approximately 3mm above the spot location and the blood dispensed onto the card with one single dispensing from the micropipette. Do not touch, press, or smear the spots.
- Air dry the cards in a card holder or other drying rack (Figure 11.14). Overnight drying (up to 16 hours) is acceptable, otherwise minimum drying time is 2 hours.
- Keep the DBS cards away from direct sunlight. Do not dry the DBS cards with a fan in an attempt to decrease drying time. Air dry only at temperature range of 15°C to 40°C
- After DBS cards have dried, place DBS card in low gas-permeability plastic bags with humidity indicator and desiccant pack to reduce humidity. See figures 11.15 and 11.16.
  - The humidity indicator should be checked periodically as needed.
  - If the indicator indicates too much humidity (color change from blue to pink- 40% to 50% level), replace the old desiccant pack and indicator card with a new one.
- Store bag in an appropriately labeled box in an ultra-low minus 70 to minus 90°C freezer. Select DBS will be requested quarterly.

**LDMS Entry:**

**LDMS Specimen Code for DBS Storage**

<b>Test</b>	<b>Primary LDMS Code</b>	<b>Additive</b>	<b>Derivative</b>	<b>Sub Add/Deriv</b>
<b>Dried Blood Spots Storage</b>	<b>BLD</b>	<b>DPE</b>	<b>DBS</b>	<b>N/A</b>

**Codes used in table:**

- BLD**                      **Blood**
- DPE**                      **Spray Dried EDTA**
- DBS**                      **Dried Blood Spot**
- N/A**                        **Not Applicable**
- Other Spec ID:**        **Not Applicable**

**Figure 11.6 Example LDMS Entry of DBS**

In addition to the illustrations below, include the date and time of specimen receipt, date and time of DBS processing (spot time), and date and time of DBS completion and storage for each aliquot. Note the primary aliquot is BLD with 5 aliquots created from the primary specimen. Each aliquot will be 25uL having its own Global Specimen ID. DBS need to be entered into LDMS and stored in appropriate location so they can be easily retrieved when necessary. Each spot will have its own Global Specimen ID.

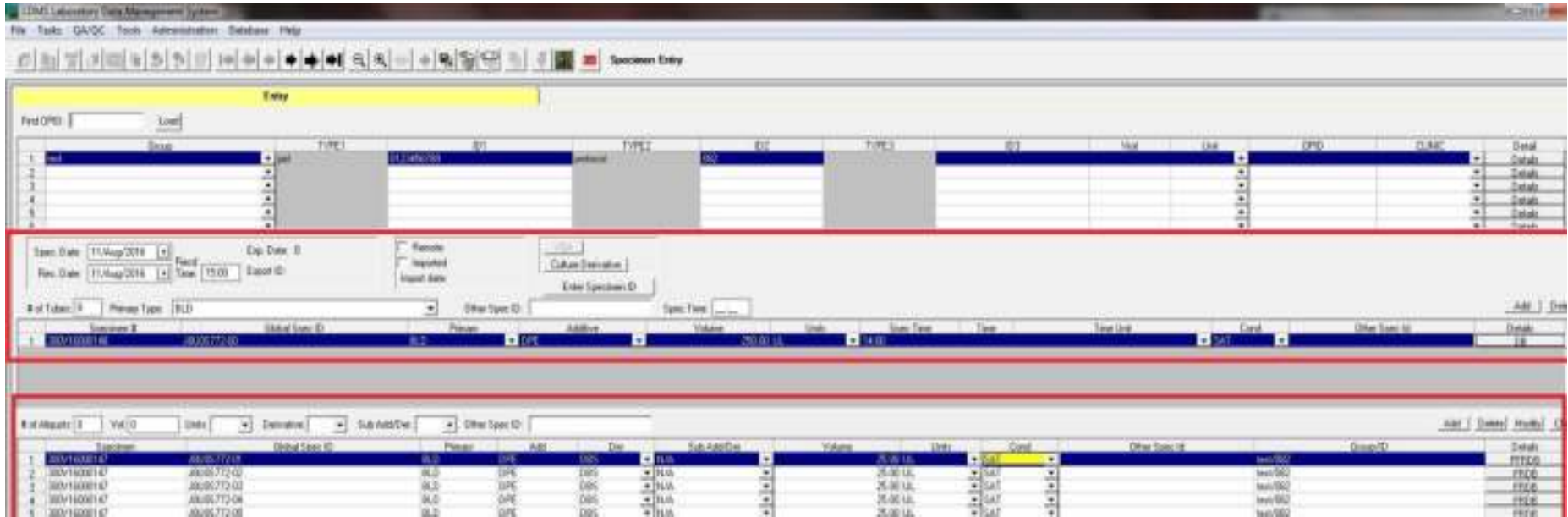


Figure 11.7 Example LDMS Entry of DBS (2)

The screenshot displays the 'Aliquot Details' dialog box in the LDMS software. The background shows a specimen management interface with a table of specimens and aliquots. The dialog box is the primary focus, containing the following sections:

- Storage:** No, Never Store, Clin: ID, Original Vol: 25, Original Vol Unit: UL.
- Condition:** SAT.
- Export:** No.
- Shipping:** No, IPK Methanol Vol is not available, IPK Vol, IPK Unit.
- Recv. Lab ID:** (empty)
- Batch No.:** (empty)
- Ship date:** (empty)
- Spec Time:** 14:00
- Reason Sample Not Collected:** (empty)
- Ship:** Mark for Shipping, Category, Intended Ship Date, Destination Lab.
- Processing Information (highlighted in red):**
  - Processing Date: 11/Aug/2016
  - Processing Time: 15:30
  - Processed By Tech Inits: DC
  - Frozen Date: 12/Aug/2016
  - Frozen Time: 08:00
  - Thaw: 0
- Comments (highlighted in red):**
  - Storage Comments:
  - Comments: Include/clarity the date and time of specimen receipts, date and time of DBS processing ("spot time"), and date and time of DBS completion and storage.

Buttons for 'OK' and 'Cancel' are visible at the bottom of the dialog box.

**Figure 11.8 Example LDMS Entry of DBS (3)**

⏪ < Participant 224 of 224 ▾ > ⏩

Project: HPTN Edit Participant ▾  
 PID: 300999990  
 OPIDs: LC-TEST  
 PROTOCOL: 083.0 Edit PROTOCOL ▾

Visits for PROTOCOL 083.0

Visit	Collection Date	ID3	Clinic	Action
4 Vst	09/Aug/2017			Edit ▾

Primary Specimens for Visit 4 Vst, 09/Aug/2017

Global Specimen ID	Status	Collection Time	Primary Type	Additive Type	Specimen Condition	Available Volume	Other Specimen ID	Specimen ID	Additional Time	Action
9001-001MDG00-000		08:00	BLD	DPE	SAT	24 ML				Edit ▾

Aliquots for 9001-001MDG00-000

Global Specimen ID	Status	Derivative Type	Sub Add/ Der Type	Specimen Condition	Available Volume	Other Specimen ID	Specimen ID	Action
9001-001MDG00-001		DBS	N/A	SAT	25 UL			Edit ▾
9001-001MDG00-002		DBS	N/A	SAT	25 UL			Edit ▾
9001-001MDG00-003		DBS	N/A	SAT	25 UL			Edit ▾
9001-001MDG00-004		DBS	N/A	SAT	25 UL			Edit ▾
9001-001MDG00-005		DBS	N/A	SAT	25 UL			Edit ▾

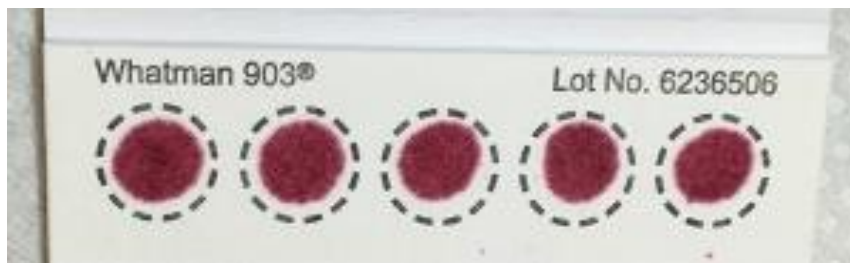
Figure 11.9 Example DBS LDMS Labels for each aliquot



Figure 11.10 Suggested labeling of DBS cards



**Figure 11.11. Example of correctly spotted DBS card (25µl spot volume)**



Note: 25µl spot volume may not completely fill target circle on DBS card.

Figure 11.12. Example of *incorrectly* spotted DBS card



Figure 11.13. Example of *incorrectly* spotted DBS card (continued)

### Invalid Specimens



1. Specimen quantity insufficient for testing.



2. Specimen appears scratched or abraded.



3. Specimen not dry before mailing.



4. Specimen appears supersaturated.



5. Specimen appears diluted, discolored or contaminated.



6. Specimen exhibits serum rings.



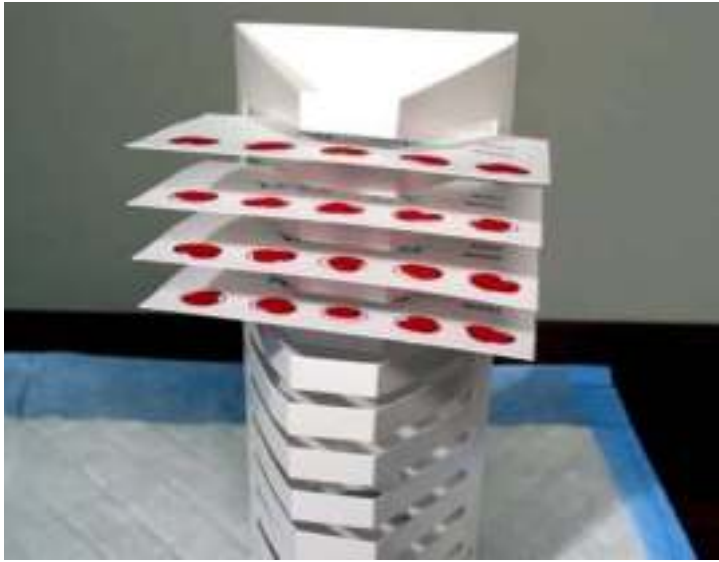
7. Specimen appears clotted or layered.



8. No blood.



**Figure 11.14. Whatman card drying rack (VWR catalogue # 89015-592)**



**Figure 11.15 Properly labeled and packaged DBS card for storage**



**Figure 11.16 Properly labeled and packaged DBS card for storage (2)**



### **DBS Shipping and Packing**

When shipping DBS, ensure specimens are shipped on dry ice. Check the desiccant packs and humidity indicators before shipping and replace if needed. Boxes should be placed in a water tight secondary containers (Tyvek bags) to protect from humidity while in transit. Make sure to generate an LDMS shipping manifest with each shipment including all requested information.

## 11.7 Whole Blood Storage for Pharmacogenomic Testing

**Specimen Type:** Whole blood collected in dried EDTA anticoagulant (“purple top”) tube.

**Specimen volume:** Minimum 1 mL whole blood

**Handling Instructions:** Whole blood is transferred to a suitable cryovial and frozen at minus 70°C to minus 90°C within 6 hours of collection.

Whole blood aliquot should be prepared from an EDTA blood tube received in the laboratory. For HPTN 084 it is acceptable to use one of the tubes received for plasma storage before it is processed for plasma storage or a sample received for HIV rapid testing after testing has been performed.

Sites will follow the instructions below or may follow site specific SOPs for whole blood storage which will include the following:

### Procedure –Stepwise

- An appropriately labeled and filled EDTA whole blood tube will be received. Transfer a minimum of 1.0mL of the whole blood to a labeled cryovial using a transfer pipet.
- Do not fill cryovials to more than  $\frac{3}{4}$  of capacity.
- Optional - Parafilm can be used to seal caps of the cryovials to prevent leakage during shipping.
- Ensure PTID, date, visit number and laboratory identifier are on the LDMS label.
- Store whole blood in an ultra-low freezer minus 70°C to 90°C until requested for shipment.
- Ship when requested on dry ice overnight for arrival on Monday through Friday only, site must follow appropriate shipping regulations.
- Batch shipment to:

Estelle Piwowar-Manning/  
Johns Hopkins University Hospital  
Department of Pathology  
Pathology Building, Room 313  
600 North Wolfe Street  
Baltimore, MD 21287  
USA

**LDMS Entry:**

**LDMS Specimen Code for Whole Blood Storage**

Test	Primary LDMS Code	Additive	Derivative	Sub Add/Deriv	Other Spec ID
Whole Blood Storage	BLD	DPE	BLD	N/A	PGEN

**Codes used in table:**

<b>BLD</b>	<b>Blood</b>
<b>DPE</b>	<b>Spray Dried EDTA</b>
<b>N/A</b>	<b>Not Applicable</b>
<b>Other Spec ID:</b>	<b>PGEN</b>

**11.8 Breast Milk collection and processing for OL participants.**

**Specimen Type:** Breast Milk.

**Specimen volume:** 5 mL unspun whole breast milk processed into 3-5 x 1 mL aliquots.

**Handling Instructions:** Whole breast milk is transferred to a suitable cryovial and frozen at minus 70°C to minus 90°C within 6 hours of collection.

**Procedure –Stepwise**

- Collect 3-5 mLs of Breast Milk in an appropriately labeled 50 mL conical tube.
- Store at 4°C (2 to 8°C acceptable) within 10 minutes of collection and send to the lab on wet ice.
- Process within 6 hours of collection.
- Transfer a minimum of 1.0mL of the whole breast milk in to a labeled cryovial using a transfer pipet.
- Log specimens into LDMS and generate LDMD labels (BMK), each aliquot should have each own individual identification number (Global Specimen).
- Store breast milk in aliquot number order
- Store the aliquots in the freezer location assigned in LDMS in the ultra-low -70°C to -90°C freezer.
- Aliquots will be requested as needed.

**LDMS Entry:**

**LDMS Specimen Code for Breast Milk Storage**

<b>Test</b>	<b>Primary LDMS Code</b>	<b>Additive</b>	<b>Derivative</b>	<b>Sub Add/Deriv</b>
<b>Whole Breast Milk Storage</b>	<b>BMK</b>	<b>Non</b>	<b>BMK</b>	<b>N/A</b>

**Codes used in table:**

**BMK**                      **Whole Breast Milk**

**NON**                      **No-Additive**

**N/A**                        **Not Applicable**

**11.9 Cord Blood collection and processing for OL participants.**

Approximately 5 mL of whole cord blood (CRD) should be drawn into spray dried K2EDTA tube for plasma storage as indicated in Tables 11-10. Sites are requested to store 2 x 1.0 mL aliquots of plasma if possible.

Sites will follow the instructions below or may follow site specific SOPs for plasma processing which will include the following:

**Specimen volume:** 5 mL unspun whole cord blood processed into 2 x 1.0 mL aliquots.

**Handling Instructions:** Whole cord blood is transferred to a suitable cryovial and frozen at minus 70°C to minus 90°C within 6 hours of collection.

**Procedure –Stepwise**

- Collect blood into lavender top blood collection tubes (K2EDTA) labeled with a SCHARP-provided PTID label. The sizes of tubes will be reviewed by the HPTN LC to ensure blood draws will yield the required number of aliquots for storage. An alternate, site-specific labeling process may be used if an SOP is in place, and HPTN LC approved, but still must use the PTID with other identifiers. Size and number of collection tubes may vary depending on local lab requirements.
- Deliver the samples to the local LDMS laboratory along with the LDMS Specimen Tracking Sheet or site-specific requisition that contains the required information.
- Using the LDMS Specimen Tracking Sheet or site-specific requisition, log the sample into LDMS (specimen type = CRD) and generate the appropriate number of LDMS

cryovial labels. The lab should store plasma in labeled cryovials. Cryovial size must be 2.0 mL. We require the use of Sarstedt tube (#72.694.006) 2 mL cryovials, or cryovials of the same dimension. Other cryovial types may only be used if specifically approved by the HPTN LC.

- Blood processing and plasma storage should be performed within 6 hours of sample collection.
- Centrifuge tube at 800 - 1000 x g for 10 minutes to separate cells and plasma.
- Carefully remove plasma and avoid disturbing the cell layer.
- Log samples into LDMS and generate LDMS labels (PL1). Each aliquot will have its own individual identification number (Global Specimen ID).
- Store plasma in aliquot number order. For example, if there is only 1.5 mL of plasma for storage: store 1.0 mL in aliquot 1, then store the remaining .5 mL of plasma in aliquot 2 and adjust the aliquot volume in LDMS to indicate .5 mL. The remaining aliquots (3,) should be entered as QNS.
- Store the aliquots in the freezer location assigned in LDMS in the ultra-low -70°C to -90°C freezer.
- Aliquots will be requested as needed.

**LDMS Entry:**

<b>Test</b>	<b>Primary LDMS Code</b>	<b>Additive</b>	<b>Derivative</b>	<b>Sub Add/Deriv</b>
<b>Whole Cord Blood Storage</b>	<b>CRD</b>	<b>DPE</b>	<b>PL1</b>	<b>N/A</b>

**Codes used in table:**

**CRD**                      **Whole Cord Blood**

**DPE**                      **No-Additive**

**N/A**                      **Not Applicable**

**11.10 Infant Blood collection and processing for OL participants.**

Approximately 500 µL to 2 mL of whole blood (if possible) should be drawn into spray dried K2EDTA tube for plasma storage as indicated in Tables 11-10. Sites are requested to store 2 x 250 µL aliquots of plasma if possible.

Sites will follow the instructions below or may follow site specific SOPs for plasma processing which will include the following:

**Procedure –Stepwise**

- Collect blood into lavender top blood collection tubes (K2EDTA) labeled with a SCHARP-provided PTID label. The sizes of tubes will be reviewed by the HPTN LC to

ensure blood draws will yield the required number of aliquots for storage. An alternate, site-specific labeling process may be used if an SOP is in place, and HPTN LC approved, but still must use the PTID with other identifiers. Size and number of collection tubes may vary depending on local lab requirements.

- Deliver the samples to the local LDMS laboratory along with the LDMS Specimen Tracking Sheet or site-specific requisition that contains the required information.
- Using the LDMS Specimen Tracking Sheet or site-specific requisition, log the sample into LDMS (specimen type = BLD) and generate the appropriate number of LDMS cryovial labels. The lab should store plasma in labeled cryovials. Cryovial size must be 2.0 mLs. We require the use of Sarstedt tube (#72.694.006) 2 mL cryovials, or cryovials of the same dimension. Other cryovial types may only be used if specifically approved by the HPTN LC.
- Blood processing and plasma storage should be performed within 6 hours of sample collection.
- Centrifuge tube at 800 - 1000 x g for 10 minutes to separate cells and plasma.
- Carefully remove plasma and avoid disturbing the cell layer.
- Log samples into LDMS and generate LDMS labels (PL1). Each aliquot will have its own individual identification number (Global Specimen ID).
- Store plasma in aliquot number order. For example, if there is only 250 µL of plasma for storage: store .250 µL in aliquot 1 in aliquot 1. The remaining aliquots (2,) should be entered as QNS.
- Store the aliquots in the freezer location assigned in LDMS in the ultra-low -70°C to -90°C freezer.
- Aliquots will be requested as needed.

**LDMS Entry:**

<b>Test</b>	<b>Primary LDMS Code</b>	<b>Additive</b>	<b>Derivative</b>	<b>Sub Add/Deriv</b>
<b>Infant Blood Storage</b>	<b>BLD</b>	<b>DPE</b>	<b>PL1</b>	<b>N/A</b>

**11.11 Required LDMS data entry scheme**

LDMS data entry is to be standardized across the sites participating in HPTN 084. This may not align with current practice or entry for other network studies.

**11.11.1 PL2 aliquots from the 20mL EDTA draw (as per protocol and SSP)**

- a. Several possible tube combinations equaling at least 20mL (per individual site chain of custody)
- b. A single primary container of EDTA whole blood is created
- c. 5 PL2 aliquots of 1.8mL are created (adjusted to actual aliquot volume as needed during storage)
- d. No other aliquots are created from this primary container
- e. See Figures 11.4 and 11.5).

### **11.11.2 DBS from EDTA whole blood (example 4mL draw)**

- a. A single primary container of 4mL EDTA whole blood is created
- b. 5 aliquots of 25uL each are created (1 for each spot on the DBS card)

### **11.11.3 Whole Blood for Pharmacogenomics (Example 4mL draw)**

- a. Occurs only once at visit 2.0 (Enrollment)
- b. Single primary container
- c. Single 1mL whole blood aliquot
- d. "PGEN" entered into primary container Other Specimen ID field (Other Spec Id)

### **11.11.4 Blood for Injectable Contraceptive Sub-Study. (additional 10 mL draw)**

- a. Plasma and DBS will be collected from selected sites at Steps 1 and 2.
- b. Follow plasma processing (see instructions above) and DBS instructions in sections 11.4 and 11.5.

### **11.11.5 Breast Milk**

- a. 5 mLs collected in a single primary container of 50mL conical tube of whole breast milk is created.
- b. 3-5 aliquots of 1.0 mL each are created.
- c. Follow breast milk processing (see instructions above) instructions in section 11.8

### **11.11.6 Cord Blood**

- a. A single primary container of 5mL K2EDTA whole cord blood is created
- b. 2 aliquots of 1.0 mL each are created.
- c. Follow cord blood processing (see instructions above) instructions in section 11.9

### **11.11.7 Infant blood**

- a. A single primary container of 500 µL to 2mL K2EDTA whole blood is created
- b. 2 aliquots of 250 µL each are created.
- c. Follow infant blood processing (see instructions above) instructions in section 11.10

## **11.12 Primary Specimen Report for HPTN 084 in PC-based LMDS**

- a. Open the LDMS "Reports" module:
  - i. Click on the "Reports" icon (under the main Menu bar) or click on the "Tasks" Menu and select "Reports" from the drop-down menu.
- b. In the Category box on the top-left of the Reports screen, highlight the "Specimen" line.
- c. In the Description box at the top of the Reports screen, highlight the "Primary Specimens Received" line.
- d. Under the "Selection Criteria" area at the bottom of the Reports screen:
  - i. In the Field box, select "Group" from the drop-down menu.
  - ii. In the Operator box, select "=" from the drop-down menu.
  - iii. In the Value box, select "HPTN" from the drop-down menu.



- iv. Click on the “Add” button, to the right of the selection criteria, to save the information in the search options box to the right, for use with your search later.
- e. Go back to the Selection Criteria area and repeat the process to enter protocol information:
  - i. In the Field box, select “Non-ACTG Prot/ID2” from the drop-down menu.
  - ii. In the Operator box, select “=” from the drop-down menu.
  - iii. In the Value box, select “084.0” from the drop-down menu.
  - iv. Click on the “Add” button, to the right of the selection criteria, to save the information in the search options box to the right, for use with your search later.
  - v. *IF the drop-down “Value” options include both “084.0” and “084” as a choice, instruction “e” (this section) should be repeated so that both are included in the saved search options (as in the figure below). If only one is an option, instruction “e” only needs to be performed once.*

**Figure 1**

	Field	Operator	Value
1	Group	=	HPTN
2	Non-ACTG Prot/ID2	=	084.0
3	Non-ACTG Prot/ID2	=	084

- f. Go back to the Selection Criteria area and repeat the process to enter search date information. The following are ways to search for one day or one month within a single search:
  - i. To search only one day:
    - 1. In the Field box, select “Received Date” from the drop-down menu.
    - 2. In the Operator box, select “=” from the drop-down menu.
    - 3. in the Value box, select the date for which you would like to check the status of the primary specimens.
    - 4. Click on “Add” box – located on to the right of the Selection Criteria.
  - ii. To search within one month:
    - 1. In the Field box, select “Received Date” from the drop-down menu.
    - 2. In the Operator box, select “>=” from the drop-down menu.
    - 3. In the Value box, select the first day of the month for which you would like to check the status of the primary specimens.
    - 4. Click on “Add” box – located on to the right of the Selection Criteria.
    - 5. In the Operator box, select “<=” from the drop-down menu.
    - 6. In the Value box, select the last day of the month for which you would like to check the status of the primary specimens.
    - 7. Click on “Add” box – located on to the right of the Selection Criteria.

8. The figure below displays what you should see in the saved area to the right of selection criteria. Lines 4 and 5 together in the figure represent the two entries for the one-month search window.

**Figure 2**

	Field	Operator	Value
3	NonACTG Prot/ID2	=	084
4	Received Date	>=	01/Nov/2017
5	Received Date	<=	30/Nov/2017

- g. There will now be multiple lines of information in the box to the right of the search criteria. The minimum lines that should be present is three, but there could be up to five lines if two protocol ID's and two date criteria have been entered. One line will be present for each of the following:
- i. The HPTN group
  - ii. The protocol number (ID2)
    1. Two lines are present if the additional protocol number (ID2) is included (e.g. 084.0 and 084 will have separate lines as in figure 1)
  - iii. The search date
    1. Two lines are present if a one-month window is to be searched (e.g. starting November 1st and ending November 31<sup>st</sup> will have separate lines as in figure 2)
- h. In the “Valid sentence” field, write a search to use all the entered and saved criteria as needed.
- i. A simple search with only 3 lines in the saved area will look like: “1 and 2 and 3” –referring to a search for HPTN samples, protocol 084.0, and the specified date.
  - ii. A search that uses two dates (for a one-month search) and two protocol ID's (to search 084.0 and 084 entries) will look like figure 3: “1 and (2 or 3) and 4 and 5” – referring to a search for HPTN samples, any 084 or 084.0 protocol entries, and the month specified between the two dates.

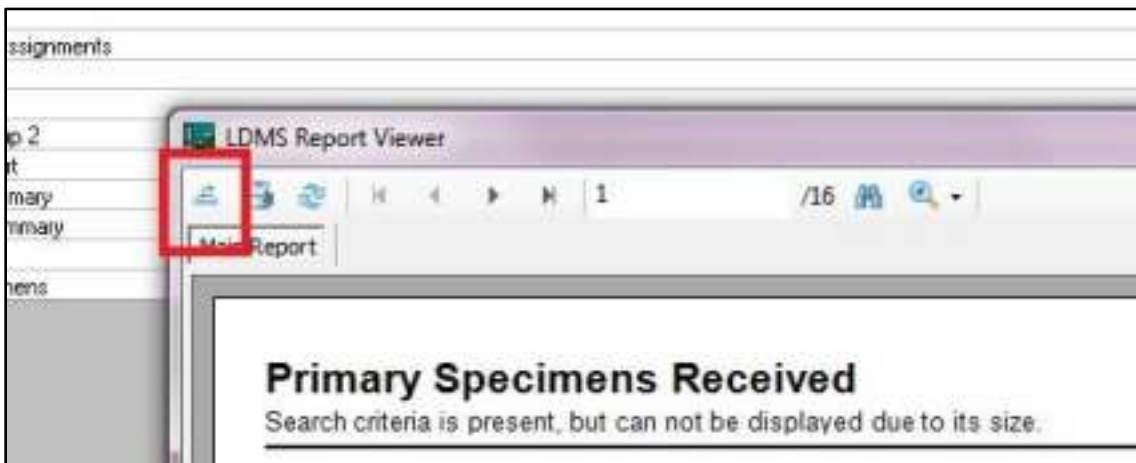
**Figure 3**

	Field	Operator
Add	3 Non ACTG Prot/ID2	=
	4 Received Date	>=
Modify	5 Received Date	<=

Valid Sentence Items: and, or, [ ], or a number  
1 and (2 or 3) and 4 and 5

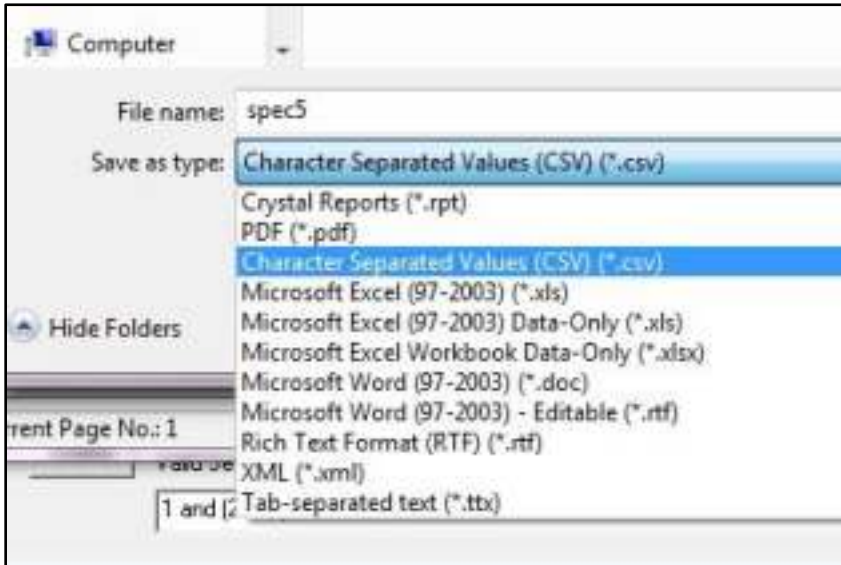
- i. Click on the “Execute” icon (the lightning bolt) at the top of the screen under the main menu bar.
- j. The “Primary Specimens Received” report will automatically generate and pop-up once completed. This provides a detailed description of each primary specimen entry.
- k. This report can then be exported into an Excel (CSV) format.
  - i. Click the “Export Report” icon in the pop-up window (figure 4).

**Figure 4**



- ii. In the “Save As” pop-up window, create a file name for the report and select to save as a “CSV” file type. See figure 5.


**Figure 5**



- a. Email reports to the HPTN 084 LC staff (Estelle Piwowa-Manning [epiwowa@jhmi.edu](mailto:epiwowa@jhmi.edu) and Yaw Agyei [yagyei1@jhmi.edu](mailto:yagyei1@jhmi.edu))

**Windows: Specimen Log Report**



1. Click on **Specimen** in the **Category** grid at the top left of the Reports screen
2. Click on **Specimen Log Report** in the Description window
3. Return to **Field** and select **Received Date**
  - a. **Operator** is '='
  - b. In **Value**, set the Current Date
  - c. Click **Add**
4. Click the **Execute**  button on the LDMS toolbar

## Webs: Specimen Log Report

This report provides the user with a specific set of information for each of their logged specimens. The report will provide the user with the participant, primary, and aliquot information for each of their specimens. The report also provides the user with the condition codes, comments, and shipping information (if available) for the given specimens. Using the search criteria below will provide the user with a list of all specimens received by the lab on a particular date

The screenshot shows the LDMS web interface. At the top, the 'Reports' menu is open, and 'Standard Reports' is selected. Below this, the 'Report Categories' dropdown is set to 'Specimen' and the 'Report' dropdown is set to 'Specimen Log Report'. In the 'Filter Criteria' section, the 'Received Date' field is set to '01/Jan/2019' with an '=' operator. The 'File Type' dropdown is set to 'PDF (\*.pdf)'. A 'Generate Report' button is visible at the bottom.

#	Field	Operator	Value
1	Received Date	=	01/Jan/2019

1. On the LDMS menu bar, hover over **Reports** and click **Standard Reports**.
2. Select the following:
  - a. Report Categories: **Specimen**
  - b. Report: **Specimen Log Report**
3. In **Filter Criteria**:
  - a. **Field**: Received Date
  - b. **Operator**: '='
  - c. **Value**=Current Date
4. Set **File Type** to PDF; Click **Generate Report**

### 11.13 Shipping of Samples to the HPTN Laboratory Center

Each site will ship plasma, whole blood, Cord blood, infant plasma, or DBS samples to the LC or designated laboratory upon request, or following a shipping schedule as determined by the LC. The site will batch the shipment, export the LDMS data, and notify the LC.

- a. The remaining plasma aliquots should be stored as per normal site standards.
- b. Other samples, such as those from Seroconverters, will also be requested on an ad-hoc basis and may be included in quarterly shipments. Separate shipping instructions will be provided at that time by LC non-protocol team members.
- c. Separate LDMS batches may be required depending on the shipping request.

Contact the HPTN LC at Johns Hopkins University (Estelle Piwowa-Manning: [epiwowa@jhmi.edu](mailto:epiwowa@jhmi.edu) and Paul Richardson: [pricha18@jhmi.edu](mailto:pricha18@jhmi.edu), +410-614-6737) to coordinate the timing and logistics of each shipment.

Sites will ship samples to the LC using the LDMS following the LC approved Shipping SOP indicating Lab 300 as the ship to lab ID number. The site should export the data to FSTRF after a batch has been made and notify the HPTN LC with the batch number.

Personnel involved in the shipping process must be IATA trained and certified for the shipping of Category B Biological specimens UN 3373 (Diagnostic) Packing Instructions 650.

## **Plasma, Cord Blood, Breast Milk and Whole blood for pharmacogenomics**

Include a copy of the shipping manifest and box map with the shipment. For dry ice shipments, use diagnostics packing code 650, UN 3373, and address the shipment to:

Estelle Piwowar-Manning/Susan Eshleman MD  
Johns Hopkins University Hospital  
Department of Pathology  
Pathology Building, Room 313  
600 North Wolfe Street  
Baltimore, MD 21287  
USA

For some shipments, an alternate address may be provided at the time of request.

Notify the HPTN LC via email ([epiwowa@jhmi.edu](mailto:epiwowa@jhmi.edu)) when the shipment has been picked up from the site by the courier/shipping company. Attach an electronic copy of the shipping manifest and LDMS batch to the email notification and include the following information in the notification: name of courier/shipping company, shipment tracking number, number of boxes shipped, date of shipment, and expected date of arrival.

## **Dried Blood Spot cards**

Storing Dried Blood Spots by individual participant will simplify the shipment process. Lists of DBS that are required to be shipped will be uploaded to the Atlas Portal. An email will be sent directly to the sites from the SDMC.

These Dried blood spot cards should also be shipped when requested. **Note: Sites can ship all samples to Johns Hopkins University, and the DBS will be forwarded to University of Colorado at Denver if indicated in the site MTA.**

Sites should ship the DBS cards directly to:

Lane Bushman  
C/O Pete Anderson  
University of Colorado at Denver  
Skaggs School of Pharmacy and Pharmaceutical Sciences  
C-238-V20, Rm V20-4410  
12850 East Montview Blvd  
Aurora, CO 80045  
USA  
Phone: 303-724-6132  
LDMS Number 533



#### **11.14 HIV QA Testing**

Selected plasma aliquots will be shipped to the HPTN LC for HIV QA testing according to the HPTN Manual of Operations; additional testing may be performed e.g. ABO typing.

When samples are received at the HPTN LC, the LC will perform additional QA and HIV testing. This will include:

- Quality assurance testing (to confirm results of in-country testing)
- Testing to confirm seroconversion events

Data from the HPTN LC will be submitted to the SDMC.

#### **11.15 Pharmacology Testing**

Plasma samples for drug levels will be collected throughout the study. These samples will be collected from all participants, although PK testing may be limited to a subset of the samples. At each injection visit a blood sample will be collected PRIOR to the injections. The actual date and time of each blood sample collection will be recorded, as well as the time of each injection. This information should be captured on the relevant CRF.

Specimens for pharmacology testing will be shipped following a shipping schedule as determined by the LC.

Pharmacology testing will be performed at the HPTN LC or at an outside laboratory designated by the HPTN LC. The primary pharmacologic assessments will be performed using assays that have been validated and approved by the Clinical Pharmacology Quality Assurance (CPQA) Committee. Results will not be returned to the sites or study participants.

Stored plasma may also be tested for the presence of other ARV drugs or other substances.

#### **11.16 Pharmacogenomic Testing**

Specimens for Pharmacogenomic analysis will be collected at the enrollment visit for participants who consent to Pharmacogenomic testing. Samples will be stored on site for shipment to the HPTN LC upon request. Assays will be performed at the HPTN LC. Results will not be returned to the sites or study participants.

### **11.17 Other Testing**

The HPTN LC will perform QA testing, including testing to determine HIV infection status in selected cases. Additional assays may be performed at the HPTN LC or a laboratory designated by the HPTN LC. This testing may include the following tests for participants who acquire HIV infection: HIV viral load, HIV resistance testing, HIV subtyping, and other tests to characterize HIV viruses and/or the host response to HIV infection. Results will not be returned to the sites or study participants, with the exception of HIV testing (if results obtained at the HPTN LC do not agree with site results) and the exception for resistance test results, noted below.

Resistance testing will be performed at the HPTN LC or a laboratory designated by the HPTN LC. This testing will be performed retrospectively at the end of the study. If real-time resistance testing is needed for clinical management, that testing should be arranged by the site outside of the study; separate specimens should be collected for that testing. For sites that do not have the capacity for local resistance testing for clinical care, results from resistance testing may be provided at the end of the study at the request of the site IoR, with approval of the HPTN LC and Protocol Chair. Results from specialized resistance testing (e.g., minority variants analysis, if performed) will not be returned to study sites.

### **11.18 Laboratory Monitoring**

LC staff will conduct periodic site visits to review in-clinic documentation, LDMS reports, specimen storage and other laboratory documentation relevant to this protocol.