Section 11. Laboratory and Specimen Management Procedures

11.1 Overview of Section 11 2
11.2 Specimen Labeling 2
11.2.1 Local Specimen Processing and Storage 3
11.2.2 Local Specimen Testing 3
11.2.3 Remote Specimen Testing 3
11.2.4 Use of the LDMS 3
11.2.5 LDMS Reconciliation 5
11.3 Protocol related testing and sample collection 6
11.3.1 HIV Testing 13
11.3.2 Hepatitis Testing 20
11.3.3 Safety Testing 20
11.3.4 Creatinine Clearance 20
11.3.5 Fasting Lipid Profile 20
11.3.6 Urinalysis Testing 21
11.3.7 Pregnancy Testing 21
11.3.8 Syphilis Testing 21
11.3.9 Urine or Vaginal Sample for GC/CT Testing. 21
11.4 Plasma Processing for Storage 21
11.5 Dried Blood Spots (DBS) 25
11.5.1 DBS Supplies: 25
11.5.2 DBS Preparation and Storage 25
11.6 Shipping of Samples to the HPTN Laboratory Center 34
11.6.1 HIV QA Testing 36
11.6.2 Pharmacology Testing 36
11.6.3 Other Testing 37
11.7 Laboratory Monitoring 37

11.1 Overview of Section 11

This section contains information on the laboratory procedures performed in HPTN 084-01.

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

1. Clinics
2. Local laboratories
3. The HPTN Laboratory Center ("LC", Baltimore, MD and Aurora, CO, 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 HPTN 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:

http://www.cdc.gov/ncidod/dhqp/bp_universal_precautions.html

Additional reference information can be requested from the HPTN LC. The information provided below is intended to standardize laboratory procedures for HPTN 084-01 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 Data and Management Center (SDMC, SCHARP) if required for this function. 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 (as found in section 13, Data Management SSP), specimen collection date and time, as well as their initials or code is fully 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 Manuals (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 and that it has been validated by the End-User. 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 two-dimensional web LDMS-generated barcode labels are below:

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 084-01 should be directed to Yaw Agyei (yagyei1@jhmi.edu) and Estelle Piwowar-Manning (epiwowa@jhmi.edu).

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

LDMS User Support at Frontier Science

LDMS user support is available 24 hours per day by telephone or email to answer your questions about using LDMS, diagnosing problems, and helping your laboratory get the most out of the software. When contacting LDMS User Support, be sure to include your LDMS laboratory number.

Please note LDMS User Support cannot be contacted during the following U.S. Holidays – Thanksgiving Day, Christmas Day, New Year's Day, Memorial Day, and Independence Day.

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

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

Email: ldmshelp@fstrf.org

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?

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 an HPTN 084-01 Specimen log report at the end of each week, and Primary Specimen report at the end of each month, and sent to the LC. In the event that the required volume or number of sample aliquots is not obtained at any time point, designated site clinic and lab staff must immediately inform the HPTN LOC, HPTN SDMC, and the LC. The HPTN LOC, SDMC, and LC 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. Emailed reconciliation reports require a documented response within one week of the original email date.

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 to 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. If participants complete Step 3 while Step 2 is still on-going, they should be followed as directed by the CMC (including HIV testing, plasma storage, and DBS storage).

Participants in Step 1 of the study who are unable to transition to Step 2 of the study for any reason other than HIV infection will be followed as directed by the CMC (including HIV testing, plasma storage, and DBS storage). If the reason is due to HIV infection, those participants will be referred for care and will be terminated from the study.

Laboratory results for safety monitoring cannot be used for multiple visits within the same calendar day. Sample test results should only be used (once) to meet the requirements of one visit and not duplicated for a second visit of the same day. Merged Study Visits: In unforeseen circumstances, and at sites with the capacity of rapidly (same day) receiving laboratory tests results, including all required HIV test results (FDA-cleared HIV rapid test, and instrumented Ab/Ag combination HIV immunoassay), missed safety visit procedures can be merged with an injection study visit. In this case, all laboratory test results must be received and reviewed prior to administration of study product without repeating laboratory testing. Although safety visit procedures are conducted, sites should use the visit code for the injection visit for all laboratory testing. Sample test results should only be used (once) to meet the requirements of one visit and not duplicated for a second visit of the same day. Meaning, one sample test results cannot have two different visit codes. The safety visit should be considered missed and documented as such.

Collect specimens and label tubes according to local regulations and the Blood Collection 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) at the time of specimen collection to prevent clotting.
- For plasma storage, approximately 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.

Note: Biological samples must be transported in a sturdy, hard-shelled closeable container with a Bio-Hazard sticker/label per local safety regulations.

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

		Step 1		
	Screening	**Day 0 Enrollment**	**Week 2**	**Week 4**
HIV testing[1]	X	X	X	X
Pregnancy[2]	X	X	X	X
HBsAg and HCV antibody testing	X			
HBsAb and HBcAb (can be done at enrolment or screening, not required at both)[3]	X[3]	X[3]		
CBC with Differential	X	X	X	X
Chemistry testing (BUN/urea, creatinine, CPK, calcium, phosphorous, glucose, amylase and lipase)[4]	Creatinine only	X	X	X
LFT (AST, ALT, total bilirubin, alkaline phosphatase)[5]	Only ALT, total bilirubin	X		X
Fasting Lipid Profile[6]		X		
Syphilis serological testing	X			
Urine GC/CT testing (urine or vaginal swab)[7]	X			
Urinalysis (protein and glucose)		X		
Plasma Storage[8]	X	X	X	X

FOOTNOTES FOR TABLE 11-1:

[1]The HIV testing algorithm is provided in the SSP Manual. Testing for acute HIV must be negative and must be performed within 14 days prior to enrolling the participant. 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 and reviewed the same day as sample collection and before product is administered.

[2]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. Confirmation of pregnancy at a subsequent visit at least 4 weeks after the initial pregnancy test is required. Participants with confirmed pregnancies will permanently discontinue oral CAB and will not transition to Step 2. They will skip to Step 3, be provided open label Tenofovir/emtricitabine (Trade name: TDF/FTC, Truvada®) as PrEP and be reviewed every 12 weeks until delivery. If pregnancy is not confirmed on subsequent testing, Step 1 participants will exit the study. Site staff will refer to their SOP for detailed management.

[3]Participants will be tested for Hepatitis B surface antibody (HBsAb), and Hepatitis B core antibody (HBcAb, total) at Screening or Enrollment. HbsAg and HCV Ab must be resulted and reviewed prior to enrollment.
[4]At Screening: Creatinine. At and after enrollment: BUN/urea, creatinine, CPK, calcium, phosphorous, glucose, amylase, and lipase.
[5]At Screening: ALT and TBili. At and after Enrollment: AST, ALT, total bilirubin, and alkaline phosphatase.
[6]Total cholesterol, HDL, triglycerides, and LDL (either calculated or measured). Participants must have fasted for at least 8 hours, preferably 12 hours prior to sample collection. Do not collect or test if <8 hrs fasting.
[7]At screening: For the GC/CT test, if sites use urine for that assay, instead of a vaginal swab. At all visits: For the pregnancy test, if sites use urine for that assay, instead of blood or plasma. At Week 2: For the urinalysis.
[8]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 SSP. Samples cannot be used by site or other lab for local purposes without specific instructions from the LC w/CMC consult.

Table 11-2: Schedule of Study Visits and Specimen Collection – Step 2. Injections

	Week 5	Week 6	Week 9	Week 10	Week 17	Week 18	Week 25	Week 26	Week 33	Week 34
HIV testing[1]	X		X		X		X		X	
Pregnancy[2]	X		X		X		X		X	
CBC with Differential	X	X	X	X	X	X	X	X	X	X
Chemistry testing (BUN/urea, creatinine, CPK, calcium, phosphorous, glucose, amylase and lipase) [3]	X	X	X	X	X	X	X	X	X	X
LFT (AST, ALT, total bilirubin, alkaline phosphatase) [4]	X	X	X	X	X	X	X	X	X	X
Fasting Lipid Profile[5] (Total Cholesterol, HDL, LDL, Triglycerides)										X
Syphilis serological testing									X	
Urine GC/CT testing (urine or vaginal swab) [6]					X				X	
Urinalysis (protein and glucose)	X	X	X	X	X	X	X	X	X	X
Plasma Storage[7]	X	X	X	X	X	X	X	X	X	X

FOOTNOTES FOR TABLE 11-2:

[1]The HIV testing algorithm is provided in the SSP Manual. Testing for acute HIV must be negative and must be performed within 14 days prior to enrolling the participant. 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 and reviewed the same day as sample collection and before product is administered.
[2]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. Confirmation of pregnancy at a subsequent visit at least 4 weeks after the initial pregnancy test is required. Participants with confirmed pregnancies will permanently discontinue oral CAB and will not transition to Step 2. They will skip to Step 3, be provided open label Tenofovir/emtricitabine (Trade name: TDF/FTC, Truvada®) as PrEP and be reviewed every 12 weeks until delivery. If pregnancy is not confirmed on subsequent testing, Step 1 participants will exit the study. Site staff will refer to their SOP for detailed management.
[3]At Screening: Creatinine. At and after enrollment: BUN/urea, creatinine, CPK, calcium, phosphorous, glucose, amylase, and lipase.
[4]At Screening: ALT and TBili. At and after Enrollment: AST, ALT, total bilirubin, and alkaline phosphatase.
[5]Total cholesterol, HDL, triglycerides, and LDL (either calculated or measured). Participants must have fasted for at least 8 hours, preferably 12 hoursprior to sample collection. Do not collect or test if <8 hrs fasting.
[6]At screening: For the GC/CT test, if sites use urine for that assay, instead of a vaginal swab. At all visits: For the pregnancy test, if sites use urine for that assay, instead of blood or plasma. At Week 2: For the urinalysis.
[7]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 SSP. Samples cannot be used by site or other lab for local purposes without specific instructions from the LC w/CMC consult.

Table 11-3: Schedule of Study Visits and Specimen Collection – Step 3. Open Label TDF/FTC Follow-Up

	Post Injection	Post-Injection	Post-Injection	Post-Injection	Post-Injection	Early Discontinuation
HIV testing[1]		X	X	X	X	X
Pregnancy[2]		X	X	X	X	X
CBC with Differential		X	X	X	X	X
Chemistry testing (BUN/urea, creatinine, CPK, calcium, phosphorous, glucose, amylase, lipase)[3]		X	X	X	X	X
LFT (AST, ALT, total bilirubin, alkaline phosphatase)[4]		X	X	X	X	X
Fasting Lipid profile[5]						
Syphilis serological testing				X		
Urine GC/CT testing (urine or vaginal swab)[6]		X	X	X	X	X
Urinalysis (protein, glucose)		X	X	X	X	
Plasma Storage[7]	X	X	X	X	X	X
DBS Storage[7]		X	X		X	

FOOTNOTES FOR TABLE 11.3:

[1]The HIV testing algorithm is provided in the SSP Manual. Testing for acute HIV must be negative and must be performed within 14 days prior to enrolling the participant. 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 and reviewed the same day as sample collection and before product is administered.

[2]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. Confirmation of pregnancy at a subsequent visit at least 4 weeks after the initial pregnancy test is required. Participants with confirmed pregnancies will permanently discontinue oral CAB and will not transition to Step 2. They will skip to Step 3, be provided open label Tenofovir/emtricitabine (Trade name: TDF/FTC, Truvada®) as PrEP and be reviewed every 12 weeks until delivery. If pregnancy is not confirmed on subsequent testing, Step 1 participants will exit the study. Site staff will refer to their SOP for detailed management.

[3]At Screening: Creatinine. At and after enrollment: BUN/urea, creatinine, CPK, calcium, phosphorous, glucose, amylase, and lipase.

[4]At Screening: ALT and TBili. At and after Enrollment: AST, ALT, total bilirubin, and alkaline phosphatase.

[5]Total cholesterol, HDL, triglycerides, and LDL (either calculated or measured). Participants must have fasted for at least 8 hours, preferably 12 hours prior to sample collection. Do not collect or test if <8 hrs fasting.
[6]At screening: For the GC/CT test, if sites use urine for that assay, instead of a vaginal swab. At all visits: For the pregnancy test, if sites use urine for that assay, instead of blood or plasma. At Week 2: For the urinalysis.
[7]Stored plasma and DBS 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 SSP. Samples cannot be used by site or other lab for local purposes without specific instructions from the LC w/CMC consult.

11.3.1 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 are reactive/positive, study drug should not be administered. **HIV rapid testing must be performed the same day and prior to administration of study drug i.e. the Turnaround Time (TAT) for the HIV rapid test assay is "same day".**

Rapid HIV test results will be reported to the appropriate study staff within the clinic.

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.

Per the HPTN 084-01 Protocol, there is no requirement to retain blood specimens used for HIV rapid testing for repeat analysis.

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

Participants with one or more reactive HIV test results at either the screening or enrollment visit 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.

The CMC 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. The CMC may request further testing and sample collections on a case by case basis.

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

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 be documented.

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, verified 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, a follow-up confirmation visit 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**. 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 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 (approximate) plasma aliquots.

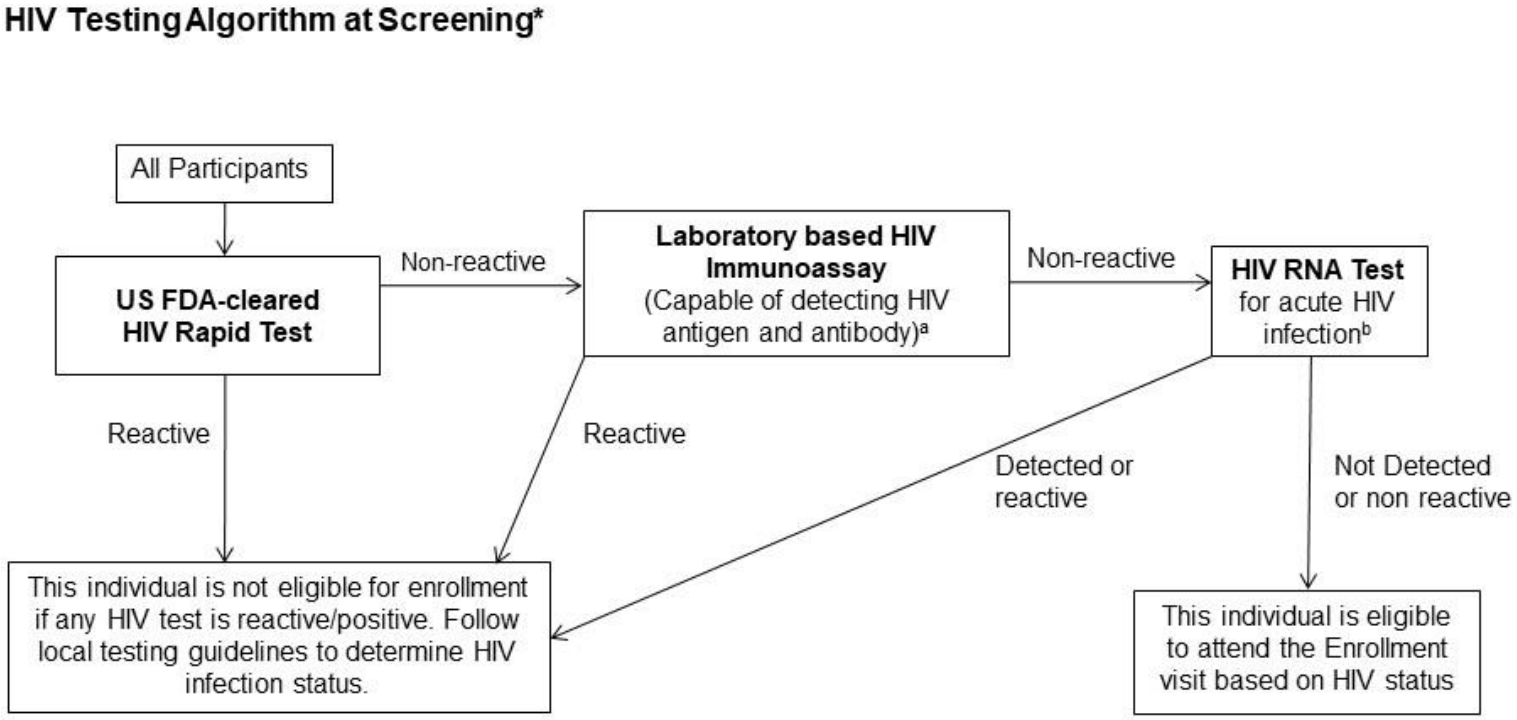
For split visits, excluding confirmation visits (held specifically to perform further HIV testing), the laboratory-based HIV instrumented assay does not need to be repeated if the split visit (i.e. X.1) occurs less than seven days from the initial visit (i.e. X.0). If the split visit is seven or more days from the initial visit, the HIV laboratory based HIV instrumented assay must be repeated. This also applies to DBS samples if regularly scheduled for that visit (i.e. repeat DBS collection and storage at 7 or more days). 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 IV of the protocol.

Participants with confirmed HIV infection during Step 3 will be followed at least for the duration of Step 3, with possible additional assessments and follow-up to be determined by the members of CMC

Figure 11.1 HIV Testing Algorithm at the Screening Visit:



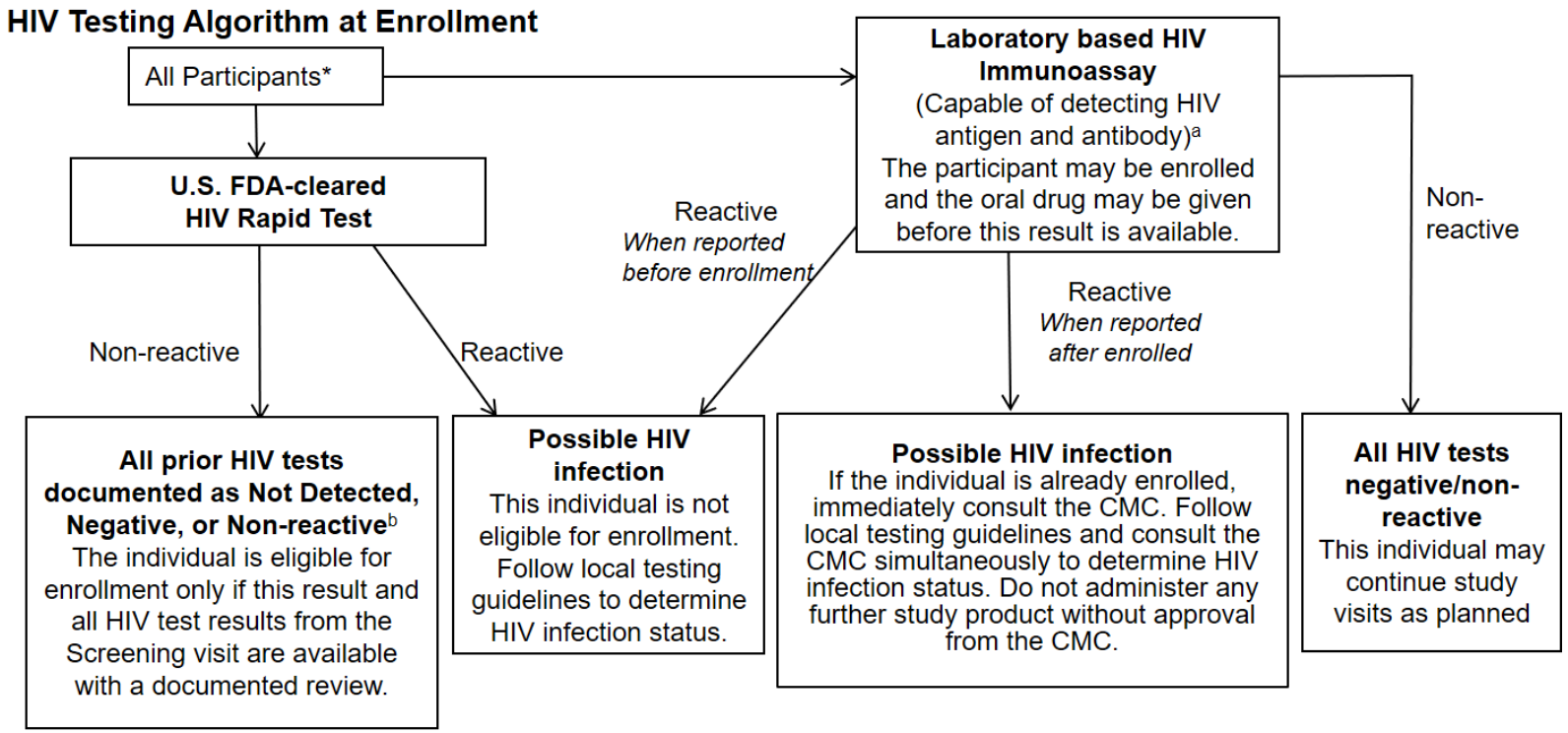
NOTES:

* Site-specific HIV testing plans must be approved by the HPTN LC before the study opens.

[a] 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 4th generation or 5th generation assay).

[b] 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:



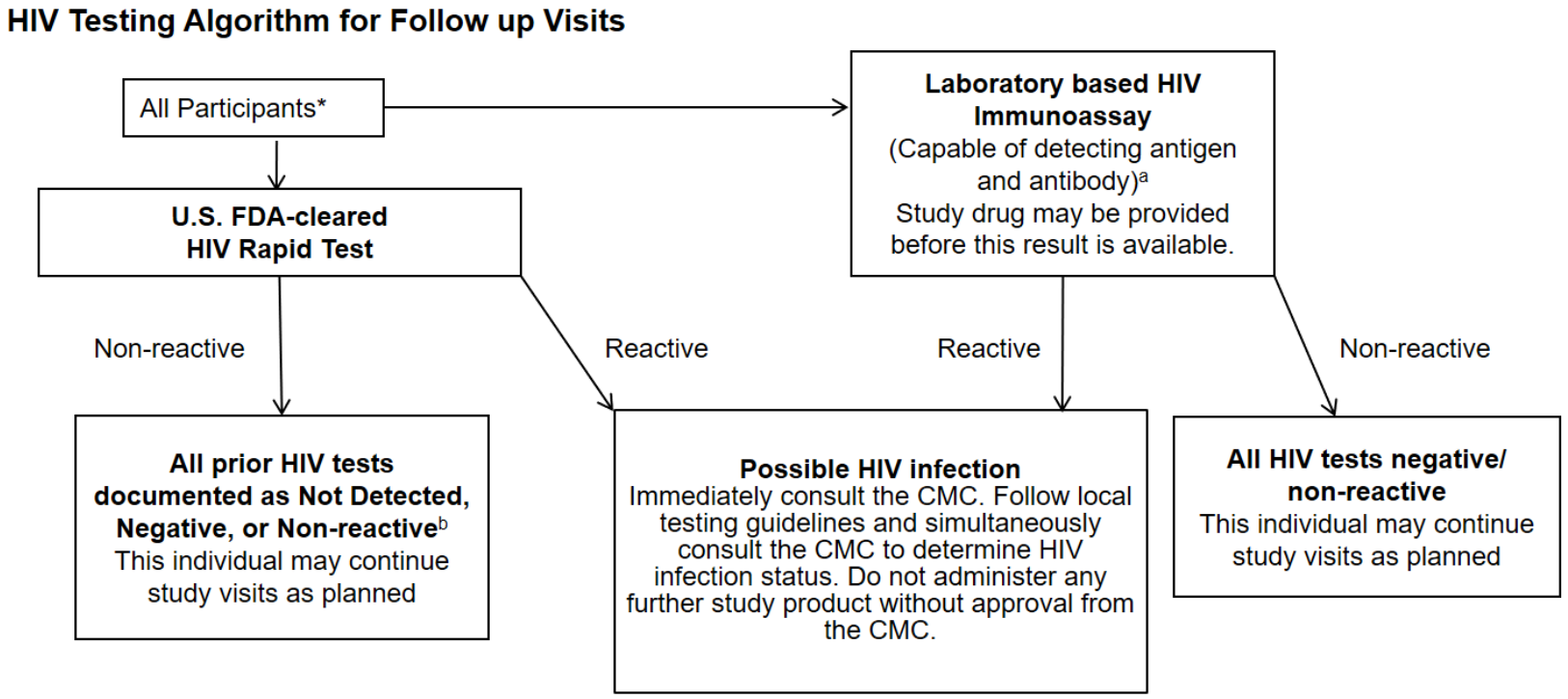
NOTES:

* 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 CMC for additional guidance once all of the test results from this visit (including the HIV RNA test) are available.

[a] 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 4th generation or 5th generation assay).

[b] 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 or not detected.

Figure 11.3 HIV Testing Algorithm at all Other Visits with HIV Testing:



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 CMC for additional guidance once all of the test results from this visit (including the HIV RNA test) are available.

[a] 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 4th generation or 5th generation assay).

[b] 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.

Table 11-4: Additional Procedures for 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[1]
HIV testing[1]	X				
CD4 cell count.	X		X		X
HIV Viral Load Testing	X		X		X
HIV resistance testing[2]	X				
Chemistry Testing (BUN/Urea, creatinine, CPK, calcium, phosphorous, glucose, amylase, lipase) [3]		X	X	X	X
LFT (AST, ALT, total bilirubin, alkaline phosphatase) [4]		X	X	X	X
Plasma Storage[5]	X	X	X	X	X
DBS storage[5]	X				

FOOTNOTES FOR TABLE 11-4:

[1] 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.

[2] Sites will 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.

[3] Required chemistry testing: BUN/urea, creatinine, CPK, calcium, phosphorous, glucose, amylase, and lipase.

[4] Required LFTs: AST, ALT, total bilirubin, and alkaline phosphatase. [5] Stored plasma and DBS will be used for Quality Assurance testing and other assessments at the HPTN LC (see Section 9) including potential assay for plasma CAB concentrations. Assessments will be performed retrospectively; results will not be returned to study sites or participants, except as noted in Section 9.0.

The CMC must be notified immediately if one or more reactive HIV test results are obtained 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 CMC.

[1] The week 48 visit should be timed as closely as possible to 52 weeks after the participant received their last injection.

The Confirmation visit for HIV testing and plasma storage should be performed on a different date than the blood draw that gave the initial reactive or positive HIV test. Contact the CMC as soon as possible if this is not feasible or conflicts with site-specific policy.

11.3.2 Hepatitis Testing

Testing for HBsAg and HCV will be performed at screening.

Testing for HBaAb and HBcAb Total will be performed at either screening or enrollment at the discretion of the site.

Sites will follow local testing arrangements for the collection and testing of samples, this will be described in the site SOPs.

Test results for HBsAg and HCVAb are required for the enrollment visit.

11.3.3 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.

11.3.4 Creatinine Clearance

Calculated creatinine clearance (estimated Glomerular Filtration Rate *eGFR*) will be performed at all visits where chemistry testing is performed, using the Modified Bedside Schwartz Equation (2009).

eGFR = (0.413 x height)/(serum creatinine)

eGFR units are mLs/minute per $1.73m^2$, when height is by cm and serum creatinine as mg/dL

11.3.5 Fasting Lipid Profile

A fasting lipid profile (total cholesterol, HDL, triglycerides, LDL – calculated or measured) will be collected at enrollment and week 34. 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 are recommended to return for sample collection and testing within 72-hours, or it is acceptable to be collected at the next scheduled 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 are NOT required prior to the issue of study product.

11.3.6 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. Per the HPTN 084-01 Protocol, there is no requirement to retain urine specimens used for urinalysis testing for repeat analysis.

11.3.7 Pregnancy Testing

Sites will follow local testing arrangements for the collection and testing of urine, plasma, or serum for beta human chorionic gonadotropin (βHCG) pregnancy test (sensitivity of ≤ 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.

11.3.8 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.

Syphilis results from the screening visit are not required prior to enrollment.

11.3.9 Urine or Vaginal Sample for GC/CT Testing.

Sites will follow local testing arrangements for the collection and testing of urine sample for GC/CT nucleic acid testing. This will be described in the site SOPs.

GC/CT results from the screening visit are not required prior to enrollment.

11.4 Plasma Processing for Storage

Approximately 20 mL of EDTA whole blood should be drawn into spray dried EDTA tubes for plasma storage at each time point indicated in Tables 11-1 to 11-4, and whenever additional HIV testing is performed. Sites are requested to store 5 x 1.8 mL aliquots of plasma if possible. The HPTN LC should be informed any time that three or fewer aliquots with 1.8mL or less are stored.

Note. The 1.8mL plasma volume stated in this SSP is an approximate volume. This can be estimated using for example the volume markings on the cryovials. The use of a precision pipette is not required for this purpose.

The manufacturer of this example tube stops gradations at 1.25mL for the 2mL cryovial. The 1.8mL needed is an approximate volume. For these cryovials, the top of the vertical striped area is an estimated maximum fill 'line' for a limit fill volume to prevent cracking of the container during freezing, and will provide an acceptable 1.8mL estimate. See photo to the right for reference (Figure 11.4) The plasma level needs to be between the two arrows for 1.8mL to be delivered and stored. The optimal level is at the indicated top arrow, near the cryovial 'ring' below the cap. Various methods for achieving the desired volume are possible. Example list, other methods are not prohibited or excluded:

- Use of a pipette with a precise measurement (not required)
- Use of a graduated disposable transfer pipette
- A marked-up a cryovial, or filled cryovial with a liquid for a comparison level (properly labeled as a blank for lab safety requirements)

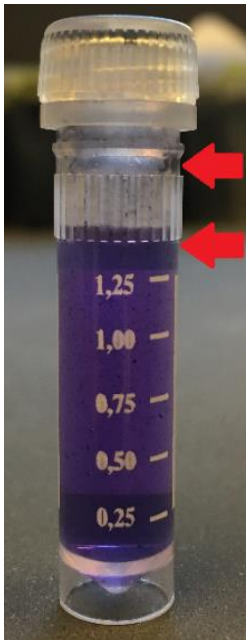


Figure 11.4

An additional approximate 20 mL 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 by the CMC and 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. 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 request the use of Sarstedt (cat# 72.694.006) 2mL Cryovials, or cryovials of the same dimensions. Reminder: Do not add more than 1.8 mL due to expansion of plasma during freezing. Do not freeze in an open rack or box. Freeze in cryoboxes with the lid in place.
    - Other cryovials 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. The use of a negative airflow biosafety cabinet is not required for this specimen processing and storage.
- 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.
    - Additional sample condition codes besides QNS, to be used as directed by the HPTN LC, include “SNP” and “SNR”.
- Store the aliquots in the freezer locations assigned in LDMS in an ultra-low minus 70° to minus 90° freezer.

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 at least for one year after the primary research paper has been published. The sites will be notified by the HPTN LC when they can destroy samples from participants that did not consent to long term storage and when the remaining samples can be destroyed. The HPTN LC will seek permission from protocol leadership and network leadership prior to this destruction process. Any samples that are collected in error etc. should not be destroyed without the permission of the HPTN LC.

LDMS Entry:

For this study, the protocol/ID2 field is 084-01

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
    - 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 11.5 through 11.6

LDMS Specimen Code for Plasma Storage

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

Codes used in table:

BLD	**Blood**
DPE	**Spray Dried EDTA**
PL2	**Plasma, Double Spun**
N/A	**Not Applicable**

- All plasma vials are stored electronically in the LDMS and physically in a 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.

11.5 Dried Blood Spots (DBS)

11.5.1 DBS 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 WB100003, or Fisher Scientific # 09-800-17).
- Humidity indicator Cards (Manufacturer # MS200032 or MS200033; ADCOA # MS20003-2 or MS20003-3; Fisher Scientific # NC9511648). 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 25uL, variable 10-100µl, or 20-200µl micropipette with appropriate filtered pipette tips. Sites should check with local suppliers for appropriate tips for their micropipettes.

11.5.2 DBS Preparation and Storage

The use of a negative airflow biosafety cabinet is not required for this specimen processing 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 as indicated in Tables 11-3 and 11-4 for complete schedules.

DBS should be prepared from an EDTA blood tube received in the laboratory. For HPTN 084-01 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 completed.

The EDTA tube should be well mixed before preparing the DBS. Pipette 25 µl of whole blood directly onto the center of each spot on the filter paper so that it is contained within the circle (Figure 11.1).

- 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 (spotted) within 6 hours of the time of collection; the actual time of collection should be recorded on the Case Report Form, as well as DBS creation time.
- 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 Figure 11.6.
    - Additional sample condition codes besides QNS, to be used as directed by the HPTN LC, include “SNP” and “SNR”.
    - Primary container and aliquot entries should have the “SHV” (short volume) condition code used as needed when incomplete volumes are obtained
    - Please remember to contact the HPTN LC when using condition codes not listed in the SSP.
- Assure the blood tube has been inverted 8 times and is 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 11.10 to 11.12 below). Return the cap to the tube and process for other lab tests (i.e. plasma processing) as needed.
    a. The pipette tip should be held approximately 3mm above the spot location and the blood dispensed onto the card with one single dispensing motion from the micropipette. Do not touch, press, or smear the spots.
- Air dry the cards in a card holder or other drying rack (Figure 11.13). Ideally

drying time should be between 2 and 16 hours. If storage cannot take place within 16 hours for example over a weekend, an appropriate comment must be made in LDMS to indicate the drying time.

- Keep the DBS cards away from direct sunlight. DBS cards should be dried at the designated lab room temperature, which should be between 15^{o}C and 40 ^{o}C. DBS cards should not be dried in excess of 40^{o}C. Do not dry the DBS cards with a fan or any heat source in an attempt to decrease drying time. Air dry only. The use of a biosafety cabinet is not required for the drying of dried blood spots for HPTN 084-01. If a cabinet is used there is no requirement for the airflow to be operational or documented for DBS purposes.
- 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 11.14 and 11.15. Indicator cards and desiccant packs should be kept in their manufacturer stock containers (airtight) until the DBS card is dried and ready for freezer storage.
- Store bag in an appropriately labeled box at -70 to -90°C.
    a. If the indicator indicates too much humidity exposure (color change from blue to pink- 40% to 50% level or higher), replace the old desiccant pack and indicator card with a new one and comment the change in LDMS.
    b. There is no need to check the humidity indicators unless DBS are handled for another purpose (i.e. shipping), and action is needed if a problem is noticed.

LDMS Entry:

For this study, the protocol/ID2 field is 084-01

DBS from EDTA whole blood (example 4mL draw) as follows:

- A single primary container of 4mL EDTA whole blood is created
- 5 aliquots of 25uL each are created (1 for each spot on the DBS card)
- See figures 11.6

LDMS Specimen Code for DBS Storage

Test	Primary LDMS Code	Additive	Derivative	Sub Add/Deriv
Dried Blood Spots	**BLD**	**DPE**	**DBS**	**N/A**

Codes used in table:

BLD	**Blood**
DPE	**Spray Dried EDTA**
DBS	**Dried Blood Spot**
N/A	**Not Applicable**

- All DBS are stored electronically in the LDMS and physically in a minus 70°C to minus 90°C freezer. Selected cards will be shipped to HPTN Laboratory Center (LC) when requested.

- In addition to the illustrations, 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.

Figure 11.5 Example LDMS Screening Visit 1.0 (Web-based). Screenshot will be updated to show 084-01

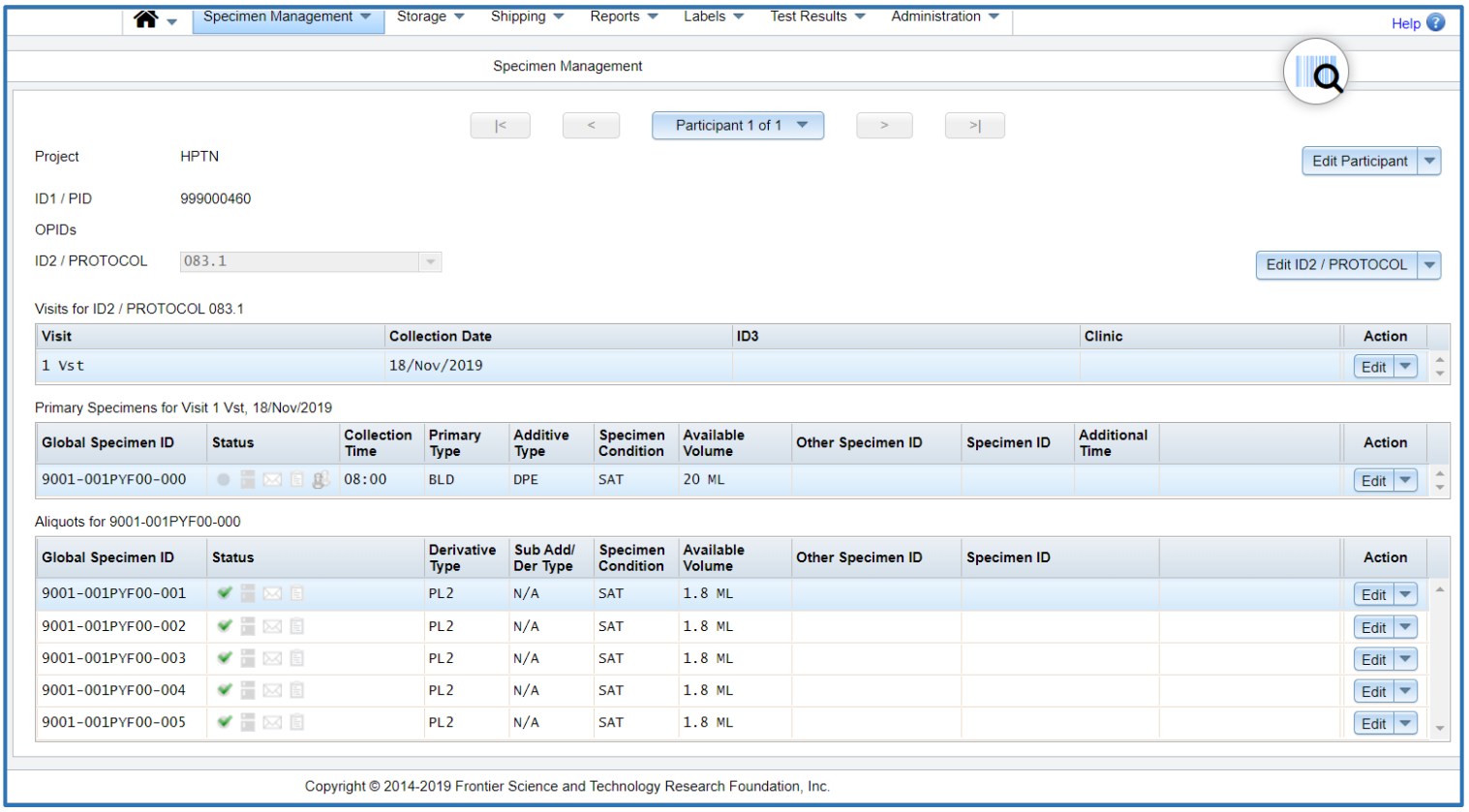


Figure 11.7 Example LDMS Step 3 Visit (Web-based).

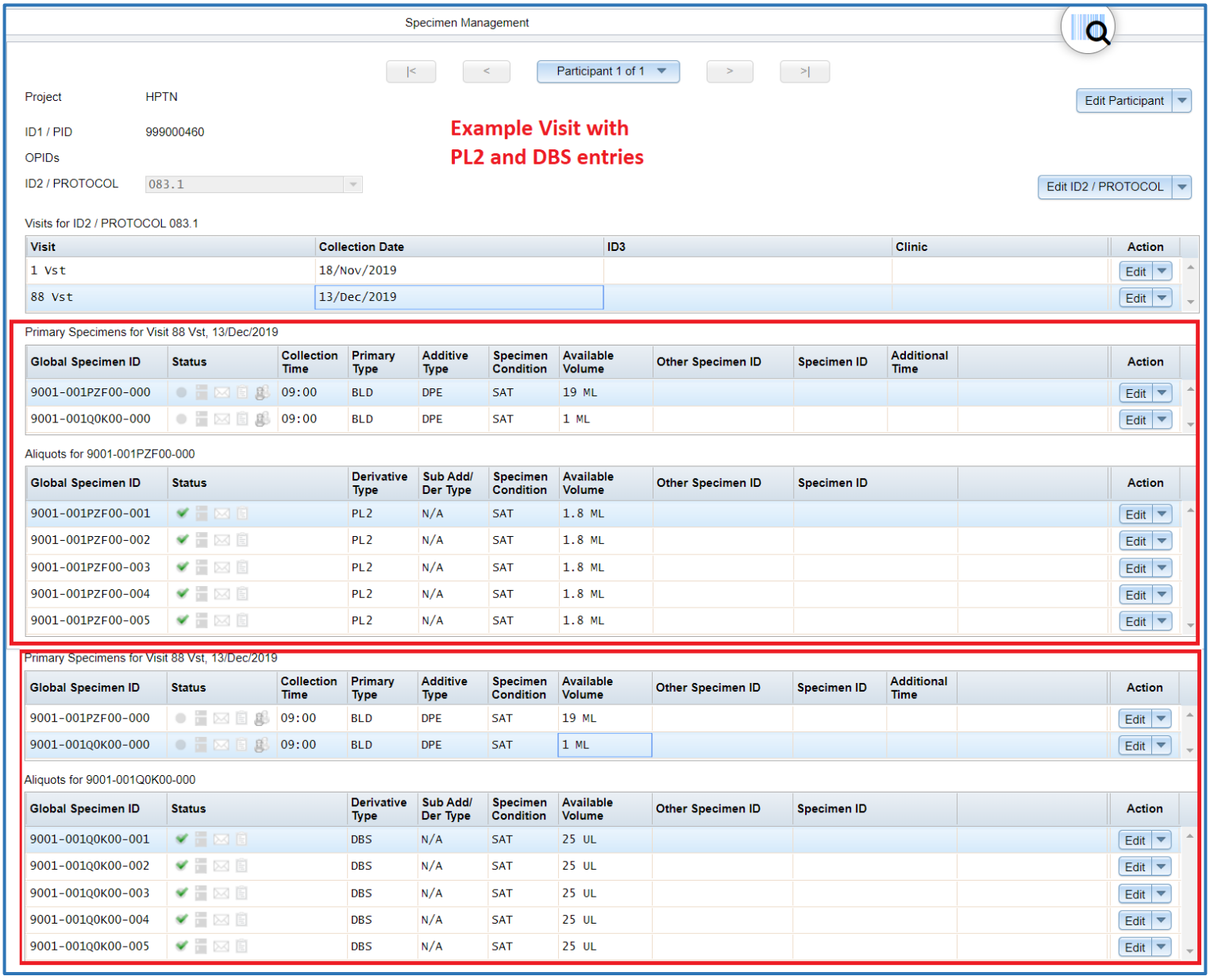


Figure 11.7 Example DBS LDMS Labels for each aliquot (Web-based)

Figure 11.8/11.9 Suggested labeling of DBS cards

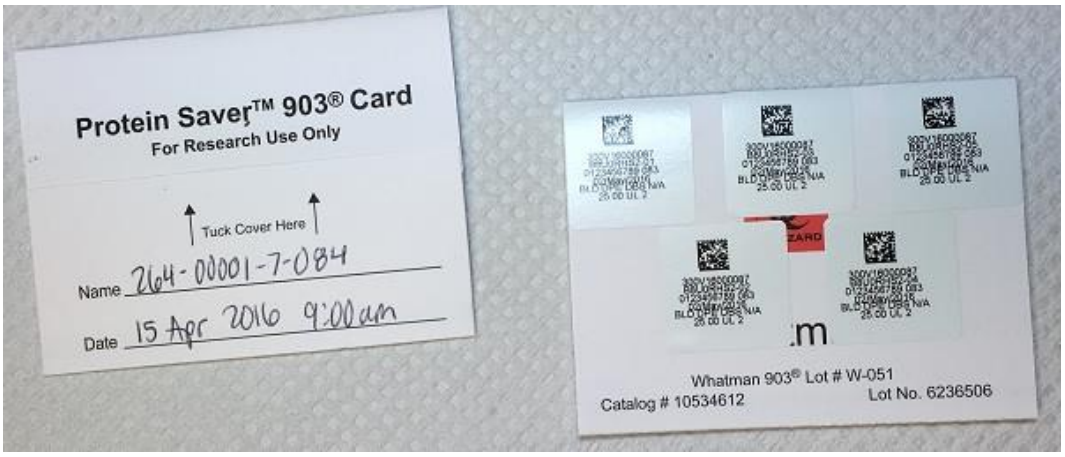
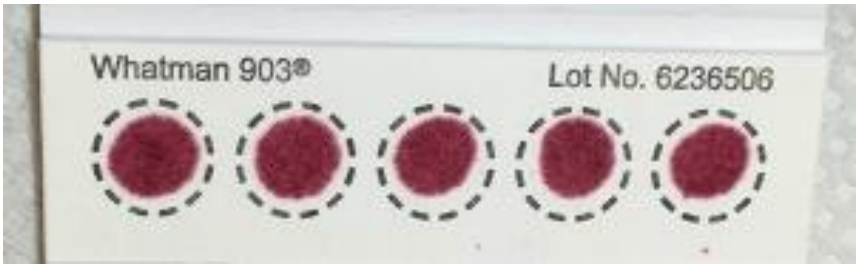


Figure 11.10 Example of correctly spotted DBS card (25µl spot volume)



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

Figure 11.11 Example of *incorrectly* spotted DBS card

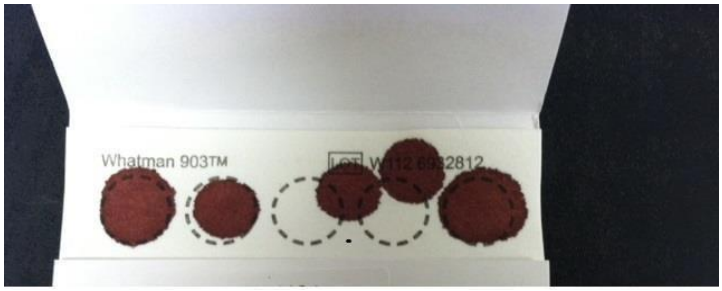


Figure 11.12 Example of *incorrectly* spotted DBS card (continued)

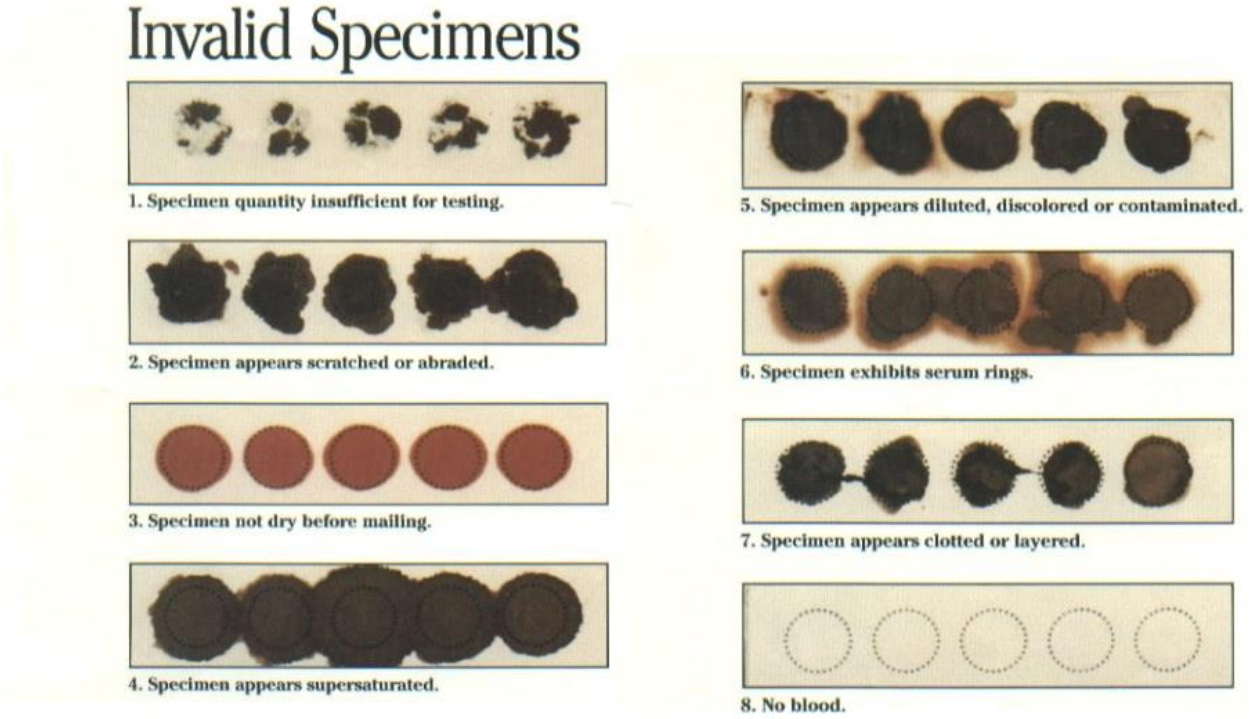


Figure 11.13 Whatman card drying rack (VWR catalogue # 89015-592)

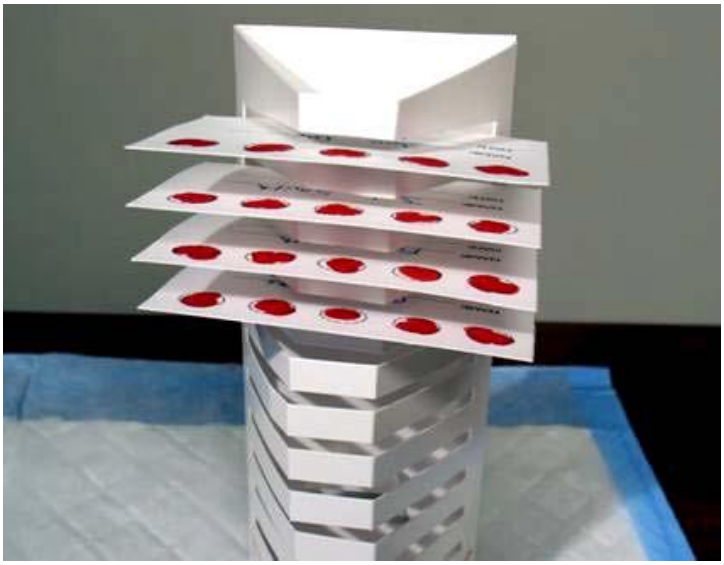


Figure 11.14 Properly labeled and packaged DBS card for storage

Figure 11.15 Properly labeled and packaged DBS card for storage (2)

11.6 Shipping of Samples to the HPTN Laboratory Center

Each site will ship plasma or DBS samples to the LC or designated laboratory upon request or following a quarterly shipping schedule as determined by the LC. The site will batch the shipment, export the LDMS data and notify the SDMC and LC. Additional samples may be specifically requested by the HPTN LC (e.g., archive/back-up samples).

Contact the HPTN LC at Johns Hopkins University (Estelle Piwowar-Manning: epiwowa@jhmi.edu, +410-614-6736) 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 the LDMS Lab number 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.

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 as indicated in the following pages, for Johns Hopkins Hospital (plasma) or the University of Colorado (DBS). For some shipments, an alternate address may be provided at the time of request. Shipment containers may be returned to sites if in suitable condition and a return slip or account number is provided. Returning of shipping containers is at the discretion of the HPTN LC.

Notify the HPTN LC via email (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
- Expected date of arrival

Plasma Shipping:

Each site is requested to keep “To Be Shipped” sample storage box (es) in their freezers.

a. Starting at Visit 2 (enrollment visit), and until the end of the study, all plasma aliquots with an LDMS global ID ending “-001” should be stored in these boxes.

b. The remaining plasma aliquots should be stored as per normal site standards.

All aliquots in these "To Be Shipped" boxes should be shipped, on a quarterly basis, during the second week of the months of February, May, August, and November for the remainder of the study.

Samples will be shipped to:

Estelle Piwowar-Manning

Johns Hopkins University Hospital

Department of Pathology

Pathology Building, Room 313

600 North Wolfe Street

Baltimore, MD 21287

USA

Phone: 410-502-0752

LDMS Number 300

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 members.

Separate LDMS batches are required for the quarterly shipments, any QA requested samples, and Seroconverter samples if they are sent in the same shipment.

DBS Shipping

DBS sample lists for shipment will be posted on the SCHARP Atlas website for each site. An Email will be sent one week before the quarterly shipments are scheduled to notify each site that the up-to-date shipping list is posted. This should allow each site to have more than one week for DBS shipment preparation (and approximately one week for plasma shipment preparation). Dried blood spot cards should also be shipped during the second week of the months of January, April, July, and October.

Storing Dried Blood Spots by individual participant will simplify the shipment process.

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

CAVP Laboratory

C-238-V20, Rm V20-4410

12850 East Montview Blvd

Aurora, CO 80045

USA

Phone: 303-724-6132

LDMS Number 533

When shipping DBS, make sure 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.

The following sections describe types of specimens to be shipped to the HPTN LC for testing:

11.6.1 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.

11.6.2 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 stored on site for shipment to the HPTN LC upon request or 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.

11.6.3 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. Results from specialized resistance testing (e.g., minority variants analysis, if performed) will not be returned to study sites.

11.7 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.