ACTG/IMPAACT LABORATORY TECHNOLOGIST COMMITTEE STANDARD OPERATING PROCEDURE			
Title:	Protocol Participation and Laboratory Processing Chart Preparation Procedures		
SOP number:	LTC-Int-001	Effective:	09Dec2022
Version:	V4.0	Last reviewed:	13Jan2014
Originator:	ACTG/IMPAACT Laboratory Technologist Committee	Pages:	12

TABLE OF CONTENTS

Title:	Protocol Participation and Laboratory Processing Chart Preparation Procedures		
SOP number:	LTC-Int-001	Effective:	09Dec2022
Version:	V4.0	Last reviewed:	13Jan2014
Originator:	ACTG/IMPAACT Laboratory Technologist Committee	Pages:	12

1 PURPOSE

The purpose of this document is to provide guidance for Laboratory Technologists serving on ACTG/IMPAACT protocol teams and as LPC reviewers.

2 BACKGROUND

The role of the LT is to help clarify the collection, transport, processing, storage and shipping of specimens for evaluations defined in the protocol SOE(s). This clarification includes documentation of specimen volumes, derivative specimen types, number, and volume of expected aliquots, specimen processing, storage, shipping and any other relevant information to assure quality specimens for protocol-defined testing. The LPC is created by the LT and documents the details for specimen handling that is not provided in the protocol document. Instructions for non-standardized processing should be included in the LPC, while routine processing is linked to standardized processing SOPs. The detailed information contained in the LPC should not be replicated in any other protocol-specific or companion documents so as to reduce redundancy and prevent errors during editing or revising.

3 SCOPE

Users of the ACTG/IMPAACT Laboratory Manual and clinical trial site staff.

4 ABBREVIATIONS

ACTG	AIDS Clinical Trials Group
CPT™	Cell Preparation Tube (BD Vacutainer® blood collection tube)
CTS	Clinical Trials Specialist
DARS	Data Availability Reports
DMC	Data Management Center
eCRF	Electronic Case Report Form
HANC	Office of HIV/AIDS Network Coordination
IATA	International Air Transport Association
IRB	Institutional Review Board
IMPAACT	International Maternal Pediatric and Adolescent AIDS Clinical Trials Group
LC	Laboratory Center
LDM	Laboratory Data Manager
LDMS	Laboratory Data Management System
LOC	Leadership and Operations Center
LPC	Laboratory Processing Chart
LS	Laboratory Specialist
LT	Laboratory Technologist
LTC	Laboratory Technologist Committee
MOP	Manual of Operations
MTA	Materials Transfer Agreement

NICHD	National Institute of Child Health and Human Development
PBMC	Peripheral Blood Mononuclear Cell
PSWP	Protocol Specific Web Page
RAG	Repository Advisory Group
SOE	Schedule of Events

5 PROTOCOL TEAM PARTICIPATION AND PROTOCOL DOCUMENTS

5.1 LTs are added early to protocol teams to provide laboratory processing guidance.

5.1.1 Participation in team calls is important. If a call time has not been established, the CTS should include the LT volunteer when polling for a call time and day.

5.1.2 The LT should notify the CTS if they are unable to participate in a call and should read the minutes from the call to keep up with the topics that were discussed.

5.1.3 Participation in team calls may change throughout the course of the protocol (development, implementation, follow-up and post-follow-up) and will vary by protocol.

5.1.4 If obligations prohibit the LT from continuing participation as a team member, it is the responsibility of the LT to notify the LTC leadership as soon as possible to determine the need for replacing a LT.

5.2 Protocol documents

5.2.1 The protocol document is the main regulatory document. The protocol document should direct readers to the LPC for processing instructions and to the MOP for collection instructions if applicable.

5.2.1.1 Clarification memos provide further explanation or more detailed information related to current protocol language.

Note: For more information see the current version of the IMPAACT Manual of Procedures Protocol Development and Modifications and/or the ACTG Protocol Development and Finalization SOP (ACTG-105).

5.2.1.2 A letter of amendment is drafted when a change in the protocol affects inclusion or exclusion criteria or changes the informed consent.

5.2.2 The purpose of the LPC is to define all specimen collection, processing, and shipping requirements. Identify unusual specimen types, processing or shipping demands early in protocol development.

Note: See Section 6 below for details regarding LPC organization and contents.

5.2.3 The MOP is a supplemental document to the protocol that is intended to assist and guide sites in the conduct of the study (For more information see the current version of the ACTG Protocol Team Handbook or IMPAACT Manual of Procedures Protocol Development and Modifications). Processing details should not be provided in the protocol or MOP. The MOP should reference the LPC for processing details.

5.3 Review of Protocol draft versions and sign-off

5.3.1 Read the entire text of each major draft version of the protocol as it is being developed; offer editorial comments and suggestions for each version. For minor versions, focus on the bolded changes. Request clarification from the team if any section of the document is unclear or seems contradictory.

5.3.2 Compare Schedule of Evaluations with the corresponding body text, footnotes, pharmacology plan, specimen collection schema and statistical section.

5.3.3 Confirm that any blood volumes and other specimen collections referenced in the informed consent form templates are accurate and correlate with the LPC.

5.3.4 Email the protocol team to request clarification for any discrepancies.

5.3.5 The LT must sign off on the final protocol version.

Note: The LPC must be completed within seven days of posting the final protocol. If the LPC must be posted with missing information (e.g., a shipping address), it should be noted that this information will be added when it is available.

5.4 Identification of Protocol-Specific Challenges

5.4.1 Unresolved issues should be brought to the LTC leadership as early as possible. Protocol-specific challenges can be raised and discussed at the beginning of each LTC conference call or by sending an e-mail to the LTC logon.

5.4.2 Examples of unusual collection and/or processing requirements include:

5.4.2.1 Leukopak processing requires the laboratory to demonstrate proficiency and be certified before receiving the first specimen. and participation in on-going proficiency testing throughout the scheduled leukopak collections (https://iqa.center.duke.edu/resources/leukapheresis-processing/enrollment; contact actg.labcenter@fstrf.org).

5.4.2.2 Biopsy or other tissue collection procedures may involve specialized reagents (e.g., formaldehyde or RPMI as a transport medium),

specialized handling, or real-time shipments.

5.4.2.3 Intensive PK collections may require specialized scheduling between laboratory and clinic to ensure that the specimens are processed and stored at the designated time frame. The LPC must state that the collection, processing and freeze times must be entered in LDMS.

5.4.3 The LT should investigate and inform the protocol team if non-standard reagents or disposables have short out-dates or other attributes that will increase sites costs.

5.4.3.1 Cost mitigation options such as centralized purchase and distribution should be considered.

5.4.3.2 Detailed guidance must be provided in the LPC and emphasized during start-up calls or laboratory training calls.

5.4.3.3 Examples of non-standardized consumables may include: PAXgene® or BD Vacutainer® CPT™ collection tubes, amber or barcoded cryovials, and specialized transport containers (i.e., temperature-controlled containers for the shipping of a leukopak or sputum).

5.5 Review of Protocol Electronic Case Report Forms (eCRFs):

5.5.1 Review all laboratory related eCRFs.

5.5.2 Ensure all primary specimens, collection times, volumes, and DMC test codes, as appropriate, are properly tracked in the eCRFs. Work with the identify LDMS specimen codes, preloads/template codes, and visit codes, as applicable.

5.5.3 Ensure all shared collection tubes have all assays delineated correctly.

5.5.4 Ensure eCRFs, SOE, LPC and LDMS preloads/templates correlate to avoid queries.

5.6 Review of Protocol Specimen Processing Budget (ACTG protocols only)

5.6.1 The protocol specimen processing budget is a portion of the total protocol budget and is specific to the specimens collected per the SOE and processed by the local network processing laboratory and detailed in section 3 of the LPC.

5.6.2 Specimens included in section 2 of the LPC are collected and sent to local testing laboratories and should not be included in the protocol specimen processing budget.

5.6.3 Protocol-specific shipping costs should be included in the specimen processing

budget.

Note: This does not include shipments to central biorepositories.

5.6.4 The LT should review the protocol specimen budget to make sure it includes all the processes defined in the SOE(s).

6 LPC PREPARATION

The LPC Template consists of a cover page and multiple sections as defined below. The cover page must include contact information and disclaimer notes, table of contents and a table highlighting non-standard reagent and/or processing or shipping requirements. The "Repeat Header Rows" option ensures the visit-specific information included in the header is carried over to tables split across pages.

6.1 LPC Section 1: Schedule of Laboratory Evaluations

6.1.1 Copy the SOE into excel or word and use this template to remove the non-laboratory-related line items and to add estimated blood volumes.

Note: Check that blood draw volume does not exceed the U.S. National Institutes of Health (NIH) recommended safety limits.

Note: In accordance with U.S. National Institutes of Health (NIH) recommendations, adult blood collection will not exceed 10.5 mL/kg or 550 mL, whichever is smaller, over any eight-week period, and pediatric blood collection will not exceed 5 mL/kg in a single day or 9.5 mL/kg in any eight-week period.

Note: The blood volumes should include both metric (mL) and US measurements (1 tablespoon = 15 mL).

Note: An example of a Blood Volume Calculator spreadsheet is posted on the LTC team site in LPC Development Tools.

6.1.2 Offer suggestions to the team for expected derivative recovery as a way to initiate discussions regarding specimen collection, processing, and aliquot expectations.

6.1.3 Share common sections 2, 3 and 5 for protocols with multiple SOEs. Headers for sections 1 and 4 can be coordinated using color coding.

6.1.4 Include a priority listing of blood collections following the SOE in the LPC as documented in the protocol or per protocol team request.

6.2 LPC Section 2: Safety/Clinical Laboratory Evaluations (Refer to Section 4 for tube types and collection volumes)

6.2.1 Define specimens that are collected and sent to a local testing laboratory.

6.2.2 Include evaluation, tube type, tests (list of analytes), and eCRF # for each line item (specimen) in the SOE.

6.2.3 Define the minimum volume and additive for each analyte.

Note: The LPC Cover Page includes a disclaimer stating that blood volumes for safety/clinical laboratory evaluations are estimates and actual blood volumes collected may differ by site.

6.3 LPC Section 3: Specimen Processing (Refer to Section 4 for tube types and collection volumes)

6.3.1 Define the specimens that are sent to local processing laboratory for storage or shipment.

6.3.2 Using the Standardized Wording Template, include evaluation, tube type, special collection notes, eCRF #, processing, and shipping instructions for each line item (specimen) in the SOE.

6.3.3 Define non-standardized collection and specimen processing instructions with assistance from the protocol team and appropriate testing laboratory personnel.

Note: Non-standard supplies or reagents should be listed in the table entitled *Protocol-Required Non-Standard Reagents and Supplies* in the LPC Template.

6.4 LPC Section 4: Evaluations by Visit

6.4.1 Include all specimens collected per the SOE by visit.

6.4.2 Include evaluation, specimen, aliquots, LDMS code, and special notes.

6.4.3 Create a separate table for each visit.

Note: Visits that contain the same collection requirements may be combined to reduce the length of the LPC.

Note: Do NOT allow rows to break across pages. Evaluations for each visit should be on one page, whenever possible.

Note: Changing the width of columns may facilitate more efficient use of space.

6.4.4 Indicate in the LPC whenever primary specimens can be combined in order to minimize total blood volumes and maximize cell recovery.

Note: The blood volumes defined in the LPC SOE must match the blood

volumes in LPC Section 4.

6.4.5 Verify unusual LDMS codes with the study LDM. Send proposed new codes to the LTC for review and approval.

Note: If aliquots are not generated (e.g., safety laboratory tests), the Aliquots and LDMS Code columns are marked not-applicable (NA).

6.4.6 Verify the preload/template name for each visit with the LDM and include it in the LPC section 4 header.

6.5 LPC Section 5: Helpful Links and Shipping Addresses

6.5.1 Confirm all shipping instructions and provide details in section 5 of the LPC.

6.5.2 Add shipping information for centralized repositories.

Note: IMPAACT LPCs should include shipping instructions and contact information for both NIAID (BRI) and NICHD (Fisher) repositories.

6.5.3 Confirm that the schedule for shipping specimens to testing laboratories is clearly defined (e.g., same day/same week or batch shipped).

- Specimens should not be shipped to the repository if testing is going to be performed within 6 months of collection.
- If specimens are to be held locally, the team must define how laboratories will be notified when to ship (e.g., Frontier Science will send a list of specimens to ship, or laboratories will batch ship specimens when a certain timepoint is reached).
- Frequent shipments to a testing laboratory will add extra burden and cost to both processing and testing laboratories. Therefore, the LT should suggest sending specimens to the repository for batch-testing at a later timepoint.
- Include information regarding any special documentation that may be required by non-LDMS receiving laboratories.

6.6 LPC Section 6: Revision History

Any protocol changes (e.g., LPC errors, clarification memos, protocol amendments, etc.) are bolded on the LPC and documented in this section.

6.7 LPC Section 7: Appendices

Appendices may include additional documents or instructions (e.g., laboratory requisitions,

detailed PK specimen processing, detailed shipping instructions, etc.).

7 LDMS TEMPLATES/PRELOADS

7.1 The use of LDMS templates/preloads is mandated by the ACTG and IMPAACT leadership.

7.1.1 Templates/preloads populate the LDMS for primary specimen collection and expected volumes and numbers of derivatives.

7.1.2 Templates/preloads comments should only include reminders for unusual processing or handling.

7.2 The LPC must be completed before the LDM can create LDMS templates/preloads.

7.3 The LT is responsible for reviewing the LDMS template/preload spreadsheet.

7.4 The LT and LDM must determine if changes to the LPC require updates to the LDMS templates/preloads.

7.5 Frontier Science deploys new LDMS templates/preloads.

7.5.1 Windows version: Changes are deployed via the LDMS export process.

7.5.2 Web version: Changes are available once deployed by Frontier Science.

8 LPC FINAL REVIEW AND POSTING

Final LPC review and sign-off is required by the team before the LPC can be posted. The protocol CTS or LS will submit the final LPC to the team and post it once sign-off is complete.

8.1 The primary LT is responsible for ensuring the LPC is complete.

8.1.1 Check that the basic format is correct.

8.1.2 Check for non-standardized processing, reagent or disposable requirements and confirm that they are presented on the first page following the Table of Contents.

8.1.3 Cross check LPC SOE against protocol SOE to ensure that all laboratory evaluations are included.

8.1.4 Confirm that laboratory-related footnotes are complete, correct, and consistent with the protocol numbering.

Note: Non-laboratory-related footnotes may be omitted at the LT's discretion.

8.1.5 Ensure that all evaluations in section 4 match the SOE and LPC sections 2 and 3.

8.1.6 Confirm that all laboratory issues are resolved.

8.1.7 Ensure that shipping details are defined.

8.2 LT should send a copy of the LPC to the protocol team as soon as the first full draft is ready.

8.2.1 The LT should highlight areas where information is needed or missing.

8.2.2 Communicate any protocol-related problems (e.g., number of aliquots, volume, or processing instructions).

8.3 If a secondary reviewer is needed, the LT must notify the LTC Leadership.

Note: The Co-LT may act as a secondary reviewer.

8.3.1 The LS on the LTC will request a reviewer.

8.3.1.1 The LS will provide the reviewer a copy of the protocol and LPC.

8.3.1.2 The LS will request that the review be completed within one week.

8.3.2 The reviewer must ensure that the LPC is consistent with the protocol; if not, notify the LT.

8.3.3 Upon completion of the review the reviewer will return the LPC and any concerns to the LT.

8.4 The LT should make any needed corrections. If major changes are identified by the LPC reviewer, the LT will send the LPC back to the entire protocol team for review.

8.5 LPCs should be posted within a week after the final protocol document is posted.

8.6 Submit the completed LPC to the LS for final team sign-off.

8.6.1 For ACTG, the LS is responsible for posting the LPC.

8.6.2 For IMPAACT, the CTS is responsible for posting the LPC.

8.7 The LT will highlight any unusual processing or reagents needed during the lab presentation of the protocol startup call.

9 NEW VERSIONS OF THE LPC

Final team sign-off is not necessary for subsequent versions if only minor modifications were made. It is

at the discretion of the LT to determine if a second reviewer and final team sign-off are required.

9.1 The LT is required to update the LPC with every protocol version.

9.1.1 Make sure the LPC version matches the current protocol version, even if no changes were made in the LPC.

9.1.2 Un-bold changes and remove strikethrough text in the previous LPC version; **bold** all new and ~~strikethrough~~ deleted information.

Note: Strikethroughs may be omitted if they would make the document difficult to read. Be sure to explain well in section 6 (Revision History).

9.1.3 Summarize all changes in section 6 of the LPC (Revision History).

9.1.4 Keep an electronic copy of each posted version of the LPC in your own records.

9.2 Update the LPC with new information from clarification memos or letters of amendment as appropriate.

9.2.1 Reference pertinent clarification memo(s) or letter(s) of amendment on the cover page of the LPC.

9.2.2 The LPC creation date will not change but the LPC revision date will change. The LPC version number will also change.

Note: Final protocol versions are whole numbers (e.g., 1.0, 2.0, etc.), but updated LPC versions are denoted by increasing decimal points (e.g., 1.1, 2.1, etc.).

9.3 If LDMS preload updates are anticipated, send the new LPC draft to the LDM as soon as possible and review the corresponding preload updates as needed.

9.4 Submit the revised LPC to the LS for final team sign-off.

9.4.1 For ACTG, the LS is responsible for posting the LPC.

9.4.2 For IMPAACT, the CTS is responsible for posting the LPC.

9.5 LPCs should be posted within a week after the posting of the new protocol version, amendment, or clarification memo.

10 DATA AVAILABILITY REPORTS (DARS, ACTG ONLY)

10.1 LTs should ensure that the protocol statisticians include them in team emails regarding review of protocol DARS.

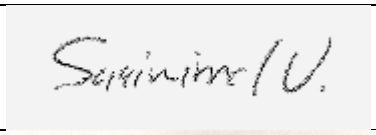
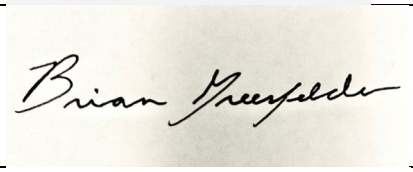
10.2 DARS is often reviewed on routine team calls.

10.3 LTs will work with team to resolve specimen related shortfalls.

INQUIRIES

Contact the ACTG/IMPAACT LTC Leadership at actg.ltcleadership@fstrf.org for questions and comments related to these procedures.

LTC LEADERSHIP SOP APPROVAL

NAME AND TITLE	SIGNATURE	DATE OF APPROVAL
Michael Leonard LTC Co-Chair		02Dec2022
Sasiwimol Ubolyam LTC Co-Chair		01Dec2022
Brian Greenfelder Co-Vice Chair		07Dec2022
Chiraphorn Kaewkosaba Co-Vice Chair		09Dec2022

Title:	Protocol Participation and Laboratory Processing Chart Preparation Procedures		
SOP number:	LTC-Int-001	Effective:	09Dec2022
Version:	V4.0	Last reviewed:	13Jan2014
Originator:	ACTG/IMPAACT Laboratory Technologist Committee	Pages:	12

REVISION HISTORY OR RECORD RETIREMENT

VERSION #	EFFECTIVE DATE	REPLACES	RATIONALE FOR [REVISION/RETIREMENT]
1.0	01Jun2011	NA	NA
2.0	13Jan2014	Version 1.0	CLSI formatting applied. Purpose and Abbreviation sections added. Protocol Review, LPC Preparation, and Protocol Completion and Posting, Including LPC Review sections extensively updated to reflect current practice.
3.0	01Apr2019	Version 2.0	Added Table of Contents. All previous sections extensively updated and new sections added to reflect current practice (Preloads and DARs).
4.0	01Dec2022	Version 3.0	All sections reviewed and extensively updated to reflect current practice.

LABORATORY SOP REVIEW

LABORATORY STAFF NAME	DATE OF CONFIRMATION OF UNDERSTANDING
	[ddMmmyyyy]
	[ddMmmyyyy]
	[ddMmmyyyy]