LAB PROCESSING CHART
IMPAACT P1101
Phase I/II Dose-finding, Safety, Tolerance and Pharmacokinetics Study of a Raltegravir-Containing Antiretroviral Therapy (ART) Regimen in HIV-infected and TB Co-infected Infants and Children

(DAIDS Document ID 11831)

A Multicenter, International Trial of the
International Maternal Pediatric Adolescent AIDS
Clinical Trials Network (IMPAACT)

Sponsored by:
The National Institute of Allergy and Infectious Diseases (NIAID), the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD),
and the National Institute of Mental Health (NIMH)

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APPENDIX I

SCHEDULE OF EVALUATIONS

	Screening[1]	On treatment study weeks						TB and/or RAL Treatment Discontinuation[17, 19]	4 Wks Off RAL treatment / On study (± 2 wks)[19]	Early Study Discontinuation or End of Study (at 12 wks off RAL treatment ± 2 wks)[19]
		Entry	Day 5 - 8	Day 14 (± 3 days)	Wk 4[14] (± 1 wk)	Wk 8[14] (± 2 wks)	Every 4 wks[15] (± 2 wks)			
CLINICAL EVALUATIONS										
Informed Consent	x									
History[2]	x	x	x	x	x	x	x	x	x	x
Physical exam[3]	x	x	x	x	x	x	x	x	x	x
Pill count[4]		x	x	x	x	x	x	x		x
LABORATORY EVALUATIONS										
Hematology[5]	1 mL	1 mL	1 mL		1 mL	1 mL	1 mL	1 mL	1 mL	1 mL
LFT[6]	1 mL	1 mL	1 mL	1 mL	1 mL	1 mL	1 mL	1 mL	1 mL	
Chemistries [7]	1 mL	1 mL	1 mL	1 mL	1 mL	1 mL	1 mL	1 mL	1 mL	
Urinalysis[8]		x								
Pregnancy test[9]	1 mL [x]	1 mL [x]	1 mL [x]	1 mL [x]	1 mL [x]	1 mL [x]	1 mL [x]	1 mL [x]	1 mL [x]	1 mL [x]
Confirmation/Documentation of HIV Infection	[0-3 mL]									
Virology										
HIV-1 RNA PCR[10]	1-3 mL	1-3 mL			1-3 mL	1-3 mL	1-3 mL	1-3 mL	1-3 mL	1-3 mL
Sequencing[13]		3 mL					3 mL[16]	3 mL[18]		
Immunology										
Lymphocyte subsets[11]		1.5 mL				1.5 mL	1.5 mL	1.5 mL		1.5 mL
Pharmacology										
Intensive PK[12]			4.5 mL							
Total Maximum Blood Volume	4 – 10 mL	8.5 – 11.5 mL	7.5 – 8.5 mL	2 – 3 mL	4 – 7 mL	5.5 – 8.5 mL	5.5 – 11.5 mL	5.5 – 11.5 mL	4 – 7 mL	3.5 – 6.5 mL

APPENDIX I FOOTNOTES

1. Screening evaluations must be performed within 30 days of Entry. Participants must be enrolled ≥ 1 week to ≤ 20 weeks after starting TB treatment. If sufficient documentation of HIV status as specified in Section 4.1.3 is not available, HIV diagnostic testing is to be done according to the definition. If testing is required to fulfill the requirements of inclusion criterion 4.1.3, the HIV-1 RNA PCR required at Screening may serve as one of the two required tests, and additional blood (1-3 mL) may be collected as Sample #1 and/or Sample #2.
2. A complete history is required at Screening; a targeted history is sufficient at subsequent visits. Targeted history should include symptoms of toxicity (such as skin rash, liver dysfunction) and diagnosis. HIV clinical classification is required at Entry only. ARV and concomitant medications will be recorded at each visit. For participants of reproductive potential, onset of sexual activity will be assessed by history. A female participant who becomes sexually active while on study will be referred for contraception as specified in Section 6.9.1; additionally, female participants will have a pregnancy test (see footnote 9 below).
3. Physical exam should include height, weight, and vital signs (temperature, blood pressure, pulse and respiratory rate). Evaluation for lymphadenopathy should be done at baseline. Evaluations for presence of jaundice, hepatosplenomegaly, skin rash, chest signs, musculoskeletal abnormalities, and joint abnormalities for TB should be performed at all study visits.
4. Adherence will be measured using the standardized IMPAACT pill count. Adherence to TB medications will be assessed at the time that study drug is initiated at Entry. Adherence to HIV and TB medications will be assessed at all on-treatment visits and at early discontinuation of study drug. The participant should be reminded of the importance of adherence and of reporting deviations in adherence at all on-treatment visits.
5. Hematology should include complete blood count (CBC) with cell differential and platelet count.
6. ALT, AST, Alkaline phosphatase, Total Bilirubin, Indirect Bilirubin and Direct Bilirubin.
7. Chemistries should include BUN, electrolytes (bicarbonate, sodium, potassium, calcium, and magnesium), glucose, creatinine, and total amylase. If total amylase is elevated, serum fractionated pancreatic amylase should be performed and recorded on the CRF. If amylase fractionation is not available, lipase may be used instead of pancreatic amylase for clinical assessment of pancreatitis.
8. Dipstick urinalysis is sufficient. The following dipstick results should be reported: specific gravity, pH, blood, ketones, glucose, protein and nitrite. Abnormal findings should be followed with complete urinalysis and microscopic examination. The following microscopic results should be reported: RBC, WBC, squamous epithelial cells, hyaline casts and granular casts.
9. Pregnancy test will be done at screening if participant is sexually active. During follow-up, sexually active females will have pregnancy testing done if clinically indicated by the study site clinician. A urine or blood pregnancy test will be done. See Section 6.9.
10. Must be performed at a DAIDS VQA-certified laboratory. Blood volume may vary from 1 – 3 mL depending on the FDA-approved method that the laboratory is VQA-certified to perform. Screening viral load must be performed within 30 days of Entry.
11. Lymphocyte subsets include CD4/CD8 counts and percentages. Must be performed at DAIDS IQA-certified laboratory.
12. Intensive PK should be scheduled so that witnessed dosing of the ARVs is as close as possible to 12 hours after the previous dosing. PK dosing within a range of 11-13 hours after the previous dose is acceptable. Participants should not ingest breast milk, formula, or any other high fat food/liquid for 2 hours prior to and 1 hour after dosing on the intensive PK day. Water and other fluids (i.e. apple/orange juice and oral rehydration solution) can be taken at any time. Participants may consume a light meal of their choice 2 hours after RAL dosing on the intensive PK day. Parents/Guardians must report that the participants have not missed any doses of the ARVs, including RAL, in the 48 hours prior to the intensive PK visit. If a missed dose is reported, the intensive PK visit must be rescheduled. Parents/Guardians should be instructed not to administer the second dose of RAL to participants until the intensive PK sampling is completed.
    - Once the intensive PK visit is scheduled, a reminder call regarding the PK visit, the required food/liquid limitations and reinforcing adherence should be made about 3 to 4 days prior to the PK visit. A follow-up call to the parent/guardian should be made 1 day prior to the PK visit to confirm adherence. If a missed dose is reported, the scheduled PK visit should be cancelled and rescheduled.

- Sampling time points: 0.5 mL is to be collected at pre-dose (0) and 0.5, 1, 2, 3, 4, 6, 8 and 12 hours post-dose.
- Doses vomited within 15 minutes may be re-dosed once, with t = 0 to then be time of repeat dosing. If dose is vomited > 15 minutes after dosing, PK must be cancelled and may be rescheduled.
- If the results of the RAL intensive PK are in question, unexpectedly low or high and may put the participant at risk for toxicity, the Protocol Team may request a repeat of the intensive PK. The site will be notified by the team and the time period for obtaining the repeat PK will be given.
- ARVs must be taken at night the day before the RAL PK. The RAL PK samples will be taken in the morning and timed to the RAL dose.

13. Refer to the LPC for shipping instructions for viral sequencing.
14. If a participant will discontinue TB treatment and RAL at the Week 4 or 8 visit due to completion of their prescribed TB treatment, the evaluations at the TB and/or RAL Treatment Discontinuation visit should also be completed. Only the evaluations that are not already being done for the Week 4 or 8 visit need to be completed.
15. These visits will only be done if a participant will continue TB treatment and RAL after the Week 8 visit.
16. If a participant is not virally suppressed by the Week 8 visit, or has viral rebound subsequently, blood will be collected for sequencing at the next visit.
17. Evaluations for TB and/or RAL Treatment Discontinuation will be performed at any of the on-treatment visits that coincide with the discontinuation of TB treatment and/or RAL or when a participant has met the criteria for virologic failure and early treatment discontinuation as defined in Sections 6.2.2 and 6.7, respectively. Only the evaluations that are not already being done for the on-treatment visit need to be completed. Discontinuation of TB treatment and RAL due to completion of prescribed TB treatment can occur anytime beginning at Week 4 depending on the duration that the participant has been on TB treatment at the time of entry.
18. If a participant discontinues RAL early due to virologic failure per Section 6.2.2, blood will be collected for sequencing at the treatment discontinuation visit.
19. Participants that discontinue treatment early for any reason will continue on study/off study drug for 3 months, and complete the TB and/or RAL treatment discontinuation, 4 weeks off RAL treatment/on study, and end of study evaluations.

Note: NIH recommendations for maximum pediatric blood draw volumes will be followed in this study. The volume of blood drawn at any study visit should not exceed 5 mL/kg in a single day and 9.5 mL/kg over any eight-week period.

Priority of draw should be as follows:
1 Safety (hematology, chemistries, LFT)
2 Pharmacokinetics
3 Virology
4 Immunology

Section 2: Safety/Clinical Laboratory Evaluation				
Evaluation	**DMC Test Code**	**Tests**		**CRF #**
Hematology	N/A	Hematology should include complete blood count with cell differential and platelet count		PE6812
Chemistry	N/A	Chemistries should include BUN, electrolytes (bicarbonate, sodium, potassium, calcium, and magnesium), glucose, creatinine, and total amylase. If total amylase is elevated, serum fractionated pancreatic amylase should be performed and recorded on the CRF. If amylase fractionation is not available, lipase may be used instead of pancreatic amylase for clinical assessment of pancreatitis.		PE6817
Liver Function Test (LFT)	N/A	ALT, AST, Alkaline phosphatase, Total Bilirubin, Indirect Bilirubin and Direct Bilirubin		PE6817
Urinalysis	N/A	Dipstick urinalysis is sufficient. The following dipstick results should be reported: specific gravity, pH, blood, ketones, glucose, protein and nitrite. Abnormal findings should be followed with complete urinalysis and microscopic examination. The following microscopic results should be reported: RBC, WBC, squamous epithelial cells, hyaline casts and granular casts *refer to CRFs for specific details*		PE0811
Pregnancy	N/A	β HCG (pregnancy test) **<u>Pregnancy test will be done at screening if participant is sexually active. During follow-up, sexually active females will have pregnancy testing done if clinically indicated by the study site clinician. A urine or blood pregnancy test will be done.</u>** **See Section 6.9**	Urine β-HCG (urine test must have a sensitivity of 15-25 mIU/ml)	F0847
Lymphocytes CD4+/CD8+	CD4/CD8	CD4/CD8 cell counts and percentages	Must be performed at DAIDS IQA-certified laboratory	LBW0054

Section 3: Specimen Processing – Refer to Section 4 for tube types and collection volumes					
Evaluation	**Tube Type**	**Special Collection Notes**	**CRF # DMC Test Code**	**Processing**	**Shipping**
Confirmation/ Documentation of HIV Infection	EDTA	If sufficient documentation of HIV status as specified in Section 4.1.3 is not available, HIV diagnostic testing is to be done according to the definition		N/A	Send to local certified Lab

Section 3: Specimen Processing – Refer to Section 4 for tube types and collection volumes					
Evaluation	**Tube Type**	**Special Collection Notes**	**CRF # DMC Test Code**	**Processing**	**Shipping**
Plasma HIV-1 RNA PCR	EDTA	Must be performed at a DAIDS VQA-certified laboratory. Blood volume may vary from 1 – 3 mL depending on the FDA-approved method that the laboratory is VQA-certified to perform. Screening viral load must be performed within 30 days of Entry.	F3008 F3109 RNAHIV	**Blood processing method will be dependent upon your testing labs requirements,** **Please communicate with the VQA certified lab for samples processing and volumes.**	Send to local VQA-certified lab.
Viral sequencing	EDTA	At the completion of the study, viral sequencing will be done in batch for all participants from their baseline samples.	F3008	Spin blood at 800xg for 10 min. Remove plasma; respin plasma at 800xg for 10 min. Freeze 2 x equal aliquots at -70/80° C. Store one vial as the primary and store the other vial as the retention sample. Store samples in separate boxes. LDMS spec code: BLD/EDT/PL2	Primary samples will be stored and batch shipped to University of Washington (LDMS #238) at Teams' request or end of Study. See the end of the LPC for shipping instructions.
Intensive PK	EDTA	Process within one hour of collection. See appendix footnote 12 for further details Intensive PK sampling time points are at pre-dose (0) and 0.5, 1, 2, 3, 4, 6, 8 and 12 hours post-dose. **For each time point: 0.50 mL of blood will be drawn.**	PKW0335	Plasma processing-Centrifuge blood within one hour of collection at 1000 x g for 10 minutes at room temperature. Freeze 2 x equal aliquots at -70/80° C. Store one vial as the primary and store the other vial as the retention sample Record volumes in the LDMS. Freeze both aliquots at -70/80° C LDMS spec code: BLD/EDT/PL1	**Day 5-8 Intensive PK will ship to UAB real-time. Primary vials only** LDMS spec. code: BLD/EDT/PL1 LDMS time/unit: 0 pre-dose or ____ Hour as needed SEE SHIPPING CHART AT END OF LPC **Include copies of the CRFs**

Section 4: Evaluations by Visit

Screen: Must be completed within 30 days of Entry. Participants must be enrolled ≥ 1 week to ≤ 20 weeks after starting TB treatment. If sufficient documentation of HIV status as specified in Section 4.1.3 is not available, HIV diagnostic testing is to be done according to the definition.

Evaluation	Specimen	CRF	Aliquots	LDMS Code	Special Notes
Hematology	1ml EDTA Blood	PE6812	N/A	N/A	Send to local lab.
Liver Function test	1ml Blood in NON or SST	PE6817	N/A	N/A	Send to local lab.
Chemistries	1ml Blood in NON or SST	PE6817	N/A	N/A	Send to local lab.
HIV-1 RNA PCR	1-3ml Blood in EDTA	F3008/3109	N/A	N/A	Send to local VQA-certified lab.
Pregnancy Test	Urine or 1 ml BLD	F0847	N/A	N/A	Pregnancy test must be done on all female participants of reproductive potential and sexually active
Confirmation/Documentation of HIV Infection	5ml Blood in EDTA		N/A	N/A	Send to local certified Lab See Section 4.1.3 for further details

Entry: Must be completed within 30 days of study Screening

Evaluation	Specimen	CRF	Aliquots	LDMS Code	Special Notes
Hematology	1ml EDTA Blood	PE6812	N/A	N/A	Send to local lab.
Liver Function test	1ml Blood in NON or SST	PE6817	N/A	N/A	Send to local lab.
Chemistries	1ml Blood in NON or SST	PE6817	N/A	N/A	Send to local lab.
Pregnancy Test	Urine or 1 ml BLD	F0847	N/A	N/A	Pregnancy test must be done on all female participants of reproductive potential and sexually active.
Lymphocyte subsets	1.5 ml EDTA Blood	LBW0054	N/A	N/A	Lymphocyte subsets include CD4/CD8 counts and percentages. Must be performed at DAIDS IQA-certified laboratory.
HIV-1 RNA PCR	1-3ml Blood in EDTA	F3008 /3109	N/A	N/A	Send to local VQA-certified lab.
Urinalysis	2ml of Urine	PE0811	N/A	N/A	Send to local lab.
Viral Sequencing	3ml Blood in EDTA	F3008	Spin blood at 800xg for 10 min. Remove plasma; respin plasma at 800xg for 10 min. Freeze 2 x equal aliquots at -70/80° C. A primary and retention aliquot Store samples in separate boxes.	BLD/EDT/PL2	At the completion of the study, viral sequencing will be done in batch for all participants from their baseline samples or upon request by the Protocol Team.

Day 5-8					
Evaluation	**Specimen**	**CRF**	**Aliquots**	**LDMS Code**	**Special Notes**
Hematology	1ml EDTA Blood	PE6812	N/A	N/A	Send to local lab.
Liver Function test	1ml Blood in NON or SST	PE6817	N/A	N/A	Send to local lab.
Chemistries	1ml Blood in NON or SST	PE6817	N/A	N/A	Send to local lab.
Intensive PK	0.50 ml EDTA Blood for each time point Intensive PK sampling time points are at pre-dose (0) and 0.5, 1, 2, 3, 4, 6, 8 and 12 hours post-dose.	PKW0335	Freeze in two aliquots at -70/80° C, a **primary** and retention aliquot	BLD/EDT/PL1	Process within 1 hr. of collection. **Ship DAY 5-8 Intensive PKs to UAB REAT-TIME <u>Primary vials only.</u>** Participants should not ingest breast milk, formula, or any other high fat food/liquid for 2 hours prior to and 1 hour after dosing on the intensive PK day

DAY 14: +/-3 days					
Evaluation	**Specimen**	**CRF**	**Aliquots**	**LDMS Code**	**Special Notes**
Liver Function test	1ml Blood in NON or SST	PE6817	N/A	N/A	Send to local lab.
Chemistries	1ml Blood in NON or SST	PE6817	N/A	N/A	Send to local lab.

Week 4: +/-7 days					
Evaluation	**Specimen**	**CRF**	**Aliquots**	**LDMS Code**	**Special Notes**
Hematology	1ml EDTA Blood	PE6812	N/A	N/A	Send to local lab.
Liver Function test	1ml Blood in NON or SST	PE6817	N/A	N/A	Send to local lab.
Chemistries	1ml Blood in NON or SST	PE6817	N/A	N/A	Send to local lab.
HIV-1 RNA PCR	1-3ml Blood in EDTA	F3008/3109	N/A	N/A	Send to local VQA-certified lab.

Week 8: (± 2 Weeks)					
Evaluation	**Specimen**	**CRF**	**Aliquots**	**LDMS Code**	**Special Notes**
Hematology	1ml EDTA Blood	PE6812	N/A	N/A	Send to local lab.
Liver Function test	1ml Blood in NON or SST	PE6817	N/A	N/A	Send to local lab.
Chemistries	1ml Blood in NON or SST	PE6817	N/A	N/A	Send to local lab.
HIV-1 RNA PCR	1-3ml Blood in EDTA	F3008/3109	N/A	N/A	Send to local lab.
Lymphocyte subsets	1.5 ml EDTA Blood	LBW0054	N/A	N/A	Lymphocyte subsets include CD4/CD8 counts and percentages. Must be performed at DAIDS IQA-certified laboratory.

Every 4 weeks after Week 8 (± 2 Weeks) These visits will only be done if a participant will continue TB treatment and RAL after the Week 8 visit					
Evaluation	**Specimen**	**CRF**	**Aliquots**	**LDMS Code**	**Special Notes**
Hematology	1ml EDTA Blood	PE6812	N/A	N/A	Send to local lab.
Liver Function test	1ml Blood in NON or SST	PE6817	N/A	N/A	Send to local lab.
Chemistries	1ml Blood in NON or SST	PE6817	N/A	N/A	Send to local lab.
HIV-1 RNA PCR	1-3ml Blood in EDTA	F3008/3109	N/A	N/A	Send to local VQA-certified lab.
Viral Sequencing	3ml Blood in EDTA	F3008	Spin blood at 800xg for 10 min. Remove plasma; respin plasma at 800xg for 10 min. Freeze 2 x equal aliquots at -70/80°C. A primary and retention aliquot Store samples in separate boxes.	BLD/EDT/PL2	If a participant is not virally suppressed by the Week 8 visit, or has viral rebound subsequently, blood will be collected for sequencing at the next visit. At the completion of the study, viral sequencing will be done in batch for all participants from their baseline samples, or upon request by the Protocol Team.
Lymphocyte subsets	1.5 ml EDTA Blood	LBW0054	N/A	N/A	Lymphocyte subsets include CD4/CD8 counts and percentages. Must be performed at DAIDS IQA-certified laboratory.

TB and/or RAL Treatment Discontinuation					
Evaluation	**Specimen**	**CRF**	**Aliquots**	**LDMS Code**	**Special Notes**
Hematology	1ml EDTA Blood	PE6812	N/A	N/A	Send to local lab.
Liver Function test	1ml Blood in NON or SST	PE6817	N/A	N/A	Send to local lab.
Chemistries	1ml Blood in NON or SST	PE6817	N/A	N/A	Send to local lab.
Lymphocyte subsets	1.5 ml EDTA Blood	LBW0054	N/A	N/A	Lymphocyte subsets include CD4/CD8 cts and percentages. Must be performed at DAIDS IQA-certified laboratory.
HIV-1 RNA PCR	1-3ml Blood in EDTA	F3008/3109	N/A	N/A	Send to local VQA-certified lab.
Viral Sequencing	3ml Blood in EDTA	F3008	Spin blood at 800xg for 10 min. Remove plasma; respin plasma at 800xg for 10 min. Freeze 2 x equal aliquots at -70/80° C. A primary and retention aliquot Store samples in separate boxes.	BLD/EDT/PL2	If a participant discontinues RAL early due to virologic failure per Section 6.2.2, blood will be collected for sequencing at the treatment discontinuation visit. At the completion of the study, viral sequencing will be done in batch for all participants from their baseline samples, or upon request by the Protocol Team.

4 Weeks Off RAL treatment / On study (± 2 weeks)					
Evaluation	**Specimen**	**CRF**	**Aliquots**	**LDMS Code**	**Special Notes**
Hematology	1ml EDTA Blood	PE6812	N/A	N/A	Send to local lab.
Chemistries	1ml Blood in NON or SST	PE6817	N/A	N/A	Send to local lab.
Liver Function test	1ml Blood in NON or SST	PE6817	N/A	N/A	Send to local lab.
HIV-1 RNA PCR	1-3ml Blood in EDTA	F3008/3109	N/A	N/A	Send to local VQA-certified lab.

Early Study Discontinuation or End of Study (at 12 Weeks Off RAL treatment ± 2 weeks)					
Evaluation	**Specimen**	**CRF**	**Aliquots**	**LDMS Code**	**Special Notes**
Hematology	1ml EDTA Blood	PE6812	N/A	N/A	Send to local lab.
Lymphocyte subsets	1.5 ml EDTA Blood	LBW0054	N/A	N/A	Lymphocyte subsets include CD4/CD8 counts and percentages. Must be performed at DAIDS IQA-certified laboratory.
HIV-1 RNA PCR	1-3ml Blood in EDTA	F3008/3109	N/A	N/A	Send to local VQA-certified lab.

Section 5: Helpful Links and Shipping Addresses

ACTG/IMPAACT Laboratory Manual, Shipping Information and other useful information:
http://www.hanc.info/labs/labresources/Pages/informationActgImpaactLabs.aspx

Intensive PK

UAB LDMS Lab #191
University of Alabama at Birmingham
Attn: Kedria Walker
Dept. of Pharmacology and Toxicology
1670 University Blvd.
Volker Hall Room 270
Birmingham, AL 35294-0019
USA
Email: kedria@uab.edu.
Phone: 205-975-2461
Fax: 205-934-6201

PK samples must be shipped directly to UAB on **DRY ICE.**

Real-Time
Day 5-8 Intensive PK (Primary sample vials only) will be shipped to UAB real-time.

Ship samples on Monday or Tuesday only. Notify the lab of shipment by e-mail or Fax which should include Courier and Airbill #. Include copies of the CRFs

End of Study shipments
Held at site until requested
Day 5-8 Intensive PK retention samples will be held at your site until the end of study.

Viral Sequencing samples

University of Washington LDMS lab #238
Dr. Lisa Frenkel
Attn: Dr. Ingrid Beck
University of Washington- Children's Hospital of Seattle
1900 Ninth Ave
Seattle WA 98101
Phone -206–884-3440
Fax- 206-884-7311
email: Frenkellabshipments@seattlechildrens.org

All viral sequencing samples must be shipped to U. WASH on **DRY ICE.**

Viral Sequencing primary aliquots only will be batch shipped to U WASH lab 238 at Teams' request or at end of Study**.**

Ship samples on Monday or Tuesday only. Notify the lab of shipment by e-mail or Fax which should include Courier and Airbill #.

Held at site until requested
Viral sequencing retention samples will be held at the site until requested by Team to ship.

Revisions 12th Sept 2014

- Added Chemistry testing will be done at the 4 Weeks Off-treatment/On-study visit
- Added detailed list of chemistries
- Changed shipping address for Viral sequencing samples

Revisions 25th June 2015
Schedule of Evaluations

- Changed the title of the TB and RAL discontinuation visit, 4 weeks off treatment/on study, and early discontinuation or end of study visit to clarify the treatment that is referenced for participant management.
- Added confirmation/documentation of HIV infection to screening visit.
- Day 14 visit was added as an additional safety visit for clinical monitoring following initiation of full ARV regimen.
- Included pregnancy testing at screening if participant is clinically indicated and reports no sexual activity to verify exclusion criteria prior to enrollment.
- Chemistries were added to the 4 weeks off treatment/on study visit to enhance participant safety and clinical monitoring.
- Footnote 8 (re-numbered 7 in protocol) has been modified to clarify interpretation of chemistries and delineate further testing and management of elevated amylase.
- Footnote 15 (re-numbered 14 in protocol) has been modified to also apply to Week 8 visit. Footnote 16 has been removed to reflect this change.
- Footnotes 18 and 20 (re-numbered 16 and 18 in protocol) have been modified to further clarify blood collection for sequencing.

Revisions 24th April 2017

- Adjusted blood volume for PK time-sampling and aliquoting instructions
- Updated aliquots for PK sampling