SUMMARY OF CHANGES

INCLUDED IN THE FULL PROTOCOL AMENDMENT OF:

IMPAACT P1026s
Pharmacokinetic Properties of Antiretroviral and Related Drugs During Pregnancy and Postpartum

(DAIDS Document ID 10040)

IND # 64,535 held by NIAID

THE AMENDED PROTOCOL IS IDENTIFIED AS:

Version 9.0, Dated 22 September 2014

Information/Instructions to Study Sites from the Division of AIDS

The information contained in this protocol amendment impacts the IMPAACT P1026s study and must be submitted to site Institutional Review Boards and/or Ethics Committees (IRBs/ECs) as soon as possible for review and approval. This amendment impacts the study informed consent forms (ICFs); all study sites must prepare updated ICFs and obtain IRB/EC approval of the updated forms. Approval must also be obtained from other site regulatory entities if applicable per the policies and procedures of the regulatory entities. All IRB/EC and regulatory entity requirements must be followed.

Upon obtaining IRB/EC approval and any other applicable regulatory entity approvals, all sites should immediately begin implementing this amendment and using the updated ICFs. After all required approvals are obtained; updated ICFs should be used for all new participants. In addition, previously enrolled participants, at the next study visit, must be re-consented using the updated ICFs unless otherwise directed by the IRB/EC.

All study sites must submit an amendment registration packet to the DAIDS Protocol Registration Office (PRO); however, approval from the DAIDS PRO is not required prior to implementing the amendment.

This Summary of Changes, Version 9.0 of the protocol, corresponding site-specific ICFs, and all associated IRB/EC and regulatory entity correspondence should be retained in each site’s essential document files for IMPAACT P1026s.

Summary of Revisions and Rationale

This protocol amendment adds additional study arms for newly approved or soon to be approved antiretroviral drugs likely to move into use during pregnancy; adds additional arms to look at the interaction of ARVS with hormonal contraceptives, closes fully enrolled arms; closes arms that have not had many recent enrollments; adds infant washout pharmacokinetic (PK) sampling; removes references to procedures for subjects co-enrolled in P1025; incorporates prior protocol Clarification Memoranda and Letters of Amendment; and includes other minor updates, corrections, and clarifications. The changes and rationale are summarized briefly below, generally in order of first appearance in the protocol.
Throughout the protocol, the version number was updated to Version 9.0 and the version date was updated to 22 September 2014.

The protocol team and site investigator rosters were updated to reflect current membership and contact details; the glossary was also updated.

The background, rationale and attendant references were updated to remove information regarding the study drugs for arms that were closed; add information regarding the study drugs included in the new arms; add information regarding infant washout PK sampling. Sections 1.1, 1.31, 1.33, 1.35, 1.5, 1.7 and 1.8.

Due to the closure of IMPAACT P1025, and the fact that no subjects co-enrolled in P1025 remain in follow-up on P1026s, all references to P1025 have been deleted from the protocol; protocol sections and appendices have been renumbered accordingly.

The development of safe and effective combination antiretroviral regimens for use in neonates shortly after birth has become increasingly important as early diagnosis of neonatal HIV infection has become routine. The first step in developing safe and effective neonatal combination ARV regimens is to describe washout elimination kinetics of transplacentally-acquired drugs. Currently, the infants of women enrolled in P1026s during pregnancy are also enrolled and followed in the study. This amendment adds sampling from these infants at four time points from birth through nine days of life for characterization of ARV washout kinetics. To incorporate this addition, protocol sections were updated as follows:

- In the Schema and Section 2.26, a new secondary objective was added.
- Secondary objective 4 in the Schema and Section 2.24 was modified to include genotyping of infants participating in washout PK sampling.
- In Section 3.0 paragraphs 1 and 3 were modified to add infant washout PK sampling.
- Section 3.13 was added to clarify the timing of infant enrollment and to reference the criteria and procedures for infants undergoing washout PK sampling.
- Section 3.5 was added to specify the timing of sample collection and instructions for storage/processing of samples.
- Section 4.3 was added to specify the criteria for infant enrollment
- Section 4.4 was added to specify criteria for enrolled infants to undergo washout PK sampling.
- Sections 8.1, 8.22, 8.41, 8.42, and 8.6 were modified to discuss accrual for and analysis of infant washout PK sampling data.
- Sections 9.1, 9.243, 9.3, 9.323, and 9.326 were modified to describe analysis of infant PK sampling.
- Appendix II was modified to include sampling time points and volumes for washout PK sampling and pharmacogenetics.
The following modifications have been made to the study arms.

- Three new antepartum arms – elvitegravir/cobicistat, dolutegravir, tenofovir alafenamide fumarate (TAF) – were added.
- Two new postpartum arms – efavirenz (EFV) plus oral contraceptives and EFV plus implanted contraceptives – were added.
- Two antepartum arms were closed due to futility - tipranavir/ritonavir and didanosine delayed release (Videx®EC).
- Three antepartum arms - nelfinavir, maraviroc and rilpivirine were closed to further enrollments however, follow-up of participants in the maraviroc and rilpivirine arms will continue under v9.0. (Participants in the nelfinavir arm have completed follow-up.)
- Two postpartum arms that were fully enrolled – lopinavir/ritonavir (LPV/RTV) plus oral contraceptives, and LPV/RTV plus implanted contraceptives – were closed.

- Section 1.3 is updated to include the rationales for the closure of version 8.0 study arms
- The Schema and Sections 4.111 and 4.114 were updated to remove closed/fully enrolled arms and add new arms.
- The Schema and Section 2.13 were updated to reflect closure of the LPV/RTV postpartum contraception arms and the addition of the EFV postpartum contraception arms.
- In the Schema (Population section), Sections 3.0, 4.111, and 4.3, and Appendix IA (footnote 17) a note was added indicating that participants enrolled under v8.0 to arms that were not continued under v9.0 and who have not completed their last visit upon site conversion to v9.0 will provide consent to v9.0 and undergo all procedures as specified under v9.0.
- Sections 3.11 and 3.12 were added to clarify the timing of maternal enrollment during pregnancy and postpartum, respectively.
- Section 3.22, Hormonal Contraceptive PK Sampling is updated to reflect the closure of the LPV/RTV postpartum contraception arms and addition of EFV postpartum contraception arms.
- APPENDIX III: Maternal Intensive PK Sampling Schedule for Antiretroviral Medicines, Tuberculosis Treatment and Hormonal Contraceptives has been updated with the regimens for the closed arms removed and the regimens for the new arms added.
- APPENDIX IV: Dietary Recommendations for Antiretroviral Medicines, Tuberculosis Medicines and Hormonal Contraceptives has been updated.
- APPENDIX V: Maternal PK Parameter Targets has been updated to remove closed arms and add new arms.

- In Section 3.0, 1st paragraph and eligibility criterion 4.17 the upper limit of the enrollment timeframe for women enrolling prior to delivery has been modified from 34 6/7 weeks to 37 6/7 weeks. Also in Appendix IA, IB, and IC the 3rd trimester visit window has been modified from 30 to 37 weeks to 30 to 38 weeks.

- The timing of infant enrollment has been clarified to indicate that infants of mothers enrolled during pregnancy are to be enrolled, in-utero, immediately after maternal enrollment. Sections 3.13 and a note after maternal eligibility criterion 4.113 are added.

- Eligibility criterion, 4.114, 1st bullet has been corrected to indicate that the drug regimen must consistent of atazanavir/ritonavir/tenofovir 300/100/300 mg q.d. postpartum and starting combined oral (from hormonal) contraceptives formulated with 30-35 ug ethinyl estradiol” for consistency throughout the protocol.
To reflect the latest version of the IMPAACT definition of HIV-1 Infection for Eligibility in IMPAACT Clinical Trials, Section 4.15 is updated.

The requirement to only use innovator (i.e. brand name or non-generic) formulations of ARV, TB drugs and contraceptives has been modified allowing generic formulations with approval of the protocol team. Eligibility criterion 4.13 is added and the text in Section 5.0 has been updated and moved to newly added Section 4.7.

Section 5.1, Toxicity Monitoring has been updated to remove closed arms and add new arms.

Section 5.3, Criteria for Discontinuation were updated to reflect infant participation.

References to the Manual for Expedited Reporting of Adverse Events to DAIDS (referred to as the DAIDS EAE Reporting Manual), dated January 2010 and the DAIDS Table for Grading the Severity of Adult and Pediatric Adverse Events were updated to reflect the latest versions, Sections 6.1 and 6.3.

Section 6.2, 1st paragraph is updated to clarify that reporting requirements are for both mothers and infants. This is not a change from v8.0

Section 6.2 is modified to indicate that Grade 3 total or indirect bilirubin for mothers on atazanavir does not require expedited reporting.

The list of disallowed medicines in Section 7.0 was updated to reflect the current study drug regimens.

Schema, Sections 3.0, and 8.42 were updated to project the number of anticipated maternal and infant enrollments under Version 9.0

Section 9.31, Laboratory Analysis and Reporting was modified to allow additional pharmacology laboratories, including the Pharmacology Laboratory of the University of Cape Town for processing of plasma samples.

The window for the initial PK sampling visit for women enrolled during antepartum and postpartum has been widened from within 72 hours to within 5 days of subject enrollment to ease operational challenges associated with obtaining the specimens, Section 3.11, Appendix IA-footnote 9, Appendix IB-footnote 8, Appendix IC - footnote 6 and Appendix ID footnote 12.

The window for the maternal delivery visit has been defined as +/- 4 days from the date of delivery with the day of delivery considered as day 0 - Appendix IA-footnote 15, IB-footnote 14 and IC – footnote 9.

The window for the maternal 3rd trimester visit has been modified from 30 to 37 weeks to 30 to 38 weeks. – Appendix IA, IB and IC.

Documentation of HIV-infection has been added to Appendix IA, IB and ID – table and footnotes 1 in each Appendix. This allows for protocol specified HIV testing to be done, to confirm HIV infection, if protocol specified documentation of HIV test results is not available in a participant’s chart.
• An indicator X has been added to the 30 – 38 week visit column for genotyping Appendix IA and IB to clarify that this sample is collected once at first PK evaluation which can occur after enrollment at either 20 – 26 weeks or 30 – 38 weeks.

• The window for the infant birth visit has been defined as birth through 3 days of life with the day of birth considered as day 0 - Appendix II – footnote 8.

• Infant feeding status and mitochondrial disorders have been added as part of history/chart abstraction at birth and all follow-up visits, Appendix II.

• Pharmacogenetic sampling for genotyping has been added at entry to Appendix IC– table and footnote 8.

• The timing and instructions for diabetes screening has been clarified to indicate that testing must be done once while on increased dose DRV or LPV/r, between 24 weeks gestation and delivery. An X has been added as an indicator to the 30 weeks to delivery visit column.

• Infant HIV infection status has been added to the table in Appendix II at all timepoints. This is not a change in evaluations from V8.0.

• Blood volumes have been updated in Appendix IA, IB, IC, ID and II.

• Table A, Guidelines for Using Schedule of Evaluations (Appendices I-A through I-D) and Sample Informed Consent Forms (Appendices VI-A through VI-D) were updated to reflect removal and re-numbering of appendices.

• Clarifications and modifications included in all prior protocol Clarification Memoranda and Letters of Amendment have been incorporated.

• Other minor corrections and clarifications were incorporated throughout the protocol.

Modifications to the Sample Informed Consent Forms

Modifications to the sample informed consent forms are shown below. New text is indicated in bold.

Appendix VI-A:

INTRODUCTION

You and your baby are being asked to take part in the research study named above because you are infected with the Human Immunodeficiency Virus (HIV), the virus that causes AIDS, and you are pregnant and are taking one or more of the following HIV medicines during your pregnancy: darunavir/ritonavir twice daily, efavirenz, etravirine, rilpivirine, maraviroc, rilpivirine, elvitegravir/cobicistat, dolutegravir, tenofovir alafenamide fumarate (TAF), lopinavir/ritonavir (African sites only).

WHY IS THIS STUDY BEING DONE? 1st paragraph, last 2 sentences

We will also see how well the medicines get into vaginal secretions where they may help to keep
the amount of HIV in the vagina at a lower level. The amount of medicine found in blood from your baby’s umbilical cord will be compared to the amount of medicine in your blood at the time of delivery. **We will also look to see how much of the HIV medicine you took is getting into your baby and how safe these medicines are for you and your baby.**

**During Pregnancy**

- You will need to come to the clinic to make sure you are eligible for the study before you enroll. This may be done as part of your first study visit when you are 20-26 weeks pregnant or 30-38 weeks pregnant, so a separate visit will not be required. **We may test you for HIV to confirm your status.** At each visit, a history and physical exam, and routine blood tests will be done. Blood will also be drawn to check how well your body is able to fight infection and to check the amount of HIV in your blood. The total amount of blood for these tests is 13 – 16 mL (2½ -slightly more than 3 teaspoons).

- **Checking the Amount of HIV Medicine in Your Blood, 2nd paragraph**

  If you enter the study when you are 20-26 weeks pregnant, repeat blood samples will be taken to measure the amount of HIV medicine in your blood. These blood samples will be repeated when you are 30-38 weeks pregnant. A small plastic catheter (soft tube) will be placed in a vein in your arm for an extended period of time, so that blood can be drawn multiple times, without having to stick you with a needle several times. The tube will stay in place until all of the blood samples are drawn. Depending on the medicine(s) you are taking and the time you usually take them, 7 blood samples over 12 hours, or 8 blood samples over 24 hours will be taken. The total amount of blood taken for these tests will be between 28-35 mL (5½ to 7 teaspoons).

- **Genetic Testing**

  Some of your blood collected for other tests will be used for genetic testing. **Also, if you agree, between birth and 9 days after birth, your baby will have one drop of blood taken for genetic testing of your baby.** This test is to see if there are differences in specific genes that may affect the levels of some HIV medicines. Some people break down medicines differently based on their DNA and this can change the levels of the medicines in their bodies. You may decide that you do not want your or your baby’s DNA to be tested either now or at another time, by contacting your care provider during the study. You can still participate in this study even if you make this decision. This test will be done later in the study so you will not receive the results of this test. Please read the following statement carefully and then mark your initials in the appropriate space provided:

  I agree to allow my DNA to be tested.

  Yes_______  No_________ Initials ________ Date ________

  I agree to allow my baby’s DNA to be tested.

  Yes_______  No_________ Initials ________ Date ________
• Additional study tests if you are taking darunavir/ritonavir twice daily or lopinavir/ritonavir (African sites only), 1st paragraph, 3rd sentence

If you have not had a test to check for gestational diabetes done as standard of care by your primary care physician, between 24 weeks gestation and delivery, some blood will be taken after a sweet drink to check the level of glucose (blood sugar) in your blood.

After Delivery, 1st paragraph, 1st sentence

If you are taking efavirenz, etravirine, maraviroc, rilpivirine, elvitegravir/cobicistat, dolutegravir, or tenofovir alafenamide fumarate (TAF), you will be seen in the clinic 6-12 weeks and 24 weeks after you deliver your baby.

Study Visits for Your Baby

After your baby is born, your baby will be examined 3 times during the study: from birth to 3 days after birth, 5-9 days after birth, and again at 6 months of age. During these visits, your baby will be weighed and measured and information about your baby’s health will be recorded from his/her medical records. Your baby, if able, will have blood samples taken to determine how much of the antiretroviral medication you took during pregnancy got into your baby and how long it takes to go away. Your baby will have blood samples taken at three time points between birth and 2 days and a fourth sample taken between 5 and 9 days after birth. About 1 mL, or less than ¼ teaspoon (sites-add locally relevant description of blood volume) of blood will be taken for each sample. The total amount of blood taken for these tests will be around 3 – 4 mL, about 1 teaspoon (sites-add locally relevant description of blood volume).

Each of your baby’s study visits will last about [sites add local information about time for study visits].

WHY WOULD THE DOCTOR TAKE ME/MY BABY OFF THIS STUDY EARLY?

The study doctor may need to take you and your baby off the study early without your permission if:

Risks of Drawing Blood

Blood drawing may cause fainting or lightheadedness or some discomfort. Other risks include bleeding or bruising where the needle enters the body. A small blood clot may form where the needle enters the body or swelling of the surrounding skin may occur. There is also a small risk of a minor infection at the blood draw site. Blood drawing from your baby can also be done by heel stick. Heel stick may cause some discomfort, bleeding or bruising at the site of the heel stick. There is a small risk of infection at the site of the heel stick.

WHAT ABOUT CONFIDENTIALITY?, 2nd paragraph

[For US Sites]

People who may review your/your baby’s records include: the U.S. Food and Drug Administration (FDA), (insert Name of Site) IRB, National Institutes of Health (NIH), the Office for Human Research Protection, study staff, and study monitors. Any publication of this study will not use your/your baby’s name or identify you/your baby personally.
WHY IS THIS STUDY BEING DONE?, 1st paragraph

The correct amount of tuberculosis medicines needed during pregnancy to treat tuberculosis infection is not known. When tuberculosis medicines are taken together with the HIV medicines efavirenz, lopinavir/ritonavir and nevirapine, the TB medicines may decrease the amount of the HIV medicines in the blood, so that the correct doses of the these HIV medicines to protect your baby from HIV infection while being safe for you and your baby is not known. In this study, we will measure levels of tuberculosis medicines and these HIV medicines in HIV-infected pregnant women. We will compare the levels of tuberculosis medicines to those in HIV-uninfected pregnant women on the same tuberculosis medicines. We will also compare the levels of HIV medicines to those in non-pregnant adults without tuberculosis on the same HIV medicines. If it is found that the your blood levels of the HIV medicines are too low, a new dose may be recommended that is not yet approved by the Food and Drug Administration (FDA). We will also see how well the medicines get into vaginal secretions where they may help to keep the amount of HIV in the vagina at a lower level. The amount of medicine found in blood from your baby’s umbilical cord will be compared to the amount of medicine in your blood at the time of delivery. We will also look to see how much of the HIV medicines you took are getting into your baby and how safe these medicines are for you and your baby and how safe these medicines are for you and your baby.

During Pregnancy

- You will need to come to the clinic to make sure you are eligible for the study before you enroll. This may be done as part of your first study visit when you are 20-26 weeks pregnant or 30-38 weeks pregnant, so a separate visit will not be required. **We may test you for HIV to confirm your status.** At each of these visits you will have a history and physical exam, and routine blood tests. Blood will also be drawn to check how well your body is able to fight infection and to check the amount of HIV in your blood. The total amount of blood for these tests is 13 – 16 mL (about 2½ to slightly more than 3 teaspoons).

- **Checking the Amount of HIV Medicine in Your Blood,** 2nd paragraph
  If you enter the study when you are 20-26 weeks pregnant, repeat blood samples will be taken to measure the amount of HIV medicine in your blood. These blood samples will be repeated when you are 30-38 weeks pregnant. A small plastic catheter (soft tube) will be placed in a vein in your arm for an extended period of time, so that blood can be drawn multiple times, without having to stick you with a needle several times. The tube will stay in place until all of the blood samples are drawn. Depending on the medicine(s) you are taking and the time you usually take them, 7 blood samples over 12 hours, or 8 blood samples over 24 hours will be taken. The total amount of blood taken for these tests will be between 31-35 mL (about 7 teaspoons).

- **Genetic Testing**
  Some of your blood collected for other tests will be used for genetic testing. **Also, if you agree, between birth and 9 days after birth, your baby will have one drop of blood taken for genetic testing of your baby.** This test is to see if there are differences in specific genes that may affect the levels of some HIV medicines. Some people break
down medicines differently based on their DNA and this can change the levels of the medicines in their bodies. You may decide that you do not want your or your baby’s DNA to be tested either now or at another time, by contacting your care provider during the study. You can still participate in this study even if you make this decision. This test will be done later in the study so you will not receive the results of this test. Please read the following statement carefully and then mark your initials in the appropriate space provided:

I agree to allow my DNA to be tested.

Yes_______      No_________ Initials ________ Date ________

I agree to allow my baby’s DNA to be tested.

Yes_______      No_________ Initials ________ Date ________

- Additional study tests if you are taking lopinavir/ritonavir, 1st paragraph, 3rd sentence

If you have not had a test to check for gestational diabetes done as standard of care by your primary care physician, between 24 weeks gestation and delivery, some blood will be taken after a sweet drink to check the level of glucose (blood sugar) in your blood.

After Delivery, 4th sentence

The total amount of blood to be drawn for these tests is between 13-48 mL (about 3 to 10 teaspoons) depending on the tests that will be done. At the 24-week visit after delivery, you will have a history and physical exam, and routine blood tests. Blood will also be drawn to check how well your body is able to fight infection and to check the amount of HIV in your blood. The total amount of blood for this visit is 13 mL (slightly more than 2 teaspoons).

Study Visits for Your Baby

After your baby is born, your baby will be examined 3 times during the study: from birth to 3 days after birth, 5-9 days after birth, and again at 6 months of age. During these visits, your baby will be weighed and measured and information about your baby’s health will be recorded from his/her medical records. Your baby, if able, will have blood samples taken to determine how much of the antiretroviral medication you took during pregnancy got into your baby and how long it takes to go away. Your baby will have blood samples taken at three time points between birth and 2 days and a fourth sample taken between 5 and 9 days after birth. About 1 mL, or less than ¼ teaspoon (sites-add locally relevant description of blood volume) of blood will be taken for each sample. The total amount of blood taken for these tests will be around 3 – 4 mL, or about 1 teaspoon (sites-add locally relevant description of blood volume).

Each of your baby’s study visits will last about [sites add local information about time for study visits].

WHY WOULD THE DOCTOR TAKE ME/MY BABY OFF THIS STUDY EARLY?

The study doctor may need to take you and your baby off the study early without your permission if:
Risks of Drawing Blood

**Blood drawing may cause** fainting or lightheadedness or some discomfort. Other risks include bleeding or bruising where the needle enters the body. A small blood clot may form where the needle enters the body or swelling of the surrounding skin may occur. There is also a small risk of a minor infection at the blood draw site. **Blood drawing from your baby can also be done by heel stick. Heel stick may cause some discomfort, bleeding or bruising at the site of the heel stick. There is a small risk of infection at the site of the heel stick.**

**WHAT ABOUT CONFIDENTIALITY?, after for US sites**

For sites outside the U.S.,
Efforts will be made to keep your/your baby’s personal information confidential. We cannot guarantee absolute confidentiality. Your/your baby’s personal information may be disclosed if required by law. Any publication of this study will not use your/your baby’s name or identify you/your baby personally.

Your/your baby’s records may be reviewed by the Ministry of Public Health in your country, the FDA, the Office of Human Research Protections (OHRP), the NIH, (insert name of site) IRB, Ethics Committee (EC), study staff, and study monitors.

Appendix VI-C

**WHY IS THIS STUDY BEING DONE?**

The correct amount of tuberculosis medicines needed during pregnancy to treat tuberculosis infection is not known. In this study, we will **measure the levels of tuberculosis medicines in the blood of pregnant and postpartum women. We will also look to see how safe these medicines are for you and your baby.**

**During Pregnancy**

You will need to come to the clinic to make sure you are eligible for the study before you enroll. This may be done as part of your first study visit when you are 20-26 weeks pregnant or 30-38 weeks pregnant, so a separate visit will not be required. At each of these visits you will have a history and physical exam, and routine blood tests. You will be given the results of these tests. About 6 mL (slightly more than one teaspoon) of blood will be drawn at each visit.

- **Checking the Amount of Tuberculosis Medicine in Your Blood**

If you enter the study when you are 20-26 weeks pregnant, repeat blood samples will be taken to measure the amount of tuberculosis medicine in your blood. **These blood samples will be repeated when you are 30-38 weeks pregnant. A small plastic catheter (soft tube) will be placed in a vein in your arm for an extended period of time, so that blood can be drawn multiple times, without having to stick you with a needle several times. The tube will stay in place until all of the blood samples are drawn. Seven (7) blood samples will be taken over 12 hours. The total amount of blood taken for these tests will be 17 mL (about 3 ½ teaspoons) depending on the number of tuberculosis medicines you are taking. You will be asked to provide the times of your previous two...**
doses of medicine and to describe the time and amount of your previous two meals. Before these repeat blood samples are taken, the study staff will review with you any dietary recommendations related to the tuberculosis medicines you are taking. The tuberculosis drug levels and testing will be done in batches later in the study, so you and your doctor won’t get results of these tests.

**After Delivery**

You will be seen in the clinic 2-8 weeks and 24 weeks after you deliver your baby. At the 2-8 week visit after delivery, you will have a history and physical exam, and routine blood tests. You will be given the results of these tests. If you are still taking tuberculosis medicines, repeat blood samples will be taken to check the amount of tuberculosis medicine in your blood like what was done during your pregnancy. The total amount of blood to be drawn at this visit is **between 6 - 23 mL (about 2 – 5 teaspoons)** depending on the tests that will be done. At the 24-week visit after delivery, you will have a history and physical exam, and routine blood tests. The total amount of blood drawn for this visit is 6 mL (slightly more than one teaspoon).

**Study Visits for Your Baby**

After your baby is born, your baby, will be examined 3 times during the study: **from birth to 3 days** after birth, **5-9 days** after birth, and again at 6 months of age.

Each of your baby’s study visits will last about [sites add local information about time for study visits].

**Genetic Testing**

Some of your blood collected for other tests will be used for genetic testing. Also, if you agree, between birth and 9 days after birth, your baby will have one drop of blood taken for genetic testing of your baby. This test is to see if there are differences in specific genes that may affect the levels of some medicines. Some people break down medicines differently based on their DNA and this can change the levels of the medicines in their bodies. You may decide that you do not want your or your baby’s DNA to be tested either now or at another time, by contacting your care provider during the study. You can still participate in this study even if you make this decision. This test will be done later in the study so you will not receive the results of this test. Please read the following statement carefully and then mark your initials in the appropriate space provided:

I agree to allow my DNA to be tested.

Yes______  No_______  Initials _______  Date ________

I agree to allow my baby’s DNA to be tested.

Yes______  No_______  Initials _______  Date ________

**Risks of Drawing Blood**

**Blood drawing may cause** fainting or lightheadedness or some discomfort. Other risks include bleeding or bruising where the needle enters the body. A small blood clot may form where the
needle enters the body or swelling of the surrounding skin may occur. There is also a small risk of a minor infection at the blood draw site. **Blood drawing from your baby can also be done by heel stick. Heel stick may cause some discomfort, bleeding or bruising at the site of the heel stick. There is a small risk of infection at the site of the heel stick.**

**WHAT ABOUT CONFIDENTIALITY?**

US Sites
People who may review your/your baby’s records include: the U.S. Food and Drug Administration (FDA), (insert Name of Site) IRB, National Institutes of Health (NIH), the **Office for Human Research Protection**, study staff, and study monitors. Any publication of this study will not use your/your baby’s name or identify you/your baby personally.

Appendix VI-D:

**WHY IS THIS STUDY BEING DONE?**

Some anti-HIV medicines interact with hormonal birth control, potentially changing the levels of the birth control (increasing the chance of side effects or of pregnancy) or of the anti-HIV drug (increasing side effects or decreasing anti-HIV activity). We want to study whether oral contraceptive pills containing the estrogen agent ethinyl estradiol or the contraceptive etonogestrel implant have significant interactions with two commonly used medicines, efavirenz and atazanavir. We want to look at the levels of efavirenz or atazanavir in your blood before you start one of the two types of hormonal birth control. Then we will measure the levels of these medicines again after you have been on birth control for several weeks and see if the levels have changed. We will also measure the levels of the hormones in your blood from the birth control and compare those levels to results from women using the same birth control but not taking antiretroviral medicines. We can see if the hormones and antiretroviral medicines interact or not and see if hormonal birth control should work as well in women on certain ARV drugs. **We will also look to see how safe these medicines are for you.**

2-12 weeks after you deliver your baby, 1st paragraph, 2nd sentence

You will need to come to the clinic to make sure you are eligible for the study before you enroll. This may be done as part of your first study visit, so a separate visit will not be required. **We may test you for HIV to confirm your status.** You will have a history and physical exam, and routine blood tests to see if it is safe for you to be in the study. Blood will be drawn to check how well your body is body is able to fight infection and to check the amount of HIV in your blood. The total amount of blood taken from these tests will be 13 – 16 mL (about 2½ to slightly more than 3 teaspoons). You will be given the results of these tests. You will be asked to sign this consent form.

If you are able to be in this study, repeat blood tests will be done to measure the amount of HIV medicine in your blood. A small plastic catheter (soft tube) will be placed in a vein in your arm for an extended period of time, so that blood can be drawn multiple times, without having to stick you with a needle several times. The tube will stay in place until all of the blood samples are drawn. Depending on the medicine(s) you are taking, 7 blood samples over 12 hours, or 8 blood samples over 24 hours will be taken. The total amount of blood taken for these tests will be 17-19 mL (about 4 teaspoons). You will be asked to provide the times of your previous two doses of medicine and to describe the time and amount of your previous two meals. Before these repeat blood samples are taken, the study staff will review with you any dietary recommendations.
related to the HIV medicines you are taking. After this first sampling, you will start the oral contraceptive pills as prescribed by your regular doctor or have the etonogestrel implant inserted by your doctor.

6 to 7 weeks after you have started hormonal contraceptives

You will come to the clinic 6-7 weeks after you have started hormonal contraceptives and the same tests that were done 2-12 weeks after you delivered your baby will be repeated. **We will ask you questions about how well you are taking your medicines.** A pregnancy test will also be done. You will take your HIV medicine at the same time of day you take your hormonal contraceptives three days before you have repeat blood samples drawn and on the day you have repeat blood samples drawn to check the levels of hormone in your blood. If you are using the etonogestrel implant 4mL (about one teaspoon) of blood will be taken from you. If you are using oral contraceptives eight (8) blood samples (about 3 teaspoons) will be taken over 24 hours. The total amount of blood taken for all these tests will be between 35-49 mL (about 7 to 10 teaspoons) depending on which contraceptive method you are using. This testing will be done in batches later in the study, so you and your doctor won’t get the results of these tests.

**WHAT ABOUT CONFIDENTIALITY?, 2nd paragraph**

**US Sites**

People who may review your/your baby’s records include: the U.S. Food and Drug Administration (FDA), (insert Name of Site) IRB, National Institutes of Health (NIH), the **Office for Human Research Protection**, study staff, and study monitors. Any publication of this study will not use your/your baby’s name or identify you/your baby personally.