Appendix III-B: Cohort 2 Sample Informed Consent Form for Study Participation

IMPAACT 2007
Phase I Safety and Pharmacokinetic Study of Maraviroc in HIV-1-Exposed Infants at Risk of Acquiring HIV-1 Infection

VERSION 1.0, 13 April 2016

You and your baby are being asked to participate in the research study named above.

This form gives information about the study. Please read it, or have it read to you, and ask any questions you may have. We will take as much time as needed for you to fully understand the study. We will ask you questions to see if we have explained the study clearly.

After you understand the study, if you decide that you and your baby will participate, you will be asked to sign or make your mark on this form. You will be offered a copy to keep.

About the Study

The International Maternal Pediatric Adolescent AIDS Clinical Trials Network (IMPAACT) and *[sites: insert site name]* are doing this study to test an anti-HIV medicine (ARV) given to babies. The medicine is called maraviroc. HIV is the virus that causes AIDS.

You and your baby are being asked to participate in this study because you are infected with HIV and there is a risk that the infection may be passed onto your baby. The transfer of HIV to newborn babies from HIV-infected mothers can occur at the time of birth.

The study will include about 70 mothers who have HIV and their babies. Your baby will receive the anti-HIV medicine being tested. Mothers will be in the study for up to 3 days and babies will be in the study for 4 months.

The person in charge of the study at this clinic is *[sites: insert name of Investigator of Record]*. The United States National Institutes of Health is paying for this study.

1. The study is being done to test the safety and blood levels of maraviroc in newborn babies

Babies born to mothers who have HIV usually take ARVs to prevent infection of HIV after birth. There are not many ARVs available for babies because many ARVs have not yet been tested in babies.

Maraviroc is an ARV that is used in adults in the United States and other countries. This study will look at whether maraviroc causes any bad side effects when given to newborn babies. It will also look at different doses of maraviroc to find what amount of maraviroc should be given to protect newborns.

2. It is your decision whether or not to join the study.

Deciding to join the study with your baby is voluntary. You are free to join or not join. If you join, you can change your mind and leave the study at any time. Your decision will have no effect on the medical care that you and your baby receive at this clinic. Your access to services and the benefits and rights you normally have will not be affected.

Take your time and consider your decision carefully. If you wish, you can talk to other people about allowing your baby to join the study. You can bring other people here to learn about the study with you.

No matter what you decide about the study, you must continue to take your anti-HIV medicines. Your baby should also take anti-HIV medicine for 4-6 weeks after birth. Taking these medicines is the best known way to maintain your health and avoid passing HIV to your baby while breastfeeding.

3. Only mothers and their babies who qualify can participate in the study.

If you decide to join the study with your baby, we will first do some tests to see if you and your baby qualify. Some tests can be done while you are pregnant. Other tests will be done after your baby is born. More information about the tests is given in #4 and #5.

Finding out if you and your baby qualify

4. We will ask questions and discuss the study requirements with you.

To find out if you qualify for the study, we will:

- Review your medical records.
- Ask about your plans for feeding your baby and taking anti-HIV medicines after your baby is born.
- Talk with you about the study requirements and if you are able to meet these requirements.
- If needed, draw your blood (up to 10 mL or 2 teaspoons) for HIV testing. There are certain HIV tests that are required for mothers in this study. If the required tests are not in your medical records, we will do the tests that are needed.

These procedures may be done while you are pregnant or within 3 days after your baby is born. They will take 30-60 minutes. *[sites: modify how much time this visit will take as needed]*.

If these procedures show that you may qualify for the study, you will be given contact information for the study staff. We will stay in contact as you get closer to your delivery date and ask you to contact us when your labor begins. We will not be involved in the delivery of your baby but will arrange to see you soon after your baby is born. You are welcome to contact us or return to the clinic at any time to talk about the study.

5. After delivery, we will collect more information and examine your baby.

To find out if your baby qualifies for the study, as soon as possible after your baby is born, we will:

- Review your and your baby's medical records.
- Ask about your and your baby's anti-HIV medicines.
- Ask about your baby's health and other medicines.
- Ask about how you are feeding your baby.
- Give your baby a physical examination
- Draw your baby's blood (about 4.5 mL or 1 teaspoon) for tests. These tests include:
  - A test to look at your baby's blood cells
  - A test to check how well your baby's liver is working
  - An HIV test

- A portion of the blood will be stored for future HIV-related tests. The samples that will be tested will be chosen after the study is completed. You or the site investigator will not be told of the results because the test is for investigation only and will be done after the study is completed. We will ask you about saving these samples in a separate form.

These procedures will take about an hour *[sites: modify how much time this visit will take as needed]*. The results of some of your baby's blood tests will be available within a couple of days. We will review the results and all other information to determine if you and your baby qualify for the study.

- If you and your baby do not qualify, we will tell you this and give you information on where you and your baby can receive medical care and other services you may need. We will destroy any of your blood remaining after testing.

- If you and your baby do qualify, we will ask you to confirm your decision for you and your baby to join the study. With your confirmation, you and your baby will be entered into the study.

Entering the study

6. If you and your baby qualify, you and your baby will enter the study within 3 days after the baby's birth.

On the day when you and your baby enter the study, we will:

- Draw your blood (14 mL or about 3 teaspoons) to test the amount of HIV in your blood and for future testing.
- Ask about your health, anti-HIV medicines, and other medicines.

These procedures may take up to 3 days *[sites: modify how much time this visit will take as needed]*.

Your baby will also receive his or her first dose of maraviroc during this visit. We will show you how to give maraviroc to your baby. It is very important that you give your baby maraviroc as instructed. We will take as much time as needed for you to understand the instructions and identify strategies that will help you to give the study medicine to your baby as instructed.

Being in the study

7. After entering the study, your baby will have 5 scheduled visits over 4 months.

Visits will be more frequent in the first 12 weeks. During this time, your baby will have 4 visits, at 1, 4, 6, and 12 weeks. After that your baby will have 1 more visit at 4 months of age.

Each visit will take about 1 to 2 hours *[sites: modify how much time this visit will take as needed]*. At these visits, we will:

- Review your baby's medical records and ask you about how your baby is doing and any side effects
- Give your baby a physical examination
- Draw your baby's blood (1.5 mL - 4.5 mL or less than 1 teaspoon) for tests. These tests will check:
    - Your baby's blood cells
    - How well your baby's liver is working.
    - If your baby has HIV

- If you took efavirenz within 2 weeks before delivery, we will draw your baby's blood (about 0.5 mL or a few drops) to test the amount of efavirenz in your baby's blood.

These procedures will take about 1 to 2 hours *[sites: modify how much time this visit will take as needed]*. Babies may have more visits if they are sick or if we need to do more tests to check on their health.

8. Your baby will also participate in another study procedure. This procedure will very closely measure the amount of maraviroc in their blood.

Your baby will also have blood drawn to very closely measure the amount of maraviroc in his or her blood. This is called a pharmacokinetic (PK) test. There will be two of these tests.

This collection will happen at the Week 1 and 4 visits. You must give your baby the medicine exactly as instructed and not miss but on the day of these visits, we will ask that you not give your baby maraviroc at home before coming to the clinic. Your baby will be given maraviroc at the clinic, so that we know what time and the exact amount of maraviroc he or she took. This is called directly observed therapy.

For the PK test, your baby will stay at the clinic for up to 13 hours after your baby takes maraviroc. If your baby is taking maraviroc only once a day, your baby will need to return to the clinic 20 - 24 hours after they took the medicine. If your baby is taking maraviroc two times a day, your baby will not need to return to the clinic. The study doctor will tell you how often your baby will take the medicine before the visit.

[Sites: modify language as appropriate to indicate procedures for the intensive PK collection. A small plastic tube (like a "drip") will be placed in your baby's arm to draw blood samples. This tube is attached to a plastic needle so that we can draw blood several times. We will not need to stick your baby with a needle each time. The plastic tube will stay in place until all of the blood samples are drawn.*]*

We will draw a few drops, about 0.5 mL of blood at 5 different time points at each PK test (a total of 2.5 mL or ½ teaspoon). We will look at the amount of study medicine in your baby's blood at each of these times.

At 6 weeks after birth your baby will also have one sample of blood drawn to measure the amount of maraviroc in his or her blood. At this visit, it is important that you can tell study staff the exact time you gave the study medicine to your child. We will draw about 0.5 mL (a few drops of blood) for this test.

9. Tests for how much of the study medicine is in your baby's blood will be done at different laboratories.

We will do most of the HIV tests and tests to check your baby's blood here at our laboratory, but some of the blood tests will be done elsewhere. We will give you the results of these tests at the next scheduled visit, or sooner, if necessary. We will explain the results and give you counseling and referrals as needed.

We will also draw blood for resistance and to check the amount of maraviroc in your baby's blood here in the clinic. These tests will be done at different laboratories in the United States. Some tests may be done while the study is ongoing; others after the study is done. We will try to give you the results of these tests when they have been tested during the study or after the study is over.

10. We may stop your baby's maraviroc.

We may stop your baby's study medicine if:

- Your baby is not able to come to the study visits.
- Your baby is not able to take the study medicine.
- Your baby becomes infected with HIV.
- Continuing maraviroc may be harmful to your baby.
- You request to stop the maraviroc for your baby.

Even if your baby stops the study medicine, your baby will stay in the study, with the same schedule of visits.

If an HIV test that we do for the study shows that your baby has HIV infection, we will ask you to bring your baby to the clinic for another test. Your baby will not receive maraviroc and your baby will have additional blood drawn (8 mL or a little more than 1.5 teaspoons) for another HIV test to see if your baby truly is infected and to test for resistance to maraviroc. If the second test confirms HIV infection, your baby will stay in the study, with the same schedule of visits, but will be taken off the study medicine. At these visits your baby will have all procedures done except HIV testing and testing for how much maraviroc is in his or her blood. The study cannot provide care and treatment for babies with HIV infection, but we will give information, counseling, and referrals to where your baby can get the care and treatment they need.

11. We may take you and your baby off the study if:

- The study is stopped for any reason.
- We determine that you and your baby cannot meet the study requirements (for example, if you move away and cannot come to the clinic).
- We determine that staying in the study might harm you and your baby.

12. Please tell us if you wish you and your baby to leave the study.

You and your baby are free to leave the study at any time for any reason. The care that you and your baby receive at this clinic will not be affected, but it is important for us to know about your decision. We will ask you to bring your baby to the clinic for one last visit. At this visit we will ask questions about your baby's health and medicines, give your baby a physical examination, and draw your baby's blood (less than 1 teaspoon) for tests. We will answer any questions you may have and give you information on how to contact us in the future, if you wish.

Risks of the study

13. There is little risk from the study procedures.

Most procedures done in this study are routine medical procedures, with little risk to you and your baby. Drawing blood can cause pain, swelling, bruising, or bleeding where the needle is inserted. Rarely, drawing blood can cause fainting or infection.

14. There are some risks from maraviroc.

Maraviroc (MVC, Selzentry®) is like any other medication or drug and may have side effects. Some of the most common or most serious effects are listed below. The list does not include all of the possible side effects. These lists include the more serious or common side effects with a known or possible relationship. If you have questions about side effects not included in these lists, you can ask us.

If your baby joins the study, we will tell you about the side effects of maraviroc that your baby will take. We will also check for any side effects during the visits and tell you what to do if your baby has any side effects.

15. We will tell you about the most severe side effects first.

First, you should know about the possible severe side effects. These effects are rare, but they can cause serious health problems and can result in death:

- Liver problems. The liver is an organ near the stomach. If your baby gets liver problems, he or she might have a rash on your baby's body; yellowing of the skin or whites of the eyes; dark or tea colored urine; upset stomach or vomiting; or loss of appetite. If your baby develops any of these symptoms, stop maraviroc and contact your baby's doctor immediately.

- Heart problems, including a heart attack.

- Low blood pressure problems. Low blood pressure may cause your baby to be dizzy or faint. If your baby has kidney problems, he or she may be at an increased risk for low blood pressure. The kidneys are organs near the middle of the back and there is one kidney on each site of the body. Doctors usually find out about kidney problems from blood tests.

16. There are also more common and not severe side effects from maraviroc.

You should also know about the more common side effects. These side effects are not severe. There are many possible mild and moderate side effects. The most common ones are listed below:

<table>
<tr>
<td rowspan="4">Overall Body Effects
• Swelling of parts of the body
• Some infections, including herpes, colds, sore throat, flu and flu-like symptoms
• Muscle aches, spasms and pain
• Fever
• Rash
• Colds
• Cough
• Runny, congested nose</td>
<td>Effects on Your Child's Activity
• Sleeping problems
• Dizziness</td>
</tr>
<tr>
<td>Effects on Your Child's Belly
• Stomach pain or bloating
• Diarrhea</td>
</tr>
<tr>
<td>Effects on Your Child's Bladder
• Problems with urination</td>
</tr>
<tr>
<td>Effects on Your Child's Blood
• Low amounts of white blood cell counts (neutropenia), which could lead to risk of infection</td>
</tr>
</table>

The list above is not a complete list of all side effects for maraviroc. As a reminder, if your baby joins the study, we will tell you about the side effects of maraviroc your baby will take.

Note: Because of how maraviroc works in your baby's body, there is a possible increased risk your baby may get other infections or cancer. However, there is no evidence from clinical studies of an increase in serious infections or cancer.

Maraviroc contains soy lecithin. If your baby has or develops an allergy to soy (soya or soybeans) or peanuts, your baby may develop an allergic reaction to maraviroc. If your baby is allergic to soy or peanuts, please tell your baby's doctor immediately.

17. There may be other possible risks of maraviroc.

Immune reconstitution syndrome

In some people with advanced HIV infection, signs and symptoms from other infections or certain diseases may occur soon after starting combination ARVs but can also occur later. Some of these symptoms may be life threatening. If your baby starts having new symptoms, or if you notice that your baby's existing symptoms are getting worse after starting the ARVs, tell your doctor immediately.

The use of some strong ARV combinations may be related to unusual position of body fat and weight loss. Some of the body changes may include body fat increasing around the abdomen, stomach area, chest or neck or body fat decreasing in the face, legs, or arms.

Risk of resistance

All ARVs can cause some resistance. Resistance means that the ARVs may not work against HIV if it is taken again in the future. To stop resistance, it is important that you give your baby the study medicine and ARVs as instructed, and do not miss any doses.

18. There could be risks of disclosure of you and your baby's information.

We will make every effort to keep your baby's information private and confidential. Study records and specimens will be kept in secure locations. All specimens and most records will be labeled only with a code number. However, you and your baby's names will be written on some records. Despite our best efforts to keep you and your baby's information private, it is possible that the information could be obtained by someone who should not have it. If this were to happen, you and your baby could be treated badly or unfairly. You could feel stress or embarrassment.

[*US sites, insert:* To help us protect your privacy, we have obtained a Certificate of Confidentiality that protects us from being forced to release information that may identify you, such as by the courts or police. The certificate cannot be used in all situations, but it can be used to resist demands for information that would identify you. The certificate does not protect against requests for information from the US federal government or from the US Food and Drug Administration. Regardless of the certificate, you can release information about your participation in the study to others, if you wish.]

Benefits of the study

19. There may or may not be a benefit to your baby from being in the study.

By joining the study, you and your baby will be part of the search for anti-HIV medicines that may be better for your baby. There may or may not be a direct benefit to you or your baby by participating in this study. Your baby will have regular visits here and frequent checks on his or her health, including tests for HIV in your baby's blood. Information learned from this study may help other babies born to HIV-infected mothers at risk of HIV infection.

Other information about the study

20. There are no costs to you or your baby for being in the study.

There are no costs to you or your baby for study visits, maraviroc, or procedures. *[Sites: insert information about compensation/reimbursement here, e.g., You will be reimbursed for the cost of transport to study visits. For each visit, you will be given (specify amount).]*

21. You and your baby's study records may be reviewed by study staff and groups that oversee the study.

Groups that oversee the study include:

- *[insert name of site IRB/EC]*
- *[insert name of other site drug entities that may review records]*
- *[insert name of other site regulatory entities]*
- The United States National Institutes of Health and its study monitors
- The United States Office for Human Research Protections
- The US Food and Drug Administration
- Other U.S., local, and international regulatory entities
- The IMPAACT Network that is coordinating the study
- The companies that make the study medicine (PHIVCO)

Like the study staff, these groups are required to make efforts to keep study records private and confidential.

The results of the study may be presented publicly or published. However, no presentation or publication will use your baby's name or identify your baby personally. A description of this study will be available on ClinicalTrials.gov. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

You and your baby's study information may be disclosed to other authorities if required by law.

22. If you or your baby gets sick or injured, contact us immediately.

You and your baby's health is important to us. We will make every effort to protect you and your baby's well-being and minimize risks to you and your baby. It is possible, however, that your baby could have an illness or injury that is study-related. This means that the illness or injury occurred as a direct result of the study procedures.

If a study-related illness or injury occurs, we will treat your baby or tell you where you can get the treatment your baby needs. The cost for this treatment may be charged to you or your insurance company. There is no program for compensation either through this institution or the National Institutes of Health.

Who to contact

23. If you have questions, concerns, or problems at any time, use these contacts.

- If you have questions about the study, contact:
  [sites: insert name and telephone number of investigator or other study staff]

- If you have questions about you and your baby's rights as a research participant, or problems or concerns about how you and your baby are being treated in the study, contact:
  [sites: insert name and telephone number of IRB contact person or other appropriate person/organization]

- If you or your baby has any health or other problems that may be related to his or her study participation, contact:
  [sites: insert name and telephone number of investigator or other study staff]

- If you or your baby want to leave the study, contact:
  [sites: insert name and telephone number of investigator or other study staff]

Signatures

24. If you agree to participate in this study, and your baby, please sign or make your mark below.

Before deciding whether to join this study with your baby, make sure you have read this form, or had it read to you, and that all of your questions have been answered. You should feel that you understand the study, its risks and benefits, and what is expected of you and your baby if you decide to join.

If you decide to allow your baby to join, we will tell you any new information from this study or other studies that may affect your willingness for your baby to stay in the study. You are welcome to ask questions or request more information at any time.

You do not give up any rights by signing this form.

_____
Participant's Name (print)

Parent's Name (print) (Or Legal Guardian)	Parent's Signature	Date
Study Staff Conducting Consent Process Name (print)	Study Staff Signature	Date
Witness Name (As appropriate)	Witness Signature	Date