

APPENDIX VI

SAMPLE INFORMED CONSENT FORM FOR STUDY PARTICIPATION

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

SHORT TITLE FOR THE STUDY: P1101

Version 3.0, dated 24 April 2017

INTRODUCTION

Your child is being asked to take part in this research study because your child has the Human Immunodeficiency Virus (HIV), which is the virus that causes AIDS, and has not taken any medications for the treatment of HIV in the past 30 days. Your child also has Tuberculosis (TB) and is taking or will be starting anti-TB medications that include Rifampicin, a medication commonly used to treat TB. This study is sponsored by the National Institutes of Health (NIH). The doctor in charge of this study at this site is: (insert name of Principal Investigator). Before you decide if you want your child to be a part of this study, we want you to know about the study.

This is a consent form. It gives you information about this study. The study staff will talk with you about this information. You are free to ask questions about this study at any time. If you agree to allow your child to take part in this study, you will be asked to sign this consent form. You will get a copy to keep.

WHY IS THIS STUDY BEING DONE?

This study is being done to measure the amount of raltegravir (RAL, Isentress™) in the blood when it is taken with the anti-TB medication Rifampicin. Raltegravir is the study medication used in this study and it is a type of anti-HIV medicine called an integrase inhibitor. Integrase inhibitors work by blocking integrase, a protein that HIV needs to enter human cells and make more copies of itself. Raltegravir has been approved for the use in adults, adolescents and children ages 4 weeks to 18 years old by the United States Food and Drug Administration (FDA). The chewable tablet is approved for children ages 2 to less than 12 years old. For children under 2 years of age, this study will look at a new way to give this medicine to young children more easily. Infants and children 4 weeks to less than 2 years old will take the raltegravir chewable tablet mixed with water, juice, breast milk or formula. This study will provide the study medication raltegravir to your child.

The other medications used in this study are Rifampicin, other anti-TB medications, two anti-HIV medications that are called Nucleoside Reverse Transcriptase Inhibitors (NRTIs) and a fourth anti-HIV medication that will be chosen by your child's doctor. It is possible that the fourth ARV drug chosen by your doctor could be a combination drug of Lopinavir and ritonavir (LPV/r). This medication may need to be dose adjusted with additional ritonavir to obtain the correct dosing for your child. This would result in a fifth anti-HIV medication. Many people find the liquid form of this drug tastes bad. These medications will not be provided by the study. These medications will be provided at the clinic where your child is receiving care. You will need to obtain them through a prescription from your child's doctor.

This study will look at the levels of raltegravir in the blood and the best dose of raltegravir in HIV-infected infants and children who are taking rifampicin for the treatment of TB compared to HIV-infected infants and children who are only taking raltegravir and do not require treatment for TB with rifampicin.

This study will also look at how the anti-HIV treatment including raltegravir when it is given with rifampicin is tolerated, and the levels of raltegravir and antiretroviral drugs (ARVs) when taken together in the blood to help find out if taking raltegravir and ARVs with rifampicin is safe.

WHAT DOES MY CHILD HAVE TO DO IF HE/SHE IS IN THIS STUDY?

Your child must be taking or starting to take anti-TB medications that include Rifampicin to be in this study. Your child will be given raltegravir and will be asked to take it two times or three times a day in addition to your child's other two new anti-HIV medicines. Raltegravir will be in a chewable tablet formulation to be chewed or taken dissolved in a liquid. The study staff will explain to you how to give the medicine to your child. Levels of raltegravir in the blood will be measured about one week after starting this medicine. Then your child will begin a fourth anti-HIV medicine along with his/her anti-TB medications including rifampicin, raltegravir and the other two anti-HIV medicines. Your child will take raltegravir until he/she stops taking the anti-TB medications prescribed by his/her doctor. Your child will continue to take the third anti-HIV medicine and the other two anti-HIV medicines for 3 months after the anti-TB medicines and raltegravir are stopped.

Deciding to allow your child to join this study is voluntary. You may choose to allow your child to join or not join. If you choose to allow your child to join, you can change your mind and take your child out of the study at any time. Your choices will have no effect on the medical care that your child receives at this clinic. Your child's access to services and the benefits and rights he or she normally has will not be affected.

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

If you decide to let your child join this study, we will first do some tests to see if your child qualifies.

Screening visit:

To find out if your child qualifies for this study, we will:

- Ask about your child's medical history including questions about your child's health and what symptoms, medications, and illnesses your child has had.
- Give your child a physical examination: We will measure your child's height, weight and vital signs (temperature, blood pressure, pulse and respiratory rate).
- Draw your child's blood for the following tests: We will take a little more than 1 teaspoon (4-6 mL) of blood for routine safety tests (a CBC, or complete blood count, which shows how many red and white blood cells there are; blood chemistries, which checks the blood sugar and how well the kidneys are working; a liver function test, which shows how well the liver is working) and to measure the amount of HIV in the blood (HIV viral load). We may draw up to an additional 3 mL to confirm your child's HIV infection if there is no medical record available.
- A pregnancy test: If your child is of child bearing age and pregnancy is suspected, your child may be asked to give an additional 1 mL of blood or a urine sample to test for pregnancy.
- You will be given the results of these tests.

If you agree to allow your child to enroll in this study, and your child does not qualify to be in this study, the reasons your child cannot enroll in this study will be shared with the protocol team, including the pharmaceutical company supporting the study.

Table 1

| | Entry | Day 5 to 8 | Day 14 | Week 4 | Week 8 | Every 4 weeks | TB and/or RAL treatment discontinuation | 4 weeks off RAL treatment/on study | Final visit |
|---|-------|------------|--------|--------|--------|---------------|---|------------------------------------|-------------|
| Medical history and review of medications | X | X | X | X | X | X | X | X | X |
| Physical exam | X | X | X | X | X | X | X | X | X |
| Pill Count | X | X | X | X | X | X | X | | X |
| CBC | X | X | | X | X | X | X | X | X |
| Liver enzymes | X | X | X | X | X | X | X | X | |
| Blood chemistries | X | X | X | X | X | X | X | X | |
| HIV viral load | X | | | X | X | X | X | X | X |
| CD4/CD8 cell count | X | | | | X | X | X | | X |

Entry visit:

[Sites: add local information regarding how long the entry visit will take].

If your child qualifies for this study and you allow your child to enter the study, your child will come to the clinic for the first study visit (or the Entry visit) within 30 days after the screening visit. The following will take place at the Entry visit:

- Your child will have the examinations and tests shown in Table 1 under the column “Entry”.
- Pill count at Entry: If your child is already taking anti-TB medications, we will check how well your child is taking the medications (including missed doses).
- Blood tests: We will take a little more than 1.5 - 2 teaspoons (8.5 - 10.5 mL) of blood.
 - About 1 ½ teaspoons (5.5 - 7.5 mL) will be for the tests in Table 1. The CD4/CD8 cell count is to check how well your child’s immune system is working. The results of these tests will be provided to you/your child.
 - A little more than ½ teaspoon (3 mL) will be used for a test to check if your child’s HIV is resistant to some anti-HIV medications (HIV resistance test). This test will be done after the study is over, and you will not be given the results.
- We will also ask your child to provide a urine sample for a routine test. The results of the test will be provided to you/your child.
- Your child will start taking raltegravir and 2 other anti-HIV medicines called NRTIs.
- If your child is a female and started to have sex since the last visit (screening), or can become pregnant, your child will be asked to provide a urine sample or an additional 1 mL of blood at each visit for a pregnancy test. Your child will be asked to take birth control precautions (ways to prevent pregnancy) throughout the study period to remain in the study. If your child is pregnant, your child will not be allowed to continue on the study medicine, but will continue to come in for study visits.

Your child will be asked to return to the clinic about 4 to 10 times in about 16 to 36 weeks (or 4 to 9 months) until your child stops taking the anti-TB medications. One visit will last a little over 12 hours where the amount of raltegravir and ARVs in the blood will be measured over 12 hours (intensive pharmacokinetics or intensive PK visit). [Sites: add local information regarding how long the visits will take].

Intensive PK visit (Day 5 to 8):

Approximately one week after starting raltegravir, your child will have an intensive PK visit. The following will take place at this visit:

- You will be contacted by the study staff one day before the visit to confirm that your child took all of his/her medications during the 2 days before the visit.
- Your child will have the examinations and tests shown in Table 1 under the column “Day 5 to 8”.

- In addition to the pill count that will be done by the study staff, you will need to write down the times your child took his/her medications during the 2 days before the visit and bring it with you to the clinic.
- We will ask that you not give your child raltegravir, other anti-HIV, and anti-TB medicines at home the day of this visit. Your child will need to bring these medicines to the clinic. Your child will be given these medications in the clinic after the first blood sample for the intensive PK test is taken.
- Blood tests: We will take a little more than 1 ½ teaspoons (7.5 mL) of blood.
 - A little more than ½ teaspoon (3 mL) will be for the tests in Table 1. The results of these tests will be provided to you/your child.
 - A little less than 1 teaspoon (4.5 mL) of blood will be taken over 12 hours to measure the amount of raltegravir in your child's blood.

Your child must have taken all doses as prescribed and not missed any doses of raltegravir and his/her other anti-HIV and TB medicines the 2 days before the PK test. If your child misses a dose within 2 days before the PK test, the visit will be rescheduled. Your child should not have breast milk, formula or any other high fat liquid for 2 hours before the PK test and 1 hour after taking the study medicines at the clinic. Your child can have water or apple/orange juice at any time. We will take the first blood sample before your child takes raltegravir at the clinic. Your child can have a small meal 2 hours after taking raltegravir. We will take blood samples 8 more times at ½ hour, 1 hour, 2 hours, 3 hours, 4 hours, 6 hours, 8 hours and 12 hours after your child takes raltegravir. Your child should not be given a second dose of raltegravir until after the PK test.

Your child may be stuck by a needle 9 times or a special needle may be inserted into your child's arm so that he/she may not have to be stuck by a needle multiple times. If possible an intravenous line will be placed in your child's vein for the whole day from which blood may be drawn to avoid as much discomfort as possible.

[Sites: modify or add language as appropriate regarding your site-specific arrangements for the PK visit]

If your child vomits within 15 minutes after taking raltegravir, your child will be given another dose of raltegravir. If your child vomits more than 15 minutes after taking raltegravir, the intensive PK test will be cancelled. The test may be re-scheduled.

Your child will start taking a fourth anti-HIV drug chosen by your doctor after the PK test is completed. Your child should take the fourth anti-HIV drug at night, with the smallest amount of food or liquid (such as *formula, breast milk, mashed banana, yogurt, or maize-based porridge etc.*), and should not be mixed with water or juice.

Day 14 visit

Your child will have a visit approximately two weeks after starting raltegravir. The following will take place at this visit:

- Your child will have the examinations and tests shown in Table 1 under the column "Day 14".
- Blood tests: We will take a little less than ½ teaspoon (2 mL) of blood at this visit for the tests in Table 1. The results of the tests will be provided to you/your child.

Week 4 visit:

The following will take place approximately four weeks after your child starts taking raltegravir:

- Your child will have the examinations and tests shown in Table 1 under the column "Week 4".
- Blood tests: We will take a little more than ½ to 1 teaspoon (4-6 mL) for the tests in Table 1. The results of these tests will be provided to you/your child.
- If your child will be stopping the anti-TB medications at the week 4 visit because your child has

completed anti-TB treatment prescribed by your child's doctor, the following will also take place:

- We will take less than ½ teaspoon (1.5 mL) of additional blood for a CD4/CD8 cell count test. The results of the CD4/CD8 cell count test will be provided to you/your child.
- Your child will stop taking raltegravir at the same time the anti-TB medications are stopped. Your child will continue to take the anti-HIV medicines as instructed by your child's doctor.

Week 8 visit:

The following will take place approximately eight weeks after your child starts taking raltegravir:

- Your child will have the examinations and tests shown in Table 1 under the column "Week 8".
- Blood tests: We will take about 1 – 1 ½ teaspoons (5.5 – 7.5 mL) of blood for the tests in Table 1. The results of these tests will be provided to you/your child.
- If your child will be stopping the anti-TB medications at this visit because your child has completed anti-TB treatment prescribed by your child's doctor, your child will stop taking raltegravir at the same time the anti-TB medications are stopped. Your child will continue to take the anti-HIV medicines as instructed by your child's doctor.

Visits every 4 weeks:

If your child will continue to take the anti-TB medications and raltegravir after the Week 8 visit, your child will have visits every 4 weeks until the anti-TB medications and raltegravir are stopped. The following will take place at these visits:

- Your child will have the examinations and tests shown in Table 1 under the column "Every 4 weeks".
- Blood tests: We will take about 1 – 1 ½ teaspoons (5.5 – 7.5 mL) of blood for the tests in Table 1. The results of the tests will be provided to you/your child.
- Depending on the amount of HIV in your child's blood, we may also take a little more than ½ teaspoon (3 mL) of additional blood for an HIV resistance test. This test may be done after the study is over, and you/your child will not be given the results.
- If your child is stopping the anti-TB medications at any of these visits because your child has completed anti-TB treatment prescribed by your child's doctor, your child will stop taking raltegravir at the same time the anti-TB medications are stopped.

Early TB and/or RAL treatment discontinuation visit:

If your child needs to stop taking the anti-TB medications and/or raltegravir early, your child will have a treatment discontinuation visit. The following will take place at this visit:

- Your child will have the examinations and tests shown in Table 1 under the column "TB and/or RAL treatment discontinuation."
- Blood tests: We will take about 1 – 1 ½ (5.5 – 7.5 mL) of blood for the tests in Table 1. The results of these tests will be provided to you/your child.
- Depending on the amount of HIV in your child's blood, we may also take a little more than ½ teaspoon (3 mL) of additional blood for an HIV resistance test. This test may be done after the study is over, and you/your child will not be given the results.

Even if your child stops taking the study medicines, your child will stay in the study and return for the visits at 4 weeks and 12 weeks after stopping raltegravir described below.

Four weeks after stopping RAL visit:

Four weeks after your child stops taking raltegravir, the following will take place:

- Your child will have the examinations and tests shown in Table 1 under the column "4 weeks off RAL treatment/on study".
- Blood test: We will take a little more than ½ - 1 teaspoon (4 – 6 mL) of blood for the tests shown in Table 1. The results of the tests will be provided to you/your child.

Final visit:

Twelve weeks after your child stops taking raltegravir your child will have the last study visit. Or, if your child stops participating in the study before completing the study, your child will have a study discontinuation visit. At the last study visit or study discontinuation visit, the following will take place:

- Your child will have the examinations and tests shown in Table 1 under the column “Final visit”. A pill count will only be done if your child is discontinuing raltegravir early at this visit.
- Blood tests: We will take a little over ½ - 1 teaspoon (3.5 – 5.5 mL) of blood for the tests shown in Table 1. The results of the tests will be provided to you/your child.

The study will first enroll a small group of 6 participants into three age groups and participants in each group will take the same dose of raltegravir. If the results of the intensive PK test in a specific age group show that the level of raltegravir is too low or too high or is found not to be safe, a new group of 6 participants will be enrolled into that age group and will take a new dose of raltegravir. The enrollment of a new group of 6 participants in each age group will be done until the best dose of raltegravir is found.

When the best dose of raltegravir is found for that age group, an additional 6 participants will be enrolled in each age group and will take the best dose so that there will be a total of 12 participants that will be studied on the best dose. If the results of the intensive PK test for a specific group show that the level of raltegravir is too low or too high or is found not to be safe, a new group of 6 participants will be enrolled into that age group and will take a new dose of raltegravir. This process will repeat until the best and safe level of raltegravir is found in a group of 12 participants for a specific age group. If the best dose is not found when raltegravir is taken two times a day, it may have to be taken three times a day.

If there is a question about the results of the intensive PK test of your child, or the results are lower than what is expected or too high and may be a risk to your child, the study doctor may ask your child to have another intensive PK test. Your child’s study doctor will let you know when the intensive PK test will be repeated.

If the group that your child belongs to (whether a group of 6 or 12 participants) has raltegravir PK test levels that are either too low, too high or is found not to be safe, the entire group (including your child) will take the new dose of raltegravir that will be tested in the new group of participants, if it is considered safe to do so and your child’s group is still taking TB treatment and raltegravir. Changes in the dose of raltegravir will be done for the entire group that a participant belongs to and not on an individual basis. If the PK tests suggest that the new dose should be given three times a day, this will not apply to your child who will continue to take raltegravir twice a day. The dose of raltegravir will only be changed once for your child and the intensive PK will not be repeated after the dose is changed. Your child will continue in the study and have the rest of the visits. This will be discussed with you by the study doctor and will depend on what is safest for your child.

If your child is still taking raltegravir and the anti-TB medications when the best dose of raltegravir is found, and your child is still in the study, the study doctor will change your child’s dose of raltegravir to the best dose. Your child will continue taking the new dose of raltegravir until your child stops taking the anti-TB medications.

OTHER INFORMATION

Your child's blood samples for the intensive PK tests will be shipped to a laboratory in the United States where the tests will be performed.

Any leftover blood samples after testing is completed for this study will be destroyed.

The information collected in this study may be used for other IMPAACT-approved HIV-related research.

HOW MANY INFANTS AND CHILDREN WILL TAKE PART IN THIS STUDY?

About 36 to 108 infants and children will take part in this study.

HOW LONG WILL MY CHILD BE IN THIS STUDY?

Your child will be in this study for about 4 to 9 months.

WHY WOULD THE DOCTOR HAVE MY CHILD STOP TAKING RALTEGRAVIR EARLY?

The study doctor may need to take your child off raltegravir early without your permission if:

- Your child develops a side effect and continuing the study drug(s) may be harmful to your child.
- Your child needs a treatment that your child may not take while on the study.
- Your child is found to have multi-drug resistant (MDR) or extensively drug-resistant (XDR) TB. MDR-TB and XDR-TB happens when the bacteria that cause TB infection changes and cannot be treated by the medicines that are usually effective in treating TB. If your child is found to have MDR or XDR TB, your child will be referred to the proper doctor or clinic for care.
- Your child is not able to take the study drug(s) as required by the study.
- New information that becomes available shows that your child should stop taking the study drug(s).
- The result of the intensive PK test shows that your child has not been taking the study drugs or the level of raltegravir that your child's body is taking is abnormally high or low.
- The amount of HIV in your child's blood does not go down to the levels low enough to continue the study drug(s).
- Your child becomes pregnant or is a female that is sexually active and does not agree to take birth control precautions.

If your child must permanently stop taking the study drug(s) before your child's study participation is completed or before the study is over, the study staff will discuss other options that may be of benefit to your child. In addition, your child will have the early treatment discontinuation visit and the visits four weeks and twelve weeks after stopping the study drug(s) as described above.

After the study:

After your child has completed study participation, the study will not be able to continue to provide your child with the raltegravir that he/she received on the study. If continuing to take these or similar drugs would be of benefit to your child, the study staff will discuss how you may be able to obtain them.

WHY WOULD THE DOCTOR TAKE MY CHILD OFF THE STUDY EARLY?

The study doctor may need to take your child off the study early without your permission if:

- You do not want your child to continue or your child does not want to continue taking raltegravir or completing the required visits.

- The study doctor determines that continuing participation could be harmful to your child's health or well-being.
- Your child is not able to attend the study visits or meet the requirements of the study, which may cause harm to him/her and affect the results of the study.
- The study is cancelled by the IMPAACT Network, Office for Human Research Protections (OHRP), National Institutes of Health (NIH), the site's Institutional Review Board (IRB) or Ethics Committee (EC), the U.S. Food and Drug Administration (FDA), other government agencies, or Merck & Co., Inc. (the drug company supporting this study). An IRB or EC is a committee that watches over the safety and rights of research participants.
- An IMPAACT Study Monitoring Committee (SMC) recommends that the study be stopped early. The SMC is a group of experts who monitor the study.
- The study has to be stopped for other administrative reasons.

WHAT ARE THE RISKS OF THE STUDY?

The drugs used in this study may have side effects, some of which are listed below. Please note that these lists do not include all the side effects seen with these drugs. These lists include the more serious or common side effects with a known or possible relationship. If you have questions concerning additional study drug side effects, please ask the medical staff at your site.

For your child's safety, it is important that you tell the study doctor or nurse about all medications that your child is taking before your child starts the study, and also before your child starts taking any new medications while on the study, including medicines bought from the store or pharmacy and herbal or natural medicines. In addition, it is important that you tell the study doctor or nurse before your child enrolls in any other clinical trials while on this study.

Your child's HIV may develop resistance to raltegravir and anti-HIV drugs that are being used in this study. Drug resistance develops when the HIV changes so the anti-HIV drugs become less effective. It is possible that your child may not receive the correct dose of raltegravir, which can also lead to drug resistance. If drug resistance develops in your child, the HIV virus may not be controlled. However, the reason for adding a fourth ARV drug early in the study is to try to avoid the development of resistance to raltegravir.

Use of Combination Antiretroviral Drugs

Immune Reconstitution Syndrome: When your child is treated with a combination of at least 3 anti-HIV drugs (which is called highly active antiretroviral therapy or HAART), the way your child's body is able to fight infection may change. The immune system is the body's defense against infection. Your child's immune system may respond in a stronger way to some types of infections that your child may already have. This immune response may cause your child to become sick and the condition is then called "immune reconstitution inflammatory syndrome" or IRIS.

We do not understand who will get IRIS and who will not. IRIS can be serious or mild. It can begin soon after a person starts HIV medication for the first time. It can also begin in people who restart their HIV medications after being off (or not taking) them for some time. IRIS happens when your child's immune system recovers too quickly. It can start to "overact" and respond to other infections that may or may not have been known before starting therapy, even ones that may have already been under control.

When your child's immune system over acts this way it can cause inflammation (redness and tenderness), which is sometimes very serious. For some people, these symptoms can be life-threatening. Even though most cases of IRIS get better after a few weeks, the symptoms may be mistaken by you, and your child's

doctor as the HIV disease getting worse or another condition. IRIS can be very confusing because, as your child's immune system fights an infection, the inflammation that takes place actually makes your child's symptoms worse.

When IRIS does happen, it happens more often after the BCG injection. BCG stands for Bacille Calmette-Guerin vaccine, a vaccine that is used to prevent tuberculosis (TB) in infants. The injection site can get bigger and the glands in the right armpit may become painful. IRIS also happens more often with TB in 1 out of 10 infants. Many other bacteria and viruses can lead to IRIS. Usually, IRIS causes a return or worsening of at least some of the symptoms from an infection your child may have had before starting HAART. While some of these reactions can be serious, they usually last for a short time and can be treated without stopping the anti-HIV drugs or HAART.

The use of potent antiretroviral drug combinations may be associated with an abnormal placement of body fat and wasting. Some of the body changes include:

- Increase in fat around the waist and stomach area
- Increase in fat on the back of the neck
- Thinning of the face, legs, and arms
- Breast enlargement

Integrase Inhibitor

Raltegravir, (RAL, Isentress™)
Merck & Co., Inc.

The following side effects have been associated with the use of raltegravir:

- Rash, which can become severe or life-threatening. Contact your child's doctor right away if your child develops a rash.
- Nausea
- Headache
- Tiredness
- Weakness
- Trouble sleeping
- Stomach pain
- Dizziness
- Depression
- Suicidal thoughts and actions
- Feeling anxious, Paranoia
- Easy bleeding (decreased blood clotting, low platelet count)
- Diarrhea
- Liver failure
- Clumsiness and lack of coordination
- Changes in behavior, like low or high activity in children
- Muscle tenderness, weakness or injury which can be serious and lead to kidney damage

Serious skin and allergic reactions including a rash which can become severe or life-threatening and can be fatal. If your child develops a rash with any of the following symptoms stop using raltegravir and contact your child's doctor right away:

- Fever
- Generally ill feeling
- Extreme tiredness
- Muscle or joint aches
- Blisters or sores in mouth
- Blisters or peeling of the skin
- Redness or swelling of the eyes
- Swelling of the mouth or face
- Problems breathing

Sometimes allergic reactions can affect the body, like the liver and cause liver problems which can lead to liver failure. Contact your child's doctor right away if your child has any of the following signs or symptoms of a liver problem:

- Yellowing of the skin or whites of the eyes
- Dark or tea colored urine
- Pale colored stools/bowel movements
- Nausea/vomiting
- Loss of appetite
- Pain, aching or tenderness on the right side below the ribs

In some patients receiving raltegravir blood tests showed abnormally high levels of a muscle enzyme—creatinine kinase which may cause muscle pain, tenderness or weakness this type of muscle break down can be serious and lead to kidney damage including kidney failure. Contact your child's doctor right away if your child has any unexplained muscle pain, tenderness, or weakness.

Note: Raltegravir chewable tablets contain phenylalanine, a component of the sugar substitute aspartame. Phenylalanine can be harmful to children and adults with phenylketonuria, a birth defect that can lead to a variety of health problems.

Risks of Blood Draws

There is risk of some discomfort, bruising, or bleeding at the site where the blood is drawn. Occasionally, there is swelling in the area where the needle enters the body and a small risk of fainting and/or infection.

Other Risks

Your child may feel uncomfortable or embarrassed by some parts of your child's physical exam and with some of the questions related to sexual development and activity.

ARE THERE RISKS RELATED TO PREGNANCY?

It is not known if the study drug raltegravir harms fetuses. Tests in pregnant animals do show some risk.

Your child will have a medical history and physical exam and we will ask you or your child questions to check if your child is having sex that could lead to pregnancy. If your child is pregnant or breastfeeding, she cannot be in the study. If your child is a female and is sexually active, she must agree to use two methods of birth control to take the study medicine. Approved methods of birth control for this study include hormonal birth control, such as slow release inserts placed under or on the skin, and a medically accepted barrier method including condoms, an intrauterine device (IUD), a diaphragm or cervical cap with a cream or gel that kills sperm. If your child is a female and is sexually active while in the study and does not agree to use two of these methods of birth control, she can remain in the study, but cannot take

the study medicine. If your child is having sex while in the study, your child will be referred to their primary provider for prevention of pregnancy. Your child may also be asked to provide urine or 1 mL of blood for a pregnancy test at each visit to check if she is pregnant. If the pregnancy test is positive, the study staff will refer your child to her primary provider for counseling about pregnancy and pregnancy care and she should stop taking raltegravir. Your child will continue to come in for study visits and will be followed until the outcome of your child's pregnancy. If you think your child has started having sex or you/your child thinks she may be pregnant at any time during the study, tell the study staff right away. The study staff will talk to you/your child about your/your child's choices. If your child becomes pregnant, she will be entered in the Antiretroviral Pregnancy Registry.

Pregnancy test results will be shared confidentially with participants, even if a parent or other adult is consenting for the child's participation in the study. *[Sites should modify preceding language about confidentiality of pregnancy test results to conform to their local practice, regulations and IRB requirements.]*

ARE THERE BENEFITS TO TAKING PART IN THIS STUDY?

If your child takes part in this study, there may be a direct benefit to your child, however we do not know if being in the study will benefit your child in any way. It is also possible that your child may receive no benefit from being in this study. Your child will have regular visits and frequent checks on his or her health, including tests for the amount of HIV in your child's blood, called viral load, and for the amount of cells that fight HIV, called CD4. Information learned from this study may help others who have HIV and TB.

WHAT OTHER CHOICES DOES MY CHILD HAVE BESIDES THIS STUDY?

Instead of being in this study you have the choice of:

- treatment with prescription drugs available to your child
- treatment with experimental drugs, if your child qualifies
- no treatment

Please talk to your doctor about these and other choices available to your child. Your doctor will explain the risks and benefits of these choices.

WHAT ABOUT CONFIDENTIALITY?

Efforts will be made to keep your child's personal information confidential. Study records and specimens will be kept in secure locations. We cannot guarantee absolute confidentiality. Despite our best efforts to keep your child's information private, it is possible that the information could be obtained by someone who should not have it. If this were to happen, your child could be treated unfairly. You could feel stress or embarrassment. Your child's personal information may be disclosed if required by law. Any publication of this study will not use your child's name or identify your child personally.

Your child's records may be reviewed by the U.S. Food and Drug Administration (FDA), the Office of Human Research Protections (OHRP), (*insert name of site*) IRB/EC, National Institutes of Health (NIH), study staff, study monitors, Merck & Co., Inc. (the drug company supporting this study), and other US, local, and international regulatory entities.

WHAT ARE THE COSTS TO ME?

Taking part in this study may lead to added costs to you and your insurance company. In some cases it is possible that your insurance company will not pay for these costs because your child is taking part in a research study. *[Sites: Delete or modify as appropriate with any site-specific information regarding insurance and local costs.]*

WILL I RECEIVE ANY PAYMENT?

You and your child may receive reimbursement for some expenses for this study. You and your child may receive payment for transportation and meals.

[Sites: Delete or modify as appropriate with any site-specific information about payment.]

WHAT HAPPENS IF MY CHILD IS INJURED?

Your child's health is important to us. We will make every effort to protect your child's well-being and minimized risk to him or her. If your child is injured as a result of being in this study, the study doctor will give or refer your child for immediate treatment for your child's injuries. 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 (NIH). You will not be giving up any of your legal rights by signing this consent form.

[Sites: Delete or modify as appropriate with any site-specific information regarding insurance and local costs.]

WHAT ARE MY CHILD'S RIGHTS AS A RESEARCH PARTICIPANT?

Taking part in this study is completely voluntary. You may choose not to allow your child to take part in this study or take your child out of the study at any time. Your child will be treated the same no matter what you decide.

We will tell you about new information from this or other studies that may affect your child's health, welfare or willingness to stay in this study. If you want the results of the study, let the study staff know.

WHAT DO I DO IF I HAVE QUESTIONS OR PROBLEMS?

For questions about this study or a research-related injury, contact:

- name of the investigator or other study staff
- telephone number of above

For questions about your/your child's/baby's rights as a research participant, contact:

- name or title of person on the Institutional Review Board (IRB) or other organization appropriate for the site
- telephone number of above

SIGNATURE PAGE

If you have read this consent form (or had it explained to you), all your questions have been answered and you agree to take part in this study, please sign your name below.

Participant's Name (print)

Participant's Signature and Date

Participant's Parent or Legal Guardian (print)

Parent or Legal Guardian's Signature and Date

Study Staff Conducting
Consent Discussion (print)

Study Staff Signature and Date

Witness' Name (print)
(As appropriate)

Witness's Signature and Date

Father's Name
(If father's consent is required)

Father's Signature and Date
(If father's consent is required)