

**Appendix II**  
**Sample Consent Form for Participants Enrolling in Stage I**

DIVISION OF AIDS  
INTERNATIONAL MATERNAL PEDIATRIC ADOLESCENT AIDS CLINICAL TRIALS GROUP  
(IMPAACT)

Phase I/II, Multi-Center, Open-Label Pharmacokinetic, Safety, Tolerability and  
Antiviral Activity of dolutegravir, a Novel Integrase Inhibitor, in Combination Regimens in HIV-1  
Infected Infants, Children and Adolescents

Participants Enrolling in STAGE ONE  
P1093 Version 5.0, dated 12 July 2018

SHORT TITLE FOR THE STUDY: Safety and PK of dolutegravir in HIV-1 Infected Children

**INTRODUCTION**

You are/your child is being asked to take part in this research study because you have /your child has the Human Immunodeficiency Virus (HIV), which is the virus that causes AIDS, and because the drugs currently available may not keep the amount of HIV in your / your child's blood low enough or may cause side effects too difficult to deal with. 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 to be/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/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 study a new antiretroviral HIV medication called dolutegravir. This drug is a type of 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. The study will help find the best amount or dose of dolutegravir for infants, children and teenagers, when it is taken on its own as well as with other antiretroviral medications. This study will also find out the safety of using this medication in infants, children and adolescents and if there are any side effects from the medication. Dolutegravir has been tested in adults and children. The study drug (dolutegravir) is approved for use in children 12 years and older by the FDA [and/or local regulatory authorities].

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

If you decide to (allow your child to) enroll in this study, you / your child will be asked to come to the clinic at least 10 times over 48 weeks and then every 12 weeks for three more years. You / your child will be given dolutegravir and you / your child will be asked to take it once or twice a day for the entire study, in addition to your / your child's regular HIV medicines. Dolutegravir is available in 3 different formulations: 1) a film-coated tablet which cannot be crushed or dissolved, 2.) a liquid suspension and, 3) a tablet that can be dissolved in water. If you are/your child is 12 up to 18 years old, you/your child will take the film-coated tablet formulation of dolutegravir. You will be given instructions on how to give dolutegravir to your child and how to store the dolutegravir. If your child is between 6 to less than 12 years of age and was prescribed the liquid or dissolvable tablets of dolutegravir he/she may be allowed to switch to the film-coated tablet formulation at a later time. The study staff will let you know when your child can switch and if you request to do so.

Although the study will provide you/your child with dolutegravir, other antiretrovirals will not be provided by the study.

This study will be done in two parts – Stage one and Stage two. Stage one will enable the doctors to find the right dose of study drug for you/your child and then will keep you on that dose to look for any side effects that you/your child might experience. In Stage two the doctors will know the right dose to put you/your child on and will look at any side effects that you / your child might experience as well as how well the drug is controlling your HIV infection. You/your child will be enrolled into either Stage one or Stage two, depending on when you/your child enroll and your age / the age of your child. This consent form is for Stage one.

In this study there are 8 cohorts in Stage I – enrolling infants, children, and adolescents from 4 weeks to less than 18 years of age. Participants who have had their 18<sup>th</sup> birthday by the entry visit will not be enrolled into the study.

#### Screening:

If you are interested in taking part / allowing your child to enroll in this study, we will see if you are / your child is eligible for the study:

- We will ask your / your child's medical history including questions about your /your child's health and what symptoms, medications, and illnesses you have/your child has had.
- We will do a physical exam including height, weight and vital signs (temperature, blood pressure, pulse and respiratory rate). Doses may be modified based on the results of the weight.
- We will take a little more than 2 teaspoons (1 mL) of blood, to check for the following:
  - The amount of HIV in the blood,
  - The amount of cholesterol and triglycerides (types of fat) in the blood,
  - How well your immune system, liver and kidneys are working,
  - Other routine tests.

You will be given the results of these tests. We will also ask you/your child to provide a urine sample for routine tests. Girls and women who can have a baby will also be asked to provide a urine or blood sample to test for pregnancy. If you are / your child is engaged in sexual activity that could lead to pregnancy, you / your child will be asked to take birth control precautions throughout the study period.

#### On Study:

If you are/your child is eligible for this study, you/your child will come to the clinic at least 10 times in about 1 year. Most of the visits will last about 1-2 hours. More visits will be needed if the amount of study drug in your blood is too low or too high and your dose needs to be adjusted. You/your child will come to the clinic for the first study visit within 30 days of the screening visit.

- At each visit, a medical history will be taken and you/your child will have a physical exam. At the enrollment visit and at the week 48 visit, you/your child's stage of sexual development will be determined. For girls/women, this will be done by looking at how developed the breasts are. For boys/men, this will be done by measuring the size of the testes.
- We will draw blood at each visit. Depending upon your/your child's age, between 1- 4 teaspoons (5-17mLs) of blood will be drawn at these visits; you will be informed of results of routine blood tests. Some of the blood drawn will be stored and tested to find out how your/your child's immune system is affected by the study drug. This testing will be done after the study is over, and you will not be given the results of these tests.

- A palatability assessment will be done at Day 10, Week 4 and Week 24 to find out what you/your child thinks about the taste of the study drug.
- You/your child will be asked to come to the clinic to have blood drawn 8 times over 24 hours during one visit, approximately 5-10 days after you / your child started taking the study medication. This visit is known as an 'intensive PK visit'. Depending on your/your child's age, up to 9mLs (about 2 teaspoons) of blood will be drawn at this visit and you will be asked to withhold certain liquids and food. The study staff will give you instructions about this. These blood tests are done to measure the amount of study drug in your/your child's blood. A small plastic catheter (a needle that is placed in a vein for an extended period of time, so that blood can be drawn multiple times, without having to stick you with a needle several times) will be placed in your/your child's arm to draw these blood samples. The needle will stay in place until all of the blood samples are drawn.
- If the amount of study drug in your/your child's blood is not enough or is too high, you/your child may be asked to take a different dose and may be asked to return to the clinic for another 'intensive PK visit'. You/your child may have blood to be drawn again 8 times over 24 hours. This is to make certain that the new dose is safe. The same procedures above will be followed.
- The current instructions on what you/your child can eat and drink around the intensive PK draws are below, but these may change. If these instructions change, the study staff will let you know and provide you with different instructions.  
If you are/your child is older than 2 years old and having intensive PKs done you/your child may be asked to follow the guidelines below regarding eating and drinking around the intensive PK visit.
  - $\geq 6$  hours PRIOR to taking your medication – you/your child may eat and drink without restriction
  - $\geq 4$  to  $< 6$  hours PRIOR to taking your medication – milk, apple/orange juice and water may be consumed; No food
  - $< 4$  hours PRIOR to taking your medication – water ONLY
  - From dosing to  $< 2$  hours AFTER taking your medication – apple/orange juice and water may be consumed; No food
  - From  $\geq 2$  to  $< 4$  hours AFTER taking your medication – you may drink apple/orange juice and eat a snack/light meal (around 100-150 calories)
  - From  $\geq 4$  hours AFTER taking your medication onwards – you may eat and drink without restriction

If your child is 4 weeks to less than 2 years old and having intensive PKs done, you/your child may be asked to follow the guidelines below regarding eating and drinking around the intensive PK visit.

- No breastmilk, formula or any other high fat food/liquid for 2 hours prior to and 1 hour after dosing on the intensive PK day.
  - Water and other fluids (i.e. apple/orange juice and oral rehydration solution) can be taken at any time.
- You will have extra blood draws at three visits (week 4, week 12 and week 24). At weeks 4 and 24, you will have two blood draws. At week 12 you will only have one blood draw. The amount of blood drawn at the different study visits will be less than 1 teaspoon (0.5-1mL) depending on your /your child's age.
- If the amount of HIV virus in your/your child's blood increases too much while on this study drug, you/your child may be asked to come back to clinic to have your blood drawn to confirm the level of HIV in your blood. If the level of HIV virus in your blood is still too high, your study

doctor may ask you to stop taking the study medicine and to come back to the clinic for another visit. As part of this visit, you/your child will have an interim medical history, physical exam and approximately 3 teaspoons of blood (14-16.5mL) will be drawn for testing and storage.

- If you/your child experiences a severe liver reaction or inflammation while on the study, you/your child may be asked to come back to clinic to have less than one teaspoon of blood (2mL) drawn to check the level of dolutegravir in the blood. Additional testing as part of routine assessments for liver inflammation (e.g. checking for viruses that cause liver inflammation) may be performed as well.

#### *Long Term Follow-Up*

After you have been on study drug for approximately 48 weeks, you will enter the long term follow-up phase of the study. You will be asked to come back into clinic every 12 weeks (every 3 months) for 3 more years. Most visits will last about 30 mins.

- At each visit, a medical history will be taken and you/your child will have a physical exam. You will also be asked if you have missed taking any of your medications.
- We will draw less than 1 teaspoon of blood (3-4mL) at each visit. You will be informed of results of routine blood tests.
- As before, if the amount of HIV virus in your/your child's blood increases too much while on this study drug, you/your child may be asked to come back to clinic to have your blood drawn to confirm the level of HIV in your blood (see above).

You/your child must continue to take your/his/her anti-HIV medications during the study as prescribed by your/your child's HIV care provider. If your/your child's HIV care provider changes your/your child's anti-HIV medications during the study, you/your child can still take the study drug. You/your child will be asked questions about taking your/his/her anti-HIV medications and the times you take/he/she takes them and if you have/he/she has missed any medications.

If you/your child can become pregnant, we will collect urine or blood to test for pregnancy at each visit. We will also ask you/your child about contraception use. If you think you/if your child thinks she may be pregnant at any time during the study, tell the study staff right away.

#### *Blood and Urine Samples*

Some of your / your child's blood and urine samples will be shipped out of the country to the USA for specialized tests. These tests will tell the doctors how much study drug is in your / your child's blood and if the study drug is causing any changes in your kidneys.

#### *For Participants Receiving Granules for suspension only*

If your child is receiving the liquid he/she will need to switch to the dissolvable tablet. The study staff will inform you when your child will need to switch. This is because the company will not be making the (granule) liquid form of dolutegravir any longer. The study staff will provide instructions on how to dispense the dissolvable tablet and on the day you are scheduled to come to the clinic to begin taking the dissolvable tablets you will be asked to not give the (granule) liquid dose to your child. The first dose of the dissolvable tablet will be given in the clinic. You will be asked to come back to the clinic about 2 weeks later and will have a palatability assessment and blood drawn to confirm the level of HIV in your child's blood. If you have been on the study for more than 24 weeks at each of these visits, blood samples will be drawn at two separate times. The amount of blood drawn will be less than 1 teaspoon (0.5 -1mL)].

#### WHAT DO I / DOES MY CHILD HAVE TO DO IF I AM / HE / SHE BECOMES INFECTED WITH TUBERCULOSIS WHILE ON THIS STUDY?

If you become/your child becomes exposed to Tuberculosis (TB) while on study and requires anti-TB treatment that includes Rifampin you/your child will have to increase the dose of dolutegravir from once a

day to twice a day while taking Rifampin. After you/your child complete(s) treatment with Rifampin, you/your child will go back to taking the dolutegravir once a day depending on what other medications you/your child is taking.

You/your child will also be required to return for at least five additional follow-up visits after starting Rifampin.

- At each of these visits, a medical history will be taken and you/your child will have a physical exam and a pregnancy test. We will draw approximately 1-3 teaspoons of blood to look at the following:
  - The amount of HIV, cholesterol and triglycerides (types of fat) in your blood
  - How well your immune system, liver and kidneys are working, as well as other routine tests
- At each visit you will be asked whether you are taking your medication as instructed.
- You/your child will be asked to come to the clinic to have blood drawn 8 times over 12 hours during one visit, approximately 5-10 days after you/ your child started taking anti-TB medication. For this visit, you/your child will be asked to fast for 6 hours before your daily dose of study medication.
- The study staff will give you more instructions about this. Depending on your/your child's age, up to 13mL (about 3 teaspoons) of blood will be drawn at this visit.
- You will have extra blood draws at two visits. At weeks 4 and 12, you will have two blood draws - blood will be drawn once before you take dolutegravir and about 12 hours later. The amount of blood drawn at the different study visits will be less than 1 teaspoon (1mL) depending on your /your child's age.

#### OTHER INFORMATION

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

#### HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

About 300 children and adolescents will take part in this study

#### HOW LONG WILL I/MY CHILD BE IN THIS STUDY?

You/your child is enrolling in Stage I of the study, and so will be in the study for at least 48 weeks After that time you/your child will enter the long-term safety follow-up phase of the study. During this time, you / your child will continue to take study-provided dolutegravir and will be asked to come to clinic every 12 weeks for three more years.

#### WHY WOULD THE DOCTOR TAKE ME / MY CHILD OFF THE STUDY DRUG / THIS STUDY EARLY?

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

- Continuing the study drug may be harmful to you / your child
- You become / your child becomes pregnant while on study
- If you elect not to attend repeat PK evaluations as part of the study

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

- You are/ your child is not able to attend the study visits as required by the study
- You need / your child needs a treatment that you / your child may not take while on the study
- You are / your child is not able to take the study drug as required by the study
- The study is cancelled by the U.S. Food and Drug Administration (FDA), National Institutes of Health (NIH), the Office of Human Research Protections (OHRP), other country specific governmental agencies, IMPAACT, the drug company supporting this study (GSK), or the site's

Institutional Review Board (IRB) or Ethics Committee (EC). An IRB or EC is a committee that watches over the safety and rights of research participants

If your doctor wants you / your child to stop taking the study drug, you/your child will be asked to return to the clinic once more, four weeks after your last dose of dolutegravir, to make sure you are/your child is continuing to do well. This visit will include a history and physical exam, a blood draw and a review of your medical records.

IF MY CHILD HAS TO PERMANENTLY STOP TAKING STUDY-PROVIDED MEDICINE, OR ONCE I LEAVE THE STUDY, HOW WOULD THE STUDY MEDICINE BE PROVIDED?

During the study:

If you / your child must permanently stop taking study-provided dolutegravir before your/your child's study participation is over, the study staff will discuss other options that may be of benefit to you/your child.

After the study:

Once you / your child leaves the study, if you/they are gaining benefit from the study-provided drug, this drug may continue to be provided until it is available to you in your country, but there is no guarantee. Study clinicians will work to ensure that you/your child continue to receive appropriate care and treatment outside of the study.

WHAT ARE THE RISKS OF THE STUDY?

The drug 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 this drug. These lists include the more serious or common side effects with a known or possible relationship. It is very important that you tell your study doctor of any changes in your/your child's medical condition while taking part in the study. At any time during the study, if you believe you are/your child is experiencing any of these side effects, you have the right to ask questions on possible and /or known risks.

Possible Risks Associated with Dolutegravir

The drug used in this study, dolutegravir, has been administered to a total of 6004 participants (4814 HIV-infected and 1190 healthy) cumulative to 16 July 2017 in ongoing and completed ViiV sponsored and clinical trials ranging from Phase I to IIIb and the dolutegravir compassionate use program. The following side effects have been seen with dolutegravir:

Very Common (expected in about 100 of every 1000 people taking DTG (10%))
Nausea or feeling sick Headache Diarrhea or loose stools

Common (expected in about 10 of every 1000 people taking DTG (1%))
Cold symptoms like runny nose and sore throat; cough; flu Dizziness or feeling light headed Trouble sleeping; abnormal dreams Rash Feeling tired High temperature Pain in the stomach; vomiting Changes in kidney, liver and muscle blood tests Ocular icterus (yellowing of the whites of the eyes)

Itching (pruritus) Feelings of deep sadness and unworthiness (depression) Flatulence (gas or wind) Increase in the level of liver enzymes Increase in the level of enzymes produced in the muscles (creatinine phosphokinase) Anxiety (fear, worry)
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Uncommon (expected in about 1 of every 1000 people taking DTG (0.1%) Allergic reaction (see below) Liver toxicity (see below) An inflammatory condition which may develop as the immune system becomes stronger (immune reconstitution syndrome or 'IRIS' (see below) Suicidal thoughts and behaviors (mainly in patients who have had depression or mental health problems before) (see below)
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Most of the side effects listed above have been mild or moderate, and have not generally stopped HIV-infected patients treated with dolutegravir from getting on with their lives as normal.

In one animal study, gastric erosion (irritation of the stomach lining) was seen. This finding has not been seen in adults in studies to date. However, if you or your child feels heartburn or stomach pain or has vomiting, please contact your/your child's study doctor.

Other side effects that may show up in blood tests:

- An increase in bilirubin (a pigment produced from the breakdown of red blood cells) in the blood,
- An increase in the level of creatinine, a waste product in the blood that gets filtered by the kidneys.

Dolutegravir Hypersensitivity Reaction

Hypersensitivity reactions have also been reported with integrase inhibitors, including dolutegravir, with signs and symptoms including general feeling of being sick, skin rash, a high temperature (fever), lack of energy (fatigue), swelling sometimes of the face or mouth (angioedema) causing difficulty in breathing, blisters or peeling skin, mouth ulcers, conjunctivitis (sore eyes), and muscle or joint aches. If you/your child develop(s) any of these signs and symptoms during the study, contact you/your child's study doctor immediately, who may decide to carry out tests on you/your child liver, kidneys or blood.

Mental illness

Some people with HIV infection occasionally have feelings of depression or may have thoughts of hurting or killing themselves (committing suicide). A small number of people being treated with integrase inhibitors for HIV infection, including dolutegravir, have had suicidal thoughts and behaviors, particularly patients with a prior history of depression or mental health illness. People with HIV taking integrase inhibitors including dolutegravir have also reported depression.

Tell the study doctor if you/your child have a history of mental illness. If you/your child have thoughts of hurting or killing yourself or have any other unusual or distressing thoughts or feelings at any time during the study, you/your child should tell the study staff or go to the nearest hospital immediately.

Use of Combination Antiretroviral Drugs

Immune Reconstitution Syndrome: In some people with advanced HIV infection, symptoms from other infections or certain diseases may occur soon after starting combination anti-HIV treatment but can also

occur later. Some of these symptoms may be life threatening. If you start having new symptoms, or notice that existing symptoms are getting worse after starting your antiretroviral therapy, tell your healthcare provider right away.

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

Some patients taking combination anti-HIV therapy may develop a bone disease called osteonecrosis (death of bone tissue caused by loss of blood supply to the bone). The length of combination anti-HIV therapy, corticosteroid use, drinking alcohol, severe reduction in ability to fight off infection, higher body weight, among others, may be risk factors for developing this disease. Signs of osteonecrosis are joint stiffness, aches and pains (especially of the hip, knee and shoulder) and difficulty in movement. If you/your child notice any of these symptoms, please inform your doctor

#### Liver Toxicity

Liver toxicity in the form of abnormal liver enzymes, inflammation of the liver (hepatitis) and liver failure have occurred in HIV-infected patients receiving regimens containing dolutegravir. The liver toxicity usually occurs in the first few weeks or months of taking anti-HIV medications. These patients were also generally either taking other medications (both HIV treatment and non-HIV treatment) that are also known to cause significant liver inflammation and/or allergic reaction, or already had liver problems (such as hepatitis B or hepatitis C), or drank too much alcohol or had a combination of these. Cases of liver toxicity have also occurred in patients who do not have these risk factors.

If you/your child have (has) an unanticipated need for hepatitis C virus (HCV) therapy during the conduct of the study, the study doctor will discuss specific HCV treatment options with you. In case you/your child experience liver toxicity, the study doctor can decide to stop the administration of the study drug in order to assure your/your child's safety.

#### Other Risks

There is the risk of serious and/or life threatening side effects when non-study medications are taken with the study drug. For your/your child's safety, you must tell your/your child's HIV care provider and the study doctor or nurse about all medications you take/your child takes before the start of this study and also before starting any new medications while you are/your child is on the study. In addition, you must tell the study doctor or nurse before you enroll/enrolling your child in any other clinical trials while on this study. The use of highly active HIV medications may also be associated with altered fat metabolism including increased triglycerides (fatty acid in the blood) and/or increased cholesterol.

Other side effects besides those listed and side effects from taking these drugs together may occur. If any unusual symptoms or changes happen, you should call your/your child's doctor immediately. It is also important that while participating in the study, you do not/your child does not take any other prescription drugs or over-the-counter medications without first talking to your/your child's doctor or study nurse.

With any drug for HIV, there is a risk that the virus in your body will become resistant, which means that the drug will be less effective or not effective against your HIV. The risk that taking part in this study will cause your HIV to develop resistance to the study drug is unknown and will depend on how well the study drug works against your virus and whether instructions are followed for taking the study drug.

### Blood Drawing and Heparin Lock Risks:

Blood drawing may cause some discomfort, bleeding or bruising where the needle enters the body. A small blood clot may form where the needle enters the body or there may be swelling in the area. There is a small risk of a minor infection at the blood draw site. Lightheadedness and fainting can also occur when a needle enters the body.

### ARE THERE RISKS RELATED TO PREGNANCY?

It is not known if the drug or drug combinations in this study harm fetuses. Tests in pregnant animals do not show risk to the mother. Early results from a large study in Botswana of pregnant women showed a possible increased risk of certain types of serious birth defects involving the brain, and spinal cord in babies born to women who received dolutegravir at the time of becoming pregnant. No cases of babies born with these types of birth defects have been reported among women who started dolutegravir later in pregnancy.

If you are/your child is having sex that could lead to pregnancy, you/your child must agree not to become pregnant.

Because of the risk involved, you and your partner, or your child and their partner must use two methods of birth control that you discuss with the study staff. You must continue to use both methods until two weeks after stopping study drug. Options for birth control methods include these listed below:

- Birth control drugs that prevent pregnancy given by pills, shots, placed on the skin (e.g. patch) or placed under the skin
- Male or female condoms with or without a cream or gel that kills sperm
- Diaphragm or cervical cap with a cream or gel that kills sperm
- Intrauterine device (IUD)

Some of these are better than others in preventing pregnancy. You/your child will work with study staff to pick the options best for you. All birth control methods listed above except condoms do not reduce the risk of giving HIV to someone else. HIV-infected individuals should use a birth control method that includes condoms to keep from giving HIV to someone else.

If you think you/your child may be pregnant at any time during the study, tell the study staff right away. The study staff will talk to you about your/your child's choices. You/your child will be tested at each study visit if it is possible that you/she may be pregnant.

If you are /your child becomes pregnant while on study, you/she will not be allowed to continue on the study drug but will be asked to remain on study and come in for study visits as planned in case of safety concerns and so that the doctors can follow your/her pregnancy until your / your child's baby is born.

### ARE THERE BENEFITS TO TAKING PART IN THIS STUDY?

If you / your child take(s) part in this study, the amount of HIV in your / your child's body may go down and your/your child's immune system may become stronger, but no guarantee can be made. You/your child may receive no benefit from being in this study. Information learned from this study may help others who have HIV.

### WHAT OTHER CHOICES DO I / DOES MY CHILD HAVE BESIDES THIS STUDY?

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

- Treatment with prescription drugs available to you/your child
- Treatment with other experimental drugs, if you/your child qualify(ies)
- No treatment (NOT recommended)

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

#### WHAT ABOUT CONFIDENTIALITY?

*(For US Sites Only)*

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below. The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

People who may review your/your child's records include the U.S. Food and Drug Administration and other U.S., local and international regulatory entities, the Office of Human Research Protections (OHRP), the site IRB /EC (insert name of site IRB/EC), the National Institutes of Health, study staff, study monitors, drug companies supporting the study, and their designees.

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about you or your participation in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate of Confidentiality to withhold that information.

*(For sites outside the U.S.)*

Efforts will be made to keep your personal information confidential. We cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law. Any publication of this study will not use your name of identify you personally.

Your records may be reviewed by the Ministry of Public Health in your country, the FDA and other U.S., local and international regulatory entities, the Office of Human Research Protections (OHRP), the NIH, (insert name of site) IRB/EC, study staff, study monitors and the drug companies supporting this study.

#### WHAT ARE THE COSTS TO ME / MY CHILD?

There are no costs to you/your child for the study drug, study visits or study procedures. However, taking part in this study may lead to added costs to you and your insurance company if medical complications arise or if your doctor decides extra tests are needed. In some cases, it is possible that your insurance company will not pay for these costs because [you are/ your child is] taking part in a research study.

#### WILL I RECEIVE ANY PAYMENT?

You will receive \$XX for each study visit you attend. If you attend all study visits, you may receive up to \$XX.

#### WHAT HAPPENS IF I AM / MY CHILD IS INJURED?

If you are / your child is injured as a result of being in this study, you / your child will be given immediate treatment for your/his/her injuries. The cost for this treatment will 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/your child's legal rights by signing this consent form.

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

Taking part in this study is completely voluntary. You may choose not to take part/not to allow your child to take part in this study or leave this study/take your child out of the study at any time. Your decision will not have any impact on your participation in other studies conducted by the NIH and will not result in any penalty or loss of benefits to which you are otherwise entitled. We will tell you about new information from this or other studies that may affect your health, welfare or willingness to stay in this study. If you want the results of the study, let the study staff know.

*(For legal guardians, as applicable)*

If your child reaches the legal age of consent during the study [he/she] will be asked to provide independent consent at their next visit.

#### 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), Ethics Committee (EC) 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 Legal Guardian (print)  
(As appropriate)

\_\_\_\_\_  
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

\_\_\_\_\_  
Second Guardian (print)  
(If required)

\_\_\_\_\_  
Second Guardian's Signature and Date

**Appendix III**  
**Sample Consent Form for Participants Enrolling in Stage II**

DIVISION OF AIDS  
INTERNATIONAL MATERNAL PEDIATRIC ADOLESCENT AIDS CLINICAL TRIALS GROUP  
(IMPAACT)

Phase I/II, Multi-Center, Open-Label Pharmacokinetic, Safety, Tolerability and  
Antiviral Activity of dolutegravir, a Novel Integrase Inhibitor, in Combination Regimens in HIV-1  
Infected Infants, Children and Adolescents

Participants Enrolling in STAGE TWO  
P1093 Version 5.0, dated 12 July 2018

SHORT TITLE FOR THE STUDY: Safety and PK of dolutegravir in HIV-1 Infected Children

**INTRODUCTION**

You are/your child is being asked to take part in this research study because you have /your child has the Human Immunodeficiency Virus (HIV), which is the virus that causes AIDS, and because the drugs currently available may not keep the amount of HIV in your / your child's blood low enough or may cause side effects too difficult to deal with. 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 to be/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/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 study a new antiretroviral HIV medication called dolutegravir. This drug is a type of 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. The study will help find the best amount or dose of dolutegravir for infants, children and teenagers, when it is taken on its own as well as with other antiretroviral medications. This study will also find out the safety of using this medication in infants, children and adolescents and if there are any side effects from the medication. Dolutegravir has been tested before in adults and children. The study drug (dolutegravir) is approved for use in children 12 years and older by the FDA [and/or local regulatory authorities].

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

If you decide to (allow your child to) enroll in this study, you / your child will be asked to come to the clinic at least 10 times over 48 weeks and then every 12 weeks until the end of the study. You / your child will be given dolutegravir and you / your child will be asked to take it once or twice a day for the entire study, in addition to your / your child's regular HIV medicines. Dolutegravir is available in three different formulations: 1) a film-coated tablet that cannot be crushed or dissolved, 2) a liquid suspension and 3) a tablet that can be dissolved in water. You will be given instructions on how to give dolutegravir to your child. If your child is between 6 to less than 12 years of age and was prescribed the liquid or dissolvable tablet tablets of dolutegravir he/she may be allowed to switch to the film-coated tablet formulation, at a later time. The study staff will let you know when your child can switch, if you request to do so.

Although the study will provide you/your child with dolutegravir, other antiretrovirals will not be provided by the study.

This study will be done in two parts – Stage One and Stage Two. Stage One will enable the doctors to find the right dose of study drug for you/your child and then will keep you on that dose to look for any side effects that you/your child might experience. In Stage Two the doctors will know the right dose to put you/your child on and will look at any side effects that you / your child might experience as well as how well the drug is controlling your HIV infection. You/your child will be enrolled into Stage One or Stage Two, depending on when you enroll /your child enrolls and your age / the age of your child. This consent form is for Stage Two.

In this study there are 7 cohorts in Stage II – enrolling infants, children, and adolescents from 4 weeks to less than 18 years of age. Participants who have had their 18<sup>th</sup> birthday by the entry visit will not be enrolled into the study.

Screening:

If you are interested in taking part / allowing your child to enroll in this study, we will see if you are / your child is eligible for the study:

- We will ask your / your child's medical history including questions about your /your child's health and what symptoms, medications, and illnesses you have/your child has had.
- We will do a physical exam including height, weight and vital signs (temperature, blood pressure, pulse and respiratory rate). Doses may be modified based on the results of the weight.
- We will take about 3 teaspoons (11mLs) of blood, to check for the following:
  - The amount of HIV in the blood,
  - The amount of cholesterol and triglycerides (types of fat) in the blood,
  - How well your immune system, liver and kidneys are working,
  - Other routine tests.

You will be given the results of these tests. We will also ask you to provide a urine sample for routine tests. Girls and women of childbearing age will also be asked to provide a urine or blood sample to test for pregnancy. If you are / your child is engaged in sexual activity that could lead to pregnancy, you / your child will be asked to take birth control precautions throughout the study period.

On Study:

If you are/your child is eligible for this study, you/your child will come to the clinic at least 8 times in 48 weeks. Most of the visits will last about 1-2 hours. You/your child will come to the clinic for the first study visit within 30 days of the screening visit.

- At each visit, a medical history will be taken and you/your child will have a physical exam. If you are/your child is older than 2 years of age, at the enrollment visit and at the week 48 visit, you/your child's stage of sexual development will be determined. For girls/women, this will be done by looking at how developed the breasts are. For boys/men, this will be done by measuring the size of the testes. Girls and women of childbearing age will also be asked to provide a urine or blood sample to test for pregnancy at each visit.
- We will draw blood at each visit. Depending upon your/your child's age, between 1-5 teaspoons (5-17mLs) of blood will be drawn at these visits. You will be informed of results of routine blood tests. Some of the blood drawn will be stored and tested to find out how your/your child's

immune system is affected by the study drug. This testing will be done after the study is over, and you will not be given the results of these tests.

- A palatability assessment will be done at Day 10, Week 4 and Week 24 to assess what you/your child thinks about the taste of the study drug.
- At two visits (week 4 and week 24), blood samples will be drawn two separate times. At week 12, you will only have one blood draw. The amount of blood drawn at the different study visits will be less than 1 teaspoon (0.5-1mL) depending on your /your child's age.
- If the amount of HIV virus in your/your child's blood increases too much while on this study drug, you/your child may be asked to come back to clinic to have your blood drawn to confirm the level of HIV in your blood. If the level of HIV virus in your blood is still too high, your study doctor may ask you to stop taking the study medicine and to come back to the clinic for another visit. As part of this visit, you/your child will have an interim medical history, physical exam and approximately 4 teaspoons of blood (14-17mL) will be drawn for testing and storage.
- If you/your child experiences a severe liver reaction or inflammation while on the study, you/your child may be asked to come back to clinic to have less than one teaspoon of blood (2mL) drawn to check the level of dolutegravir in the blood. Additional testing as part of routine assessments for liver inflammation (e.g. checking for viruses that cause liver inflammation) may be performed as well.

#### *Long Term Follow-Up*

After you have been on study drug for approximately 48 weeks, you will enter the long term follow-up phase of the study. You will be asked to come back into clinic every 12 weeks (every 3 months) for 3 more years. Most visits will last about 30 minutes.

- At some visits, a medical history will be taken and you/your child will have a physical exam. You will also be asked if you have missed taking any of your medications.
- We will draw less than 1 teaspoon of blood (3-4mL) at some visits. You will be informed of results of routine blood tests.
- As before, if the amount of HIV virus in your/your child's blood increases too much while on this study drug, you/your child may be asked to come back to clinic to have your blood drawn to confirm the level of HIV in your blood (see above).

You/your child must continue to take your/his/her anti-HIV medications during the study as prescribed by your/your child's HIV care provider. If your/your child's HIV care provider changes your/your child's anti-HIV medications during the study, you/your child can still take the study drug. You/your child will be asked questions about taking your/his/her anti-HIV medications and the schedule you take/he/she takes them on and if you have/he/she has missed any medications.

If you/your child can become pregnant, we will collect urine or blood to test for pregnancy at each visit. We will also ask your child about contraception use. If you think you/if your child thinks she may be pregnant at any time during the study, tell the study staff right away.

#### *Blood and Urine Samples*

Some of your / your child's blood and urine samples will be shipped out of the country to the US for specialized tests. These tests will tell the doctors how much study drug is in your / your child's blood and if the study drug is causing any changes in your kidneys.

*[For Participants Receiving Granules for suspension only]*

*[If your child is receiving the (granule) liquid he/she will need to switch to the dissolvable tablet. The study staff will inform you when your child will need to switch. This is because the company will not be making the liquid form of dolutegravir any longer. The study staff will provide instructions on how to dispense the dissolvable tablet and on the day you are scheduled to come to the clinic to begin taking the dissolvable tablets you will be asked to not give the (granule)liquid dose to your child. The first dose of the dissolvable tablet will be given in the clinic. You will be asked to come back to the clinic about 2 weeks later and will have a palatability assessment and blood drawn to confirm the level of HIV in your child's blood. If you have been on the study for more than 24 weeks at each of these visits, blood samples will be drawn at two separate times. The amount of blood drawn will be less than 1 teaspoon (0.5-1mL) depending on your /your child's age.]*

#### WHAT DO I / DOES MY CHILD HAVE TO DO IF I AM / HE / SHE BECOMES INFECTED WITH TUBERCULOSIS WHILE ON THIS STUDY?

If you become/your child becomes exposed to Tuberculosis (TB) while on study and requires anti-TB treatment that includes Rifampin you/your child will have to increase the dose of dolutegravir from once a day to twice a day while taking Rifampin. After you/your child complete(s) treatment with Rifampin, you/your child may go back to taking the dolutegravir once a day, depending on what other medications you/your child is taking.

You/your child will also be required to return for at least five additional follow-up visits after starting Rifampin.

- At each of these visits, a medical history will be taken and you/your child will have a physical exam and we will draw approximately 1-3 teaspoons of blood to look at the following:
  - The amount of HIV, cholesterol and triglycerides (types of fat) in your blood
  - How well your immune system, liver and kidneys are working, as well as other routine tests
- At each visit you will be asked whether you are taking your medication as instructed.
- You/your child will be asked to come to the clinic to have blood drawn 8 times over 12 hours during one visit, approximately 5-10 days after you/ your child started taking anti-TB medication. For this visit, you/your child will be asked to fast for 6 hours before your daily dose of study medication.
- The study staff will give you more instructions about this. Depending on your/your child's age, up to 13mL (a little more than 4 teaspoons) of blood will be drawn at this visit.
- You will have extra blood draws at two visits. At weeks 4 and 12, you will have two blood draws – blood will be drawn once before you take dolutegravir and about 12 hours later. The amount of blood drawn at the different study visits will be less than 1 teaspoon (1mL).

#### OTHER INFORMATION

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

#### HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

About 300 children and adolescents will take part in this study

#### HOW LONG WILL I/MY CHILD BE IN THIS STUDY?

By signing this consent form, you are agreeing to / allow your child to participate in Stage II of the study. You/your child will stay in the study for at least 48 weeks. After that time After that time you/your child will enter the long-term safety follow-up phase of the study. During this time, you / your child will continue to take study-provided dolutegravir and will be asked to come to clinic every 12 weeks for three more years.

## WHY WOULD THE DOCTOR TAKE ME / MY CHILD OFF THE STUDY DRUG / THIS STUDY EARLY?

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

- Continuing the study drug may be harmful to you / your child
- You become / your child becomes pregnant while on study

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

- You are/ your child is not able to attend the study visits as required by the study
- You need / your child needs a treatment that you / your child may not take while on the study
- You are / your child is not able to take the study drug as required by the study
- If you elect not to attend repeat PK evaluations as part of the study

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

- The study is cancelled by the U.S. Food and Drug Administration (FDA), National Institutes of Health (NIH), the Office of Human Research Protections (OHRP), other country specific governmental agencies, IMPAACT, the drug company supporting this study (GSK), or the site's Institutional Review Board (IRB) or Ethics Committee (EC). An IRB or EC is a committee that watches over the safety and rights of research participants

If your doctor wants you / your child to stop taking the study drug, you/your child will be asked to return to the clinic once more, four weeks after your last dose of dolutegravir, to make sure you are/your child is continuing to do well. This visit will include a history and physical exam, a blood draw and a review of your medical records.

## IF MY CHILD HAS TO PERMANENTLY STOP TAKING STUDY-PROVIDED MEDICINE, OR ONCE I LEAVE THE STUDY, HOW WOULD THE STUDY MEDICINE BE PROVIDED?

### During the study:

If you / your child must permanently stop taking study-provided dolutegravir before your/your child's study participation is over, the study staff will discuss other options that may be of benefit to you/your child.

### After the study:

Once you / your child leaves the study, if you/they are gaining benefit from the study-provided drug, this drug may continue to be provided until it is available to you in your country, but there is no guarantee. Study clinicians will work to ensure that you/your child continue to receive appropriate care and treatment outside of the study.

## WHAT ARE THE RISKS OF THE STUDY?

The drug 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 this drug. These lists include the more serious or common side effects with a known or possible relationship. It is very important that you tell your study doctor of any changes in your/your child's medical condition while taking part in the study. At any time during the study, if you believe you are/your child is experiencing any of these side effects, you have the right to ask questions on possible and /or known risks.

### Possible Risks Associated with Dolutegravir

DTG has been administered to a total of 6004 participants (4814 HIV-infected and 1190 healthy) cumulative to 16 July 2017 in ongoing and completed ViiV sponsored and clinical trials ranging from Phase I to IIIb and the DTG compassionate use program.

The following side effects have been seen with dolutegravir:

<p><b>Very Common (expected in about 100 of every 1000 people taking DTG (10%))</b></p> <p>Nausea or feeling sick (mild to moderate) Headache (mild to moderate) Diarrhea or loose stools</p>
<p><b>Common (expected in about 10 of every 1000 people taking DTG (1%))</b></p> <p>Cold symptoms like runny nose and sore throat; cough; flu Dizziness or feeling light headed Trouble sleeping; abnormal dreams Rash Feeling tired High temperature Pain in the stomach; vomiting Changes in kidney, liver and muscle blood tests Ocular icterus (yellowing of the whites of the eyes) Itching (pruritus) Feelings of deep sadness and unworthiness (depression) Flatulence (gas or wind) Increase in the level of liver enzymes Increase in the level of enzymes produced in the muscles (creatinine phosphokinase) Anxiety (fear, worry)</p>
<p><b>Uncommon (expected in about 1 of every 1000 people taking DTG (0.1%))</b></p> <p>Allergic reaction (see below) Liver toxicity (see below) An inflammatory condition which may develop as the immune system becomes stronger (immune reconstitution syndrome or 'IRIS' (see below) Suicidal thoughts and behaviors (mainly in patients who have had depression or mental health problems before) (see below)</p>

Most of the side effects listed above have been mild or moderate, and have not generally stopped HIV-infected patients treated with dolutegravir from getting on with their lives as normal.

In one animal study, gastric erosion (irritation of the stomach lining) was seen. This finding has not been seen in adults in studies to date. However, if you or your child feels heartburn or stomach pain or has vomiting, please contact your/your child's study doctor.

Other side effects that may show up in blood or urine tests:

- An increase in bilirubin (a pigment from the breakdown of red blood cells) in the blood.
- An increase in the level of creatinine, a waste product in the blood that gets filtered by the kidney

Dolutegravir Hypersensitivity Reaction

Hypersensitivity reactions have also been reported with integrase inhibitors, including dolutegravir, with signs and symptoms including general feeling of being sick, skin rash, a high temperature (fever), lack of energy (fatigue), swelling sometimes of the face or mouth (angioedema) causing difficulty in breathing, blisters or peeling skin, mouth ulcers, conjunctivitis (sore eyes), and muscle or joint aches. If you/your child develop(s) any of these signs and symptoms during the study, contact you/your child's study doctor immediately, who may decide to carry out tests on your/your child's liver, kidneys or blood.

### Mental illness

Some people with HIV infection occasionally have feelings of depression or may have thoughts of hurting or killing themselves (committing suicide). A small number of people being treated with integrase inhibitors for HIV infection, including dolutegravir, have had suicidal thoughts and behaviors, particularly patients with a prior history of depression or mental health illness. People with HIV and taking integrase inhibitors including dolutegravir have also reported depression.

Tell the study doctor if you/your child have a history of mental illness. If you/your child have thoughts of hurting or killing yourself or have any other unusual or distressing thoughts or feelings at any time during the study, you/your child should tell the study staff or go to the nearest hospital immediately.

### Use of Combination Antiretroviral Drugs

Immune Reconstitution Syndrome: In some people with advanced HIV infection, symptoms from other infections or certain diseases may occur soon after starting combination anti-HIV treatment but can also occur later. Some of these symptoms may be life threatening. If you start having new symptoms, or notice that existing symptoms are getting worse after starting your antiretroviral therapy, tell your healthcare provider right away.

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

Some patients taking combination anti-HIV therapy may develop a bone disease called osteonecrosis (death of bone tissue caused by loss of blood supply to the bone). The length of combination anti-HIV therapy, corticosteroid use, drinking alcohol, severe reduction in ability to fight off infection, higher body weight, among others, may be risk factors for developing this disease. Signs of osteonecrosis are joint stiffness, aches and pains (especially of the hip, knee and shoulder) and difficulty in movement. If you/your child notice any of these symptoms, please inform your doctor.

### Liver Toxicity

Liver toxicity in the form of abnormal liver enzymes, inflammation of the liver (hepatitis) and liver failure have occurred in HIV-infected patients receiving regimens containing dolutegravir. The liver toxicity usually occurs in the first few weeks or months of taking anti-HIV medications. These patients were also generally either taking other medications (both HIV treatment and non-HIV treatment) that are also known to cause significant liver inflammation and/or allergic reaction, or already had liver problems (such as hepatitis B or hepatitis C), or drank too much alcohol or had a combination of these. Cases of liver toxicity have also occurred in patients who do not have these risk factors.

If you/your child has an unanticipated need for hepatitis C virus (HCV) therapy during the conduct of the study, the study doctor will discuss specific HCV treatment options with you. In case you/your child experience liver toxicity, the study doctor can decide to stop the administration of the study drug in order to assure your/your child's safety.

### Other Risks

There is the risk of serious and/or life threatening side effects when non-study medications are taken with the study drug. For your/your child's safety, you must tell your/your child's HIV care provider and the study doctor or nurse about all medications you take/your child takes before the start of this study and also before starting any new medications while you are/your child is on the study. In addition, you must tell the study doctor or nurse before you enroll/enrolling your child in any other clinical trials while on this study.

The use of potent antiretroviral drug combinations may also be associated with altered fat metabolism including elevated triglycerides (fatty acid in the blood) and/or elevated cholesterol.

Other side effects besides those listed and side effects from taking these drugs together may occur. If any unusual symptoms or changes happen, you should call your/your child's doctor immediately. It is also important that while participating in the study, you do not/your child does not take any other prescription drugs or over-the-counter medications without first talking to your/your child's doctor or study nurse. With any drug for HIV, there is a risk that the virus in your body will become resistant, which means that the drug will be less effective or not effective against your HIV. The risk that taking part in this study will cause your HIV to develop resistance to the study drug is unknown and will depend on how well the study drug works against your virus and whether instructions are followed for taking the study drug.

### Blood Drawing and Heparin Lock Risks:

Blood drawing may cause some discomfort, bleeding or bruising where the needle enters the body. A small blood clot may form at the site where the needle enters the body or there may be swelling in the area. There is a small risk of a minor infection at the blood draw site. Lightheadedness and fainting can also occur.

### ARE THERE RISKS RELATED TO PREGNANCY?

It is not known if the drug or drug combinations in this study harm fetuses. Tests in pregnant animals do not show risk. Early results from a large study in Botswana of pregnant women showed a possible increased risk of certain types of serious birth defects involving the brain, and spinal cord in babies born to women who received dolutegravir for HIV treatment at the time of becoming pregnant. No cases of babies born with these types of birth defects have been reported among women who started dolutegravir later in pregnancy.

If you are/your child is having sex that could lead to pregnancy, you/your child must agree not to become pregnant or make a female pregnant.

Because of the risk involved, you and your partner, or your child and their partner, must use two methods of birth control that you discuss with the study staff. You must continue to use both methods until two weeks after stopping the study drug. Options for birth control methods include these listed below:

- Birth control drugs that prevent pregnancy given by pills, shots, placed on the skin (e.g. patch) or placed under the skin
- Male or female condoms with or without a cream or gel that kills sperm
- Diaphragm or cervical cap with a cream or gel that kills sperm

- Intrauterine device (IUD)

Some of these are better than others in preventing pregnancy. You/your child will work with study staff to pick the options best for you. All birth control methods listed above except condoms do not reduce the risk of giving HIV to someone else. HIV-infected individuals should use a birth control method that includes condoms to keep from giving HIV to someone else.

If you think you/your child may be pregnant at any time during the study, tell the study staff right away. The study staff will talk to you about your/your child's choices. You/your child will be tested at each visit during the study if it is possible that you/she may be pregnant. If you are /your child becomes pregnant while on study, you/she will not be allowed to continue on the study drug but will be asked to remain on study and come in for study visits as planned in case of safety concerns and so that the doctors can follow your/her pregnancy.

#### ARE THERE BENEFITS TO TAKING PART IN THIS STUDY?

If you / your child take(s) part in this study, the amount of HIV in your / your child's body may go down and your/your child's immune system may become stronger, but no guarantee can be made. You/your child may receive no benefit from being in this study. Information learned from this study may help others who have HIV.

#### WHAT OTHER CHOICES DO I/DOES MY CHILD HAVE BESIDES THIS STUDY?

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

- Treatment with prescription drugs available to you/your child
- Treatment with other experimental drugs, if you/your child qualify(ies)
- No treatment (NOT Recommended)

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

#### WHAT ABOUT CONFIDENTIALITY?

*(For U.S. sites only)*

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below. The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

People who may review your/your child's records include the U.S. Food and Drug Administration and other U.S., local, and international regulatory entities, the Office of Human Research Protections (OHRP), the site IRB /EC (insert name of site IRB/EC), the National Institutes of Health, study staff, study monitors, drug companies supporting the study, and their designees.

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about you or your participation in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate of Confidentiality to withhold that information.

*(For sites outside the U.S.)*

Efforts will be made to keep your personal information confidential. We cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law. Any publication of this study will not use your name of identify you personally.

Your records may be reviewed by the Ministry of Public Health in your country, the FDA and other US, local, and international regulatory entities, the Office of Human Research Protections (OHRP), the NIH, (insert name of site) IRB/EC, study staff, study monitors and the drug companies supporting this study.

#### WHAT ARE THE COSTS TO ME / MY CHILD?

There are no costs to you/your child for the study drug, study visits or study procedures. However, taking part in this study may lead to added costs to you and your insurance company if medical complications arise or if your doctor decides extra tests are needed. In some cases it is possible that your insurance company will not pay for these costs because you/ your child are taking part in a research study.

#### WILL I RECEIVE ANY PAYMENT?

You will receive \$XX for each study visit you attend. If you attend all study visits, you may receive up to \$XX.

#### WHAT HAPPENS IF I AM / MY CHILD IS INJURED?

If you are / your child is injured as a result of being in this study, you / your child will be given immediate treatment for your/his/her injuries. The cost for this treatment will 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/your child's legal rights by signing this consent form.

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

Taking part in this study is completely voluntary. You may choose not to take part/not to allow your child to take part in this study or leave this study/take your child out of the study at any time. Your decision will not have any impact on your participation in other studies conducted by the NIH and will not result in any penalty or loss of benefits to which you are otherwise entitled. We will tell you about new information from this or other studies that may affect your health, welfare or willingness to stay in this study. If you want the results of the study, let the study staff know.

*(For legal guardians, as applicable)*

If your child reaches the legal age of consent during the study [he/she] will be asked to provide independent consent at their next visit.

#### 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 Legal Guardian (print)  
(As appropriate)

\_\_\_\_\_  
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

\_\_\_\_\_  
Second Guardian (print)  
(If required)

\_\_\_\_\_  
Second Guardian's Signature and Date

**Appendix IV**  
**Sample Informed Consent Form for Specimen Storage and Future Use**

**DIVISION OF AIDS**  
**INTERNATIONAL MATERNAL PEDIATRIC ADOLESCENT AIDS CLINICAL TRIALS**  
**GROUP (IMPAACT)**

Phase I/II, Multi-Center, Open-Label Pharmacokinetic, Safety, Tolerability and  
Antiviral Activity of dolutegravir, a Novel Integrase Inhibitor, in Combination Regimens in HIV-1  
Infected Infants, Children and Adolescents

P1093 Version 5.0, dated 12 July 2018

You have decided to allow your child to join the study named above/You are participating in the study named above. As part of the study, you/your child will have blood drawn and urine collected. After these samples are tested for the study, there may be some samples that are left over. We call these extra samples. The IMPAACT Network would like to keep these extra samples and use them for other research in the future.

This form gives information about use of extra samples. Please read it, or have it read to you, and ask any questions you may have. After we discuss the information with you, you will record your decisions on use of extra samples at the end of the form.

*(For legal guardians, as applicable)*

*If your child reaches the legal age of consent during the study [he/she] will be asked to provide independent consent at their next visit.*

**1. It is your decision whether or not to allow the extra samples to be used.**

You are free to say yes or no, or to change your mind at any time. Your decision will not affect your/your child's participation in the study. If you say no, all extra samples will be destroyed.

**2. If you agree, your child's extra samples will be kept in a repository.**

A repository is a secure facility that is used to store samples. The IMPAACT Network repository is in the United States. There is no limit on how long the samples will be kept *[sites may insert time limits or additional site-specific requirements here if required by local authorities]*.

**3. Extra samples could be used for different types of research.**

Extra samples may be used for research on HIV, the immune system, and other diseases. The research may be done in the United States or in other locations.

If you agree, the extra samples could also be used for research that looks at your/your child's genes.

Any research done with the extra samples must be reviewed and approved by the IMPAACT Network. The research must also be approved by an ethics committee. The role of an ethics committee is to review the research plan and protect the rights and well-being of the persons whose samples will be used.

**4. There is little risk to you/your child.**

When extra samples are used for research, they are labeled with a code number only. To protect your child's privacy, no names are used. However, information such as age, gender, HIV status, and other health information may be linked to the samples. Information on which study ARVs you/your child received and you/your child's immune system responses to the ARVs may also be linked to the samples.

There may be some risks from tests of you/your child's genes. If others found out the results of these tests, they could treat you badly or unfairly. However, this is almost impossible because the results of these tests will not be in you/your child's study records and they will not be given to you.

**5. There may be no benefit to you/your child.**

The research done with extra samples is not expected to give any information relevant to your child's health. The results will not be given to you and will not be part of your study records.

**6. You will not be paid for use of your/your child's samples.**

There is no cost to you for use of your child's extra samples. The samples will not be sold and you will not be paid for use of the samples. It is possible that research done with the samples could lead to a new discovery or a new product. If this happens, there is no plan to share any money with you or your child.

**7. Information from research using extra samples may be reviewed by groups that oversee the research.**

These groups include:

- The IMPAACT Network
- The ethics committees that review and approve the research
- Government and other agencies that pay for the research
- Government and other agencies that monitor the research
- Other local, US, and international regulatory entities

The people who do research with the extra samples and the groups listed above are required to make efforts to information private and confidential.

The results of research done with extra samples may be presented publicly or published. However, no presentation or publication will use your/your child's name or identify your child personally.

**8. If you have any questions, concerns, or problems related to your/your child's extra samples, use these contacts.**

- If you have questions about use of your/your child's extra samples, contact:  
*[sites insert name and telephone number of investigator or other study staff]*.
- If you later change your mind about use of your/your child's extra samples, contact:  
*[sites insert name and telephone number of investigator or other study staff]*.
- If you have questions about your/your child's rights as a research participant, or problems or concerns about how your child is being treated in the study, contact:

*[sites insert name and telephone number of IRB contact person or other appropriate person/organization].*

**9. Signatures**

**If you agree to let your/your child's extra samples be used, please sign or make your mark below.**

\_\_\_\_\_ I allow my/my child's extra samples to be used for research on HIV, the immune system, and other diseases. I also allow my child's samples to be used for tests of his or her genes.

\_\_\_\_\_ I allow my/my child's extra samples to be used for research on HIV, the immune system, and other diseases. I do not allow my child's samples to be used for tests of his or her genes.

\_\_\_\_\_ I do not allow my/my child's extra samples to be used for any research.

\_\_\_\_\_  
Participant's Name (print)

\_\_\_\_\_  
Parent's Name (print)  
(Or Legal Guardian)

\_\_\_\_\_  
Parent's Signature

\_\_\_\_\_  
Date

\_\_\_\_\_  
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