

TEMPLATE*

CONSENT TO BE A RESEARCH SUBJECT

Solid Organ Transplantation in HIV:
Multi-Site Study
HIVTR Version 7.0
July, 2009
[Kidney, Liver]



*Note: The Kidney and Liver consents have been combined in this template.
Sites should create separate consents for each organ.
Sections of the consent that are organ or site specific have been marked in
[bold, brackets] and should be modified accordingly .

Consent to be a Research Subject

Solid Organ Transplantation in HIV: Multi-Site Study

[Kidney, Liver]

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CONSENT TO BE A RESEARCH SUBJECT

Solid Organ Transplantation in HIV: Multi-Site Study

[Kidney, Liver]

BACKGROUND/PURPOSE

A research study is being conducted to look at the safety of **[kidney, liver]** transplants and how well they work in persons living with HIV infection. The main questions being studied include 1) do post-transplant medications (immunosuppressants) that are used to prevent the body from rejecting the new **[kidney, liver]** make HIV infection worse, 2) does HIV infection make the transplanted **[kidney, liver]** not work as well, and 3) how do the drugs used to treat HIV infection (antiretrovirals) and immunosuppressant medications interact with each other in the body.

People with HIV infection are at risk for **[kidney, liver]** disease for the same reasons that people without HIV infection are at risk, and also because of HIV-related **[kidney, liver]** disease. Due to improvements in the treatment of HIV, HIV-infected patients may now be better candidates for a transplant. Up until recently, people with HIV infection have often not been offered a transplant because of concerns that the drugs (immunosuppressants) required for organ transplantation might worsen the patient's HIV infection. This concern is a major focus of this study.

Approximately **[150 kidney, 125 liver]** patients will be enrolled in this study over several years at medical research centers throughout the United States. Total study participation will be five years from the day you/your child receives a transplant.

You/your child is being asked to participate in this research study because you/your child is HIV-positive and has end-stage **[kidney, liver]** disease. If you/your child agree to participate and sign this consent form, the following will occur:

PRE-TRANSPLANT PROCEDURES

A. Pre-transplant Screening Procedures

Tests will be done to see if you/your child can be in this study. These are called “screening” tests. Some of these tests will be done by your/your child’s primary medical care provider (the person that sees you/your child for regular visits and checkups). All test results that may affect your/your child’s health or treatment will be discussed with the primary medical care provider. You/your child may also receive these results from the study coordinator if you would like them.

1. Medical History Review, Physical Examination and Blood Tests

The study doctors will review all of your/your child’s medical history, all the medications you/your child is taking, and how you/your child is feeling physically. You/your child will have a complete physical examination and a chest x-ray. About 3 tablespoons of blood **[and a sputum sample (include if cluster 1 or 2)]** will be drawn to look at you/your child’s overall health and how well you/your child’s immune system (the body’s natural defense against illness) is working. The blood tests will also look for any current or past infections. A sample of urine will be tested to determine how well the kidneys work.

2. TB and Vaccination Screening

You/your child will be asked to have a skin test for tuberculosis (TB, and infection of the lungs and other organs) called a PPD test. For this test, a small injection is placed just under the skin of the arm. If you/your child tests positive, or have tested positive in the past and has never been treated for TB, you/your child will begin a 9-month course of medications before being eligible to receive a transplant. If you/your child has ever had a positive skin test for TB, you/your child will have chest x-rays instead of a skin test.

Your/your child’s study doctor will review what vaccinations you/your child has had in the past. Your/your child’s study doctor will let you know if you need to get additional or new vaccinations. Certain vaccines will only be given if you/your child’s T-cells (cells that help fight infection) are above a certain number.

3. Cervical PAP Smears

Females who are sexually active will have a PAP smear (a test that looks for changes in cells of the cervix) performed by your/your child’s primary medical care provider. For this procedure, you/your child will have a pelvic examination and an instrument called a speculum will be used to

examine your/your child's cervix. A small plastic brush and a wooden spatula will be used to collect cells for examination.

If the test results are abnormal, you/your child's primary medical care provider and the study doctors will discuss the results so that arrangements for appropriate follow-up can be made. If treatment is required, referrals will be made outside of the study.

4. Pregnancy, Pregnancy Testing, and Birth Control

It is not known what effect most immunosuppressive medications have on pregnancy or unborn babies. It is known, however, that the use of MMF (a type of immunosuppressive medication) during pregnancy can cause increased rates of pregnancy loss and birth defects. Therefore, if you/your child is participating in sexual activity that could lead to pregnancy, you/your child must use two reliable methods of birth control simultaneously, be surgically sterile (from a hysterectomy or tubal ligation), have a partner who is sterile, or be post-menopausal for the entire duration of the study. Women taking MMF should begin using the two forms of contraception four weeks prior to starting treatment and continue use for six weeks after the last treatment dose of MMF. Since you/your child has HIV, a condom may be the best option since it will prevent HIV transmission, not just pregnancy, and no other form of birth control adds this benefit. Because of the possible interaction between some of the medications you/your child might be taking and birth control pills, birth control pills alone should not be used as a means of birth control while participating in this study.

In addition, if you/your child is a female who can have children, you/your child must have a negative pregnancy test prior to enrollment in the study and immediately prior to the transplant procedure. If you/your child become pregnant during the study you should notify the study doctor immediately. The outcome of any pregnancy test will be recorded.

Because the immunosuppressive medications may enter the breast milk, you/your child will not be allowed to participate in this study if breast-feeding.

5. Hepatitis Infection

[KIDNEY]: If you/your child has hepatitis C (a liver infection), you/your child will be asked to have their liver specialist (hepatologist) perform a liver biopsy if you/your child has not already had one. If you/your child has a bleeding disorder (bleeds easily, can not form blood clots quickly), a blood problem specialist (hematologist) will be involved in your/your child's clinical care. If you/your child does not have a hepatologist, your/your primary medical care provider will refer you/your child to one.

For the biopsy, the biopsy site will be cleaned and a numbing medicine will be injected into the area where the biopsy will be done. Usually a small cut (less than ¼ inch in size) is made in the skin. A small needle is inserted just under the skin and a small piece of the liver is removed. You/your child will be asked not to breath and to remain completely still during this procedure. Medications may be given to help you/your child relax. You/your child will be asked to sign a separate consent form for this procedure.

If the liver biopsy shows cirrhosis (advanced and serious damage to the liver), you/your child will not be eligible to receive a kidney transplant without receiving a liver transplant unless your/your child's doctors feel that a liver transplant is not medically appropriate at this time.

If the biopsy results are abnormal and show damage to the liver but not cirrhosis, hepatitis C treatment may be necessary. Your/your child's doctors will discuss various treatment options with you/your child.

Before treatment options are discussed, 2 teaspoons of blood will be collected for blood tests to look at what type of hepatitis C you/your child has and how much virus is in the blood. You/your child will also have a CT scan (a type of x-ray) of the liver. Medications may be given to help you/your child relax during this procedure.

[LIVER]: If you/your child has either Hepatitis B or C infection, pre-transplant treatment recommendations will be made by the study liver specialist about treatment.

6. Neurologic (Brain Function) Testing and Possible MRI Testing with Possible Spinal Tap

If you/your child's doctor feels it is necessary, you/your child will have a MRI (Magnetic Resonance Imaging study) of the head. For this procedure, you/your child will lie down on a narrow bed, which will then be placed in a tunnel that is open at each end. This test takes about one hour. Medications may be given to help you/your child relax during this procedure..

Based on the MRI results, it may be necessary to obtain a sample of your/your child's cerebrospinal fluid (the fluid surrounding your/your child's brain and spine). For this procedure, you/your child will be asked to curl up sideways on a table with the knees drawn up to the chest. A numbing medicine will be applied to the site where the fluid is to be withdrawn. A thin needle is inserted between two bones in the lower back. Once the

needle is in place, no more than 2 teaspoonfuls of fluid are withdrawn. The procedure usually takes about 30 minutes.

7. Quality of Life Testing

You/your child will be asked to complete a quality of life questionnaire in clinic before the transplant and then again at 1, 2, and 5 years after the transplant. This questionnaire is designed to look at your/your child's overall quality of life and the impact disease has had on your/your child's physical, mental and social functioning on a day-to-day basis. The questionnaire should take approximately 20-30 minutes to complete.

B. Organ Waiting List

If the results of all of the screening procedures determine that you/your child is eligible to participate in the study, and if you/your child agrees to continue participation, you/your child will be put on a waiting list that is kept by a national organization that distributes organs. Waiting for a **[kidney, liver]** could take months to years. Participation in this study does not guarantee that an organ will become available, nor does it increase your/your child's chances of receiving one.

C. Donor Consent for Living Donation

If you/your child has a potential donor(s) who decides to be evaluated for the ability to donate, he or she will be notified of your/your child's participation in a research study and will be asked to review and sign an informed consent document. This informed consent document will explain that you/your child has HIV infection and that we don't know how well people with HIV infection who undergo transplant do. The potential donor will be informed of the study and asked to sign the consent form when they are first evaluated if you agree. It is possible to delay telling the potential donor until initial test results confirm that the person may be an appropriate donor, but before any invasive tests are performed (tests that can have more than a very small risk).

D. Pre-Transplant Ongoing Eligibility Tests

While you/your child is waiting for an available **[kidney, liver]**, about ½ tablespoon of blood will be drawn every three months for T cell counts and viral load measurements. You/your child must have a primary medical care provider who has experience in the care of patients with HIV infection. Your/your child's primary medical care provider will perform these tests and fax the results to the research staff. Continued eligibility will be determined based on the most recent T-cell count and viral load test results. We will request these results from your /your child's primary medical provider every 12 weeks. They must be done not more than 16 weeks before the transplant for you/your child to be eligible for the study.

POST-TRANSPLANT PROCEDURES

A. Post-Transplant Hospitalization

Post- transplant hospitalization may last several days to weeks. During hospitalization for the transplant, you/your child will be seen daily for a review of medications and any symptoms you/your child may be having. A physical examination will be performed as indicated based on symptoms or abnormal tests.

B. Post-Transplant Study Clinic Visits

Because you/your child is HIV+ and participating in this study, there will be more study visits than would be required for someone without HIV who is getting a transplant. After hospitalization, you/your child will have at least 13 clinic visits in the first year. You/your child will be seen every 3 months in Years 2 and 3 and every 6 months in Years 4 and 5. Some of these visits may occur at your/your child's local doctor's office. However, visits at week 12, 26, 52, and year 2 must occur at **[NAME OF TRANSPLANT CENTER]**. Most visits will include a brief physical examination, a review of symptoms and medications, and collection of blood for laboratory tests.. A repeat TB skin test will be done annually at your/your child's primary medical care provider's office. The quality of Life Questionnaire that you/your child completed before the transplant will be repeated at years 1, 2 and 5 after the transplant. Women will have a repeat cervical Pap smear every 6 months. All test results that may affect your/your child's health or treatment will be discussed with the primary medical care provider. You/your child may also receive these results from the study coordinator if you would like them.

C. Medications

You/your child will be treated with immunosuppressive medications which may include cyclosporine, tacrolimus or sirolimus, mycophenolate mofetil (MMF) and prednisone. Other medications may be given if the **[kidney, liver]** is rejected (not accepted by the body)

Antiretroviral therapy will consist of combinations of approved drugs for the treatment of HIV and will be guided by the study doctors in consultation with you/your child's primary medical care provider.

Because test-tube studies have shown negative interactions between MMF and AZT (retrovir) or d4T (zerit), you/your child's primary medical care provider will be advised to try not to use AZT and d4T as part of antiretroviral therapy.

You/your child will also need to take many medications to prevent infections that are common in people who have had a transplant. If your/your child's T-cells decrease, you/your child will also need to take medications to prevent other infections that are common in people with AIDS and low T-cell counts. Study staff will discuss all other medications with you/your child and explain why they are necessary.

For safety reasons, you/your child should keep research staff informed about any medications (over-the-counter or prescription) you/your child is taking or intends to take while enrolled in this study. Additional tests and evaluations will be performed as clinically necessary to monitor your/your child's condition.

D. Hepatitis Monitoring

[KIDNEY]: If you/your child tests positive for the hepatitis C virus, you/your child's hepatitis C viral load will be followed with blood tests. A repeat liver biopsy will be done at 6 months, 2 ½ and 5 years after transplant and as needed.

[LIVER]: If you/your child tests positive for the hepatitis B and/or C viruses, your/your child's hepatitis B and/or C viral load will be followed with blood tests. A liver biopsy will be done at 6 and 12 months, then yearly after the transplant, or at other times as determined by the doctors. For the biopsy, the biopsy site will be cleaned and a numbing medicine will be injected into the area where the biopsy will be done. Usually a small cut (less than ¼ inch in size) is made in the skin. A small needle is inserted just under the skin and a small piece of the liver is removed. You/your child will be asked not to breath and to remain completely still during this procedure. Medications may be given to help you/your child relax. You/your child will be asked to sign a separate consent form for this procedure.

E. Specimens for Research Studies and Storage of Specimens

About one cup of the blood drawn **[and a sputum sample (include if cluster 1 or 2)]** will be collected at specified study visits. In addition biopsy slides will be collected from any scheduled or unscheduled biopsy performed throughout the duration of the study, **[UCSF and Mt. Sinai KIDNEY: as well as kidney biopsy tissue from any kidney rejection episodes,]** and will be shipped to laboratories participating in this study for research tests, or will be frozen and stored for future research studies. Samples will be stored with a coded number at a central storage bank or at participating laboratories. Only the study doctors will know who the samples belongs to. Unused samples will be discarded after 5 years unless additional funding is available to continue storing them.

It is possible that some of these samples will be used for tests that are not directly related to this study. These tests may not be done for several months to years, and it is possible these studies may never be performed. You/your child may be provided with information from the future tests that may be important to your/your child's clinical care if the testing is validated and considered standard of care. You/your child can refuse to have blood stored and still participate in the

study. You/your child may agree or refuse to have blood samples stored by checking a box at the end of this consent form.

F. Genetic Testing

You/your child will be asked to have genetic testing performed on stored blood **[UCSF and Mt. Sinai KIDNEY: or biopsy tissue]**. In these studies, you/your child's blood **[UCSF and Mt. Sinai KIDNEY: or biopsy tissue]** will be looked at for certain types of genes responsible for influencing how the body reacts to HIV, infections that can occur in HIV-infected persons, and certain medications. If samples are selected for genetic testing, they will not contain any personal identifiers such as your/your child's name or ID number. Genetic testing is an optional part of this study. You/your child may refuse genetic testing, which will not affect you/your child's participation in this study. If you/your child agree to participate in this part of the study, you/your child will have the option of discontinuing from the genetic blood testing at any time by telling research staff.

G. Total Blood

For adults, older children, and adolescents, approximately **[TBD]** pints of blood will be collected in Year 1; a little more than **[TBD]** cup will be collected in Year 2; less than **[TBD]** cup will be collected in Years 3 and 4; and about **[TBD]** will be collected in year 5. For pediatrics, the total amount of blood collected will depend on your/your child's weight, with less blood drawn from smaller children. **[Depends on options, and cluster and will be provided to each site by administrative core staff]**

H. Early Study Discontinuation

You/your child may be removed from the study without you/your child's consent for the following reasons:

- You/your child is a female who becomes pregnant or who is breast-feeding a young child and has not yet received a transplant;
- You/your child are no longer eligible to participate;
- The study doctors decide that continuing in the study would be harmful to you/your child;
- You/your child is unable to keep appointments or follow study instructions;
- The study is cancelled.

The study staff may contact you after study discontinuation to find out about any serious medical problems you/your child has developed, for as long as you are willing to be contacted.

If you/your child wish to withdraw from the study before the transplant, no additional follow-up will be necessary. If you/your child withdraws after receiving a transplant, you/your child will continue to be followed every 6 months for 5

years after the transplant if you are willing. The follow-up will involve questions about your/your child's health, T-cell count and viral load.

I. Other Research Studies

[Note to sites: If applicable to your center. See appendix A for appropriate text to include in your version of the consent.]

RISKS AND DISCOMFORTS

A. Waiting Period

Because you/your child may have a long wait for a **[kidney, liver]**, you/your child may no longer meet the eligibility requirements for a transplant within this study once an organ becomes available.

B. Donor Consent

You/your child may not want to tell you/your child's potential donor(s) about the HIV infection and you/your child may feel that there is some personal risk to telling them. Potential donor(s) may decide not to donate when they are told of your/your child's participation in research and/or you/your child's HIV infection. You/your child can choose not to tell your/your child's potential donor about the HIV infection, but the potential donor will not be evaluated for donation.

C. Transplant Procedure

[Kidney, Liver] transplantation in an HIV-infected individual is investigational. There may be risks that are currently unknown. All the risks associated with the operation and immunosuppression which are not specific to people with HIV will be explained to you/your child separately. You/your child will be asked to sign a non-study surgical consent prior to the transplant that explains these risks.

D. Inadvertent Disclosure of HIV Status

During the course of care in the clinic or hospital, it is difficult to control the information that may be discussed by health care providers about specific diagnoses or medications. It is possible that someone who does not know you/your child's HIV status could find out about it in this setting.

E. Study Procedures

1. Collection of Blood

Collection of blood may cause slight discomfort, pain, bleeding or bruising at the injection site. Rarely, fainting or infection may occur.

2. Cervical PAP Smear

This procedure may be slightly uncomfortable from the position and the speculum. Slight bleeding may occur.

3. Liver Biopsy

In approximately 1 case in 1000, liver biopsy may result in significant bleeding and surgery may be required. The risk of death from a liver biopsy is approximately 1 case in 10,000. In rare cases, biopsy may result in damage to other tissues that are near the liver. In about 1 case in 50, temporary significant pain will occur after the biopsy procedure.

4. CT Scan

CT scans involve a small amount of radiation (like an X-ray) and are considered safe. You may experience discomfort from lying still or anxiety from being in an enclosed space. The dye used for the CT scan may cause an allergic reaction (difficulty breathing, swelling, hives, itching and rarely, sudden death). If you are pregnant, you cannot have a CT Scan because of possible risk from the radiation.

5. MRI

Because the MRI machine acts like a large magnet, it could move iron-containing objects in the MRI room during the examination, which could in the process harm you/your child. Loose metal objects, like pocket knives or key chains, are not allowed in the MRI room. If you/your child has a piece of metal in the body, such as a fragment in your/your child's eye, aneurysm clips, ear implants, spinal nerve stimulators, or a pacemaker, you/your child will not be allowed into the MRI room. You/your child may be bothered by feelings of claustrophobia (feeling scared of the small tunnel where the test is done) and by the loud banging noise during the procedure. Temporary hearing loss has been reported from this loud noise, which is why you/your child will wear earplugs. You/your child may experience a reaction to the dye used for this procedure, which could cause difficulty breathing, swelling, hives, itching, and sudden death.

The risks to a fetus from MRI are unknown.

6. Lumbar Puncture (Spinal Tap)

Lumbar puncture may cause local discomfort, pain, decreased blood pressure and rarely, infection at the site of injection. The most common complication is headache, caused by leaking of cerebral spinal fluid after the procedure. In some cases the headache may be severe and may last

several days to a week. Very rarely will the headache last for several weeks. If headache occurs you/your child will be offered pain medication.

7. Sub-Studies

[If applicable. See appendix A for appropriate text.]

8. Internet-Based Data Collection

Data from this study will be entered into a computerized database through a secured web site. All information will be saved and transmitted in a coded form. Only authorized personnel requiring a password will be permitted to enter data. There is risk, although minimal, of unauthorized persons obtaining confidential information.

F. Drug Risks

1. Transplant Immunosuppression Medications

Transplant immunosuppression medications may worsen your/your child's HIV infection, which could result in a more rapid progression to AIDS, increased opportunistic infections, and death. These drugs weaken the immune system, causing an increased chance of getting other infections and cancers. These drugs may also result in a more rapid progression of viruses that affect the liver, including hepatitis B and hepatitis C.

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 of 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, you may ask the medical staff.

a. Cyclosporine

In one study of patients with advanced HIV disease (AIDS) cyclosporine resulted in an increased risk of AIDS-related infections. Common side effects include headache, diarrhea, nausea, vomiting, hair growth, shaking and numbness, kidney problems, elevated blood sugar (diabetes), and high blood pressure. Cyclosporine is known to cause side effects in the unborn child and should not be taken by pregnant or breast-feeding women.

b. Tacrolimus

Common side effects include increased liver enzymes, headache, diarrhea, nausea and vomiting, shaking, difficulty falling asleep or staying asleep, and numbness. Uncommon but more serious side

effects may include seizures, diabetes, kidney problems, and high blood pressure.

c. Sirolimus

Common side effects include high blood pressure, rash, and increased liver enzymes (usually temporary and not harmful; very rarely, these increases can indicate irreversible liver damage), cholesterol, and triglycerides (fats in the blood). Less common side effects may include hepatic artery thrombosis (a blood clot in the liver), a decrease in platelets (blood cells involved in clotting), a decrease in white blood cells (cells that fight infection), headache, indigestion, nose bleed, infection, irritation of the mouth, and anemia (low red blood cell count).

d. Cyclosporine, Tacrolimus and Sirolimus in Combination with Antiretrovirals

It is not known how immunosuppressive medications will interact with treatments for HIV. Combination treatment may cause increased side effects. There is also the possibility that the combination of these drugs may increase or decrease the levels in blood of the antiretroviral medications. If the levels are decreased, this may cause incomplete suppression of the HIV virus, causing the antiretroviral medications to become ineffective and resulting in a worsening of my/my child's HIV disease.

e. Mycophenolate Mofetil (MMF)

Common side effects of MMF are diarrhea, nausea, vomiting, abdominal pain, constipation, loss of appetite, and indigestion. Anemia (a decrease in red blood cells), low platelet counts, and low white blood cell counts have also been observed. MMF use during pregnancy can cause increased rates of pregnancy loss and birth defects.

f. MMF in Combination with Antiretrovirals

Studies suggest MMF makes AZT and d4T less effective against HIV, and makes ddI (didanosine) and abacavir (ziagen) more effective. It does not seem to have any effect on 3TC (epivir). It is not known if these effects will be seen in people taking these drugs. There is the possibility that the combination of these drugs may increase or decrease the levels of the antiretroviral medications, which may cause incomplete suppression of the HIV virus, causing

my/my child's antiretroviral medications to become ineffective and resulting in a worsening of my/my child's HIV disease.

g. Prednisone

Side effects include headaches, dizziness, difficulty falling asleep or staying asleep, behavioral changes (including psychosis), depression, increased appetite, weight gain, ulcers, changes in fat and muscle pattern, thinning of the skin, acne, increased blood sugar (and even diabetes) as well as an increased risk of adrenal suppression (lowering the amount of hormones the body normally produces) and increased chance of getting viral, bacterial and fungal infections. Recent reports suggest that people who use prednisone may have an increased risk of developing osteopenia (thin bones) or decreased blood supply to the hip. Prednisone may also slow the growth and development of children.

2. Serious Infection and Cancer Risk

Immunosuppressive medications may increase the risk of developing serious infections and certain cancers. Some of these infections or cancers can become life-threatening and if treatment fails, may lead to death.

3. Prophylactic (preventive) and Other Medication Risks

Each of the preventive medications has side effects and risks that will be explained to you/your child before they are prescribed. In addition, there may be interactions between these medications and the immunosuppressive and/or antiretroviral medications. These interactions could result in levels of any of these drugs being either too high and causing increased side effects, or too low and resulting in the drugs not working to prevent rejection of the kidney or to control HIV.

4. Antibiotics

There is a risk of an allergic, or more serious, anaphylactic reaction to any of the antibiotics that may need to be administered to you/your child for infection. Anaphylaxis is a life-threatening emergency that can be reversed with the appropriate medical care, but it can also lead to death in some instances.

G. Reporting of Sexually Transmittable Diseases

Positive test results for syphilis, Hepatitis B and Hepatitis C will be reported to the local Department of Health, as required by law. **[Sites should add specific HIV reporting language pertaining to their state.]**

H. New Findings

There may be risks that are currently unknown. You/your child will be informed of any new findings during the study that may affect you/your child's decision to continue participating.

I. Confidentiality

Your medical and research records will be confidential to the extent permitted by law. Efforts will be made to keep your personal information private. However, we cannot guarantee complete confidentiality. You will be identified by a code, and personal information from your records will not be released without your written permission.

No individual identities will be used in any reports or publications resulting from this study. If you/your child agree for you/your child to participate, a regular medical record will be created for you/your child at the medical center.

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/your child, 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/your child, 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).

Understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your/your child's involvement 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 to withhold that information.

Medical and research records may be reviewed by the United States agency sponsoring the research (the National Institute of Allergy and Infectious Diseases), including its representatives, agents, employees, contractors, and other persons assisting in conducting, monitoring or analyzing the study. In addition, the U.S. Food and Drug Administration, or other health authorities may review your medical and research records for regulatory purposes.

[The sites should include language such as the following if they intend to make voluntary disclosure about things such as child abuse, intent to hurt self or others, or other voluntary disclosures.] The Certificate of Confidentiality does not prevent the researchers from disclosing voluntarily, without your consent, information that would identify you/your child as a participant in the research project under the following circumstances. [The sites should state here the conditions under which voluntary disclosure would be made. If no voluntary disclosures will be made, the researchers should so state.]

TREATMENT AND COMPENSATION FOR INJURY

If you/your child is injured as a result of being in this study, treatment will be available. The costs of such treatment may be covered by **[your institution]**, depending on a number of factors. Research related injury will not be covered by the study. **[The University does not normally provide any other form of compensation for injury. For further information, call the office of the Committee on Human Research at XX or write: Committee on Human Research at XX.]**

A. Benefits

You/your child may receive no direct benefit from participating in this study. However, you/your child will be contributing to the understanding of **[kidney, liver]** transplantation in HIV-infected individuals.

B. Alternatives

You/your child may choose not to participate. If you choose for you/your child not to participate in this study, a similar non-research protocol **[is/is not]** available for transplantation **[at xx site]**. You/your child may continue on the current or prescribed therapy without receiving a transplant. In addition, You/your child may choose at any time after transplantation to discontinue you/your child's participation in the study.

C. Costs

If you/your child has insurance, all clinic visits, inpatient hospitalization, routine laboratory monitoring, procedures and x-rays will be billed to you/your child's insurance. **[UCSF: If you/your child has no insurance or your/your child's insurance does not pay for one or more of these charges, the study will pay.]** Your/your child's insurance will not be billed for any research-related tests.

D. Payment

You/your child will not be paid for participation in this study.

QUESTIONS

This study has been explained to you/your child by [your investigators] and you/your child's questions have been answered. If you have any other questions about the study or if you/your child experiences a study-related injury, you can call **[your investigators at XX]**. If you/your child have any questions about your/your child's rights as a subject participating in a research study, you/your child may contact the office of the Committee on Human Research at **[XX]**.

CONSENT

You/your child has been given copies of the signed and dated consent form and the Experimental Subject's Bill of Rights to keep.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You/your child has the right to decline to participate or to withdraw at any point in the study without jeopardy to you/your child's medical care. To participate, you/your child should sign below.

Name of Patient (if age 13 or above)

Signature of Patient

Date

The person being considered for this study is a minor or is unable to consent for himself or herself. I have been asked to give permission as a parent or legally authorized representative to include my child or ward in this study.

Name of Parent or Legally authorized representative

Signature of Parent or Legally authorized representative

Date

Name of Parent or Legally authorized representative

Signature of Parent or Legally authorized representative

Date

Name of Person Obtaining Consent

Signature of Person Obtaining Consent

Date

I agree to have blood stored for possible future tests.

Yes

No

*Subject's or
Legally Authorized
Representative's
Initials*

I agree to have genetic testing.

Yes

No

*Subject's or
Legally Authorized
Representative's
Initials*

**[UCSF, Cedars-Sinai, U Maryland, Mt. Sinai liver, Columbia, Beth Israel
Deaconess: I agree to have anal Pap smears for the detection of HPV.]**

Yes

No

*Subject's or
Legally Authorized
Representative's
Initials*

Add site Release of Medical Information form here for the primary medical care provider. This should be signed at the time consent is obtained.

APPENDIX A: LANGUAGE FOR SITE SPECIFIC SUB-STUDIES

Below is recommended text for each of the sub-studies to be included in the consent forms. If your center is participating in the sub-study (as indicated below) the suggested text should be added to your consent forms in the appropriate section as indicated.

PK Sub-Study

[UCSF only]

Procedures:

Because we do not know how the medications you/your child is taking will interact with each other, multiple blood samples and a urine sample may be collected during a day-long stay in the General/Pediatric Clinical Research Center (GCRC)/(PCRC) at various times over a 12 to 24 -hour period during study participation, as follows: prior to the transplant procedure and at Weeks 2, 12, and 26 after the transplant procedure. Participation in these studies will be determined by the type of HIV or immunosuppressive medication your are taking.

A small plastic tube will be inserted in a vein in order to avoid multiple needle sticks for the collection of these blood samples. Approximately 1 teaspoonful of blood for adults, older children and adolescents and less than half a teaspoon for younger children will be collected at each of multiple time points over 12 - 24 hours (a total of approximately 10 teaspoonfuls for adults, adolescents and older children, or 4 teaspoons for younger children). At each clinical stay you/your child will also provide a sample of urine, which will be tested for illegal drugs and prescription drugs to evaluate any interactions with your/your child's anti-HIV and/or immunosuppressive medications. This test is called a urine toxicology screen. Your/your child's clinical stay may take up to 14 or 26 hours.

You/your child may have a whole body DEXA (Dual Energy X-Ray Absorptiometry) test done. The machine takes a picture of the bones in the spine and hip and calculates their density or thickness, and can also measure the total amount of muscle, bone and fat in the body. During the scans, you/your child will be asked to change into a gown and to lie down on a padded table. You/your child will be asked to lie still, but will be able to breathe normally. Each scan takes about 5 - 10 minutes. A trained staff person will be in the room the entire time. The scans will take place at [the UCSF General Clinical Research Center in the Moffitt Hospital].

You/your child will be asked to have genetic testing performed as part of the drug level studies (pK studies). In these studies, you/your child's DNA will be analyzed to see if you/your child has certain types of genes that are responsible for influencing how the body reacts to HIV or infections that can occur in HIV-

infected persons. The study will only evaluate those genes that may have a role in responding to HIV or related infections. Samples will not contain any personal identifiers such as your/your child's name or ID number. Genetic testing is an optional part of this study. You/your child may refuse genetic testing, which will not affect you/your child's participation in this study. If you/your child agree to participate in this part of the study, you/your child will have the option of discontinuing from the genetic blood testing at any time by telling research staff.

Risks and Discomforts:

Catheter Placement - Catheter (small plastic tube placed in a vein) placement for drug level (pK) studies may cause slight discomfort, bleeding or bruising at the site of placement and rarely, infection may occur.

Confidentiality – In this study, you/your child will be tested for illegal drugs with a urine test as part of the pK studies.

DEXA – You/your child may feel some stress if the DEXA scans shows that you/your child has low bone density. Study staff will tell you the results of the bone density scan and mail a report of the bone density test to your/your child's doctors if requested. If your/your child's bone density is found to be low, your/your child's doctors may want to do blood tests or other exams.

The bone density scanner emits some radiation. The amount of radiation you/your child will get exposed to with each scan is relatively small, about one fiftieth of a chest x-ray or about the amount you would get on a cross-country airplane flight. These doses of radiation could be potentially harmful, but the risks are so small that they are difficult to measure. If you/your child has had a lot of x-rays already, you should discuss this with the study investigators or your/your child's doctor.

Anal HPV-Sub Study

[UCSF, Cedars-Sinai, U Maryland, Mt. Sinai liver, Columbia, Beth Israel Deaconess]

Procedures:

Patients who are immunosuppressed for any reason (including having HIV infection or receiving a transplant) are thought to be at a higher risk for the development of HPV (a virus)-associated cancer in the cervix as well as in the anus. The purpose of the Pap smear(s) of the anus is to look for HPV itself. The pap smear of the anus also allows for early detection of any pre-cancerous changes in the cells.

The study investigators would like to learn more about anal HPV infection and the course of anal disease over time. Because HPV infection of the anus can be

seen in both men and women, if you/your child is sexually active, you/your child will be asked to have an anal examination and a Pap smear of the anus to collect cells to test for anal HPV infection.

For the anal Pap smear, you/your child will have a swab inserted into the anal canal to collect cells and to look for HPV. If this is abnormal, you/your child will be referred to a specialist for the following exams and tests:

You/your child will have a visual examination of the anal region. An instrument called an anoscope will be inserted into the anal canal. The anoscope allows the specialist to look at the inside of the anal canal. Three percent acetic acid (diluted vinegar) will be applied to the surface of the anal canal as well as to the inside of the canal. During the anoscopy, if any areas of abnormality are seen, a biopsy (removal of a small piece of anal skin) may be required. To perform this biopsy, the anal skin will be numbed by injecting a numbing medicine (similar to that used by a dentist) with a small needle. After the skin becomes numb, a very small piece of anal skin will be removed. This biopsy skin will be sent to the Department of Pathology, at the University of California, San Francisco for examination. If the area of abnormality is large enough, a second piece of anal skin may be needed for analysis. These procedures take about 30 minutes.

If a potentially pre-cancerous area is found, your/your child's primary medical care provider and the study doctors will discuss the results so that arrangements for appropriate follow-up can be made. If treatment is required, referrals will be made outside of the study.

You/your child may choose not to participate in the studies of the anal region or you/your child may stop participating in them at any time. Your/your child's decision will not affect participation in the rest of the study. You may agree or refuse to participate in these HPV studies by checking the correct choice at the end of this consent form.

Risks and Discomforts:

Insertion of an anal swab, an anoscope and application of acetic acid may cause some discomfort. Anal biopsy may be associated with discomfort from the needle stick for anesthesia, bleeding, temporary discomfort after the anesthetic wears off and rarely, infection or allergic reaction to the anesthesia. If you/your child needs to travel to another clinic where the follow-up tests are performed, time will be required.