The Johns Hopkins Bloomberg
School of Public Health

CONSENT FORM A / NEW RESEARCH PROJECT

Title of Research Project: A Randomized Trial of HAART in Acute/Early HIV Infection Version 3.0

Principal Investigator: Joseph B. Margolick MD, PhD

Introduction:
This consent form explains the research study you are being asked to join. Please review this form carefully and ask any questions about the study before you agree to join. You may ask questions at any time after joining the study.

Purpose of Research Project:
You are being asked to take part in this study because you have been infected with HIV, possibly within the past year. HIV is the virus that causes AIDS. We now know a lot about how to treat HIV in people who have had the virus for a long time. There are many medicines approved to treat HIV. People usually take a combination of 3 – 4 medicines. Once these medicines are started, they are usually taken for many years. This is known as HAART (Highly Active Antiretroviral Therapy). However, we still do not know the best way to treat people who have been infected within the past year. We think that if we give HAART for 12 months during the first year of HIV infection, and then stop the treatment, we might be able to keep your immune system working better and increase the number of years that you can go before you need to take HAART again. We do not know this for sure; and this is what we hope to learn through this study. We are also going to study the side effects that the people taking HAART develop. We want to see if taking HAART early and only for one year leads to fewer side effects.

In order to study these questions, we will give treatment to half the people who are in this study, and half will not receive treatment. Who will receive treatment will be decided by chance. The treatment will last one year. We will then follow both the people who received treatment and those who did not. We want to see if giving treatment right away is more helpful than waiting to start treatment.

According to the current guidelines for the treatment of HIV infection, the benefits of treating people with acute or early disease are based on theory, and have not been proven in studies. We hope to answer this question through this study.

This study will be done at six centers throughout Canada and the United States. We plan to enroll 180 people into this study. Your participation in the study will last for 3 years. It is possible that we may extend the length of this study. If that happens you will be asked to sign another consent form to allow us to follow you for an additional period of time.
Procedures:

The Screening Visit:

Before you can enter this study, you will have a screening visit to find out if you can be in this study. You will have standard tests used in the care of patients with HIV.

At the screening visit we will:

- Ask you questions about your medical history
- Ask how you think you were exposed to HIV
- Ask you about any medications that you are taking
- Talk about high-risk behaviors (like using drugs or having sex without a condom)
- Draw blood for routine laboratory tests. The total blood drawn at this visit will be about 6 tablespoons and will look at your red and white blood cells (hematology), your liver and kidney (chemistry) and the amount of fats in your blood (lipids).
- Measure your T-cell count, which tells us how well your immune system is working.
- Measure the amount of HIV in your blood, or viral load.
- Test for HIV antibodies (tests which tell us you are HIV positive).
- Test your HIV drug sensitivity (genotype). This means we will find out which drugs are likely to work against your HIV infection.
- Test for Hepatitis B and Hepatitis C (diseases which can affect your liver) and syphilis.
- If you are a woman who can have a child, you will have a pregnancy test.

If these tests tell us that you were exposed to HIV infection more than 12 months ago, you will not be able to take part in this study. In that case, we will help you find a doctor who can treat your HIV infection.

If you meet certain eligibility criteria (page 11), you will be invited to come back to join the study.

The Randomization Visit:

If you want to take part in this study, you will come back for your next study visit within fourteen days. At this visit you will have a complete physical exam. Then the decision will be made as to whether you will receive Highly Active Antiretroviral Therapy (HAART) right away or you will not be treated unless it is clinically needed. This decision will be made randomly, like flipping a coin. To make this decision, we will make a telephone call to a computerized randomization center while you are with the study coordinator. You will find out then if you will be getting treatment.

If you are going to receive treatment, a study doctor will review your HIV sensitivity test. This doctor will recommend medicines that should work well for you. This will be based on what we know about treating HIV in people who have been infected for more than one year.
We will talk about these drugs with you and ask you questions about your lifestyle. We will ask you about the kinds of foods you eat and how early you get up in the morning. We want to be sure that we have chosen a combination of drugs that you will be able to take. We will tell you about the side effects of each drug, how often you will need to take it, and how it should be taken.

There are many medicines available to treat HIV. If you cannot take a particular drug, we can switch you to another one that may be easier for you to take. It is very important that you take your medicines the way that they are prescribed. It is important that you tell the study staff if you are having problems with your medicines (like side effects or missing doses). If you are on treatment and miss three monthly study visits in a row your treatment will be stopped to avoid development of resistant virus unless it is clinically indicated for it to continue. If you are in jail or prison your study treatment will be stopped. However, we will ask you to continue in the study.

We will draw blood at this visit, for hematology, chemistry, t-cells and viral load tests. We may repeat an HIV test. We will draw blood to store for future testing. The total blood drawn at the randomization visit will not be more than about 6 tablespoons.

If you are a woman who can have a baby and are randomized to begin treatment, you will have a pregnancy test each time before we give you any study medications.

**Additional Study Visits:**

Additional study visits will take place after 1 and 2 weeks. Then you will come back once a month for 1 year. At each of these visits, we will ask you questions about your health, any medications that you are taking (and any side effects you may be having), and high-risk behaviors. If you are taking medicines to treat HIV we will ask you to complete a questionnaire about how you are doing with them. Blood will be drawn and a physical exam will be done according to the schedule below.

**Weeks 1, 2**
- Blood for hematology and chemistry (about 2 tablespoons)
- Blood to test for HIV antibodies (only if your test was not positive at the last visit)
- Physical exam (only if you are having any symptoms)

**Months 1, 2, 4, 8, 10, 11**
- Blood for hematology and chemistry and viral load (about 3 tablespoons)
- Blood to test for HIV antibodies (only if your test was not positive at the last visit)
- Physical exam (only if you are having any symptoms)

**Months 3, 6, 9 and every three months until the end of the study**
- Blood for hematology and chemistry, viral load, T-cells and storage for future testing (about 6 tablespoons)
- Physical exam (only if you are having any symptoms)

**Month 12 and every twelve months until the end of the study**
• Blood for hematology and chemistry, viral load, T-cells, lipids and storage for future testing (about 6 tablespoons)
• Physical exam

After month twelve, study medicine will be stopped in all people who have been getting treatment. Some people may have one of their medicines changed for the last month before all therapy is stopped. This will be done to prevent resistance to the medication Sustiva. Before you begin HAART we will review the medications we would like you to take. If they include Sustiva we will explain when and why we will replace them with a protease inhibitor. Treatment will not be stopped if there are medical reasons why treatment should be continued. Those medical reasons include pregnancy, low T-cells or chronic hepatitis B infection. If you have been getting treatment you will come in for visits 1, 2 and 4 weeks after stopping treatment. We will draw blood for viral load and storage for future testing at these visits.

Everyone taking part in this study will come in every 3 months until the end of the study (month 36). At each visit we will ask you about how you are doing and blood will be drawn.

Each study visit should take about 30 minutes. The first two visits may take up to 1 hour. The total amount of blood drawn at each visit will be different, but will not be more than 6 tablespoons.

During the follow-up period we will watch your T-cells and your viral load closely. If at any time the study doctors think that you need treatment with antiretroviral medication, therapy will be offered.

Everyone in the study should have a primary care physician. Your primary care physician will take care of any medical problems that you have that are not related to this study. With your permission, the study staff will keep your primary care physician up-to-date on your progress in the study. If you do not have a primary care physician, we can refer you to one.

The results of all lab tests performed during the study will be shared with you, and (with your permission) with your primary care provider.

**Risks/Discomforts:**

The risks of this study include the side effects of the medicines used to treat HIV infection. There are currently 18 drugs licensed to treat HIV infection. The combinations of drugs used in this study will be selected according to the recommendations of the U.S. Department of Health and Human Services guidelines for the treatment of HIV infection.

The side effects of these drugs are well known and can include:
• nausea
• vomiting
• diarrhea
• headache
• fever
• chills
• fatigue
• malaise (flu-like symptoms)
• changes in liver, pancreas or kidney function
• decrease in the number or red blood cells (anemia)
• decrease in the number of white blood cells
• increase in the amount of “fat” in the blood (triglycerides)
• increased cholesterol
• increased blood sugar (diabetes)
• numbness and tingling in hands, feet or mouth
• difficulty concentrating
• grogginess or difficulty sleeping
• some people have a change in their body fat (lipodystrophy)
• some people may have allergic reactions to some medicines.

We will talk with you about the possible side effects of the medicines that you are going to take. You will be given written information about the drugs. It is possible that there are side effects to the medicines that are unknown at this time. We will inform you of any new information that we learn during the study.

There is a risk of increased side effects when taking a combination of drugs. There may also be other still unknown risks from taking these drugs in combination.

There is the risk of serious and/or life-threatening side effects when non-study medications are taken with study drugs. For your safety, you must tell your doctor or nurse about all the medications you are taking before you start the study and before taking any non-study medications while you are on the study.

In addition, you must tell the study staff before enrolling in any other clinical trials while you are on the study.

Another risk of taking HAART is the risk of developing resistance to medicines used to treat HIV infection. If you do not take your medicines properly, it is possible that the virus in your blood will mutate (change) and the medicines will not work well. This is called “resistance”. We know that the best way to avoid resistance is to take every dose of all of your medicines the way that we tell you. Therefore, we will make every effort to help you understand how to take your drugs. It is very important for you to let us know if you are having trouble with any of your medicines. The study staff will do everything possible to help you manage your side effects, and may change or stop your medicines, if you cannot take them properly.

Drawing blood may cause mild pain, bleeding or bruising of your skin and, very rarely, infection. Some people become lightheaded or may faint when they have blood drawn.

There is a risk that people with HIV can infect their sexual partners. We recommend that you use condoms at all times to prevent transmission of the virus to your partners.
Risks of Pregnancy:

Certain drugs used to treat HIV infection can harm a developing baby. You cannot join the study if you are pregnant. For that reason, if you are a woman who can have a baby, you will have a pregnancy test before you enter the study. We will give you another pregnancy test before you start HAART, and at every study visit when medication is dispensed. You and your partner must use one method of birth control that you discuss with the study staff. You may choose one of the birth control methods listed below:

- 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)

If you would like to use hormonal contraception (birth control pills or implants) in addition to one of the methods above, please discuss this with the study staff. These methods may be less effective when used with certain antiretroviral medications. At your request, the study doctors will see if they can devise a HAART regimen that can be used with birth control pills and which should be effective based on your resistance test.

Some anti-HIV drugs require the use of two methods of birth control. If you are taking one of these medicines, the study staff will discuss your options with you. If you become pregnant while in the study we will review the medicines that you are taking. We may change the treatment to one that is approved for use in pregnant women.

Benefits:

The knowledge that we will gain from this study is very important. Your participation will help us to understand how to treat people with acute or early HIV infection. If you are randomized to receive treatment for your HIV infection, it is possible that you may benefit from this treatment. It is also possible that you will not benefit. Any treatment given to you will be tailored to your virus. This will be based on the results of the sensitivity test (genotype) that is done at your first study visit.

You may benefit from having very close follow-up of your HIV infection and frequent monitoring of your blood work. This follow-up and all study related lab tests will be provided at no cost to you.

Costs to You:

We have asked the companies that make anti-HIV medications to donate drugs to our study participants. Some drugs may be available free of charge. However, it is possible that the results of your sensitivity test may show that you would respond better to a medicine that we do not have access to. In that case, we will ask that you use your health insurance to purchase that medicine. The study will reimburse you for any “co-pays” that you may have so that you will have no “out-of-pocket” expense. If you do not have health insurance, we will put you in contact with a social worker that can find out what services you qualify for.
Alternatives to Participation:

You may choose not to take medicines to treat HIV at this time. You may choose to receive treatment outside of this study. This choice is entirely up to you. Your decision will not affect your care at any of the Johns Hopkins Medical Institutions. You should not take part in this study if you know you definitely want to begin antiretroviral medicine at this time or if you know you definitely do not want to start taking antiretroviral medicine now. Remember, if you join this study, whether or not you receive antiretroviral medicines at this time will be determined by chance. The study staff will be happy to refer you to a doctor who can follow your HIV infection.

Confidentiality:

All information that you tell us will be kept confidential. All study data will be kept with a code or number. Your study records will be kept in a locked file cabinet in a locked office and/or on password protected computer files. No one will be able to see your study records except people working directly on the study. We will not give out any information about you unless you have given us written permission to do so.

The only people who will have access to this information will be those who are involved in the study. These people may include the researchers, study and lab personnel, and other study staff. Others who may see your information are the groups of people who make sure that the study is being done as it should be: the Committees on Human Research and staff, Audit and Compliance Officers, Legal Counsel and others including the Study Monitors who need to see your information to make sure that the study is going as planned.

Other groups of people who may be involved in the study and may need to see your information are:

- The government agency, the Office for Human Research Protection, that makes sure that we are conducting the research as planned, and the Food and Drug Administration.
- Doctors and staff at other places that are participating in this study.
- The sponsor of this study and people who the sponsor may contract with for this study. The name of the sponsor is National Institute of Allergy and Infectious Diseases.
- The Data Safety Monitoring Board.

Maryland State Law requires us to report certain diseases to the Baltimore City Health Department. Any information relating to HIV infection will be reported using a unique identification number to ensure that your identity is kept private. Information that identifies you will not be given out to people who are not working on the study, unless you give us permission. If the study staff learns of possible child abuse and/or neglect, we will be required by Maryland State Law to tell the proper authorities.

At the end of the study, whatever we learn from the research may be published in a medical journal or used for teaching. Your name or other details about your health will not be used, so
no one will be able to identify you personally.

**Leaving the Study Early:**

You can agree to be in the study now and change your mind later. If you wish to stop, please tell us right away. Leaving this study early will not stop you from getting regular medical care at Johns Hopkins. If you leave the study early, we may use your health information that we already have if it is needed for this study or any follow-up activities. If you leave the study early and give us permission, we will call you a month after your last visit to see how you are doing. If you were taking HAART at the time that you leave the study we will call you a second time (2 months after your last visit).

**You may be taken out of the study if:**

- Staying in the study would be harmful to you.
- You need treatment not allowed in this study.
- You fail to follow instructions.
- The study is cancelled.
- You show bad behavior towards study or clinic staff.
- You are under the influence of drugs or alcohol during a study visit.
- There may be other reasons that we don’t know at this time to take you out of the study.

**Compensation:**

You will be paid $15.00 for each study visit. You will be paid about $240 for year 1. You will be paid about $60 per year for each additional year. If you take part in the study for all 3 years you may receive up to $360.

**Voluntariness:**

Your participation in this research project is completely voluntary. You have the right to withdraw from the study at any time. Even if you do not want to join the study, or if you withdraw from the study, you will still have the same quality of medical care available to you at Johns Hopkins. You should ask the Principal Investigator listed below any questions you may have about this research study. You may ask him/her questions in the future if you do not understand something that is being done. The investigators will share with you any new findings that may be learned while you are taking part in this study.

**Research Related Injury:**

The Johns Hopkins Bloomberg School of Public Health, The Johns Hopkins Hospital and the Federal government do not have any program to provide compensation to you if you experience injury, or other bad effects, which are not the fault of the investigators. If you feel that you have suffered an injury the study staff and/or the people in the Office for Research Subjects office will answer your questions and/or help you find medical care.
Persons to Contact:

If you want to talk to anyone about this research study because you think you have not been treated fairly or think you have been hurt by joining the study, or you have any other questions about the study, you should call the Principal Investigator, Dr. Joseph Margolick at (410) 955-1436 or call the Office for Research Subjects at 1-888-262-3242 or FAX (410) 502-0584. Either the Principal Investigator or the people in the Office for Research Subjects office will answer your questions and/or help you find medical care if you feel you have suffered an injury. You will be given a 24 hour pager number and email addresses to contact study staff in case of clinical problems or questions. Dr. Gallant may be paged at (410) 283-2686 and Dr. Barditch may be paged at (410) 283-1051.

If you have read this document and you have been given the chance to ask any questions now or at a later time or if the document has been read and explained to you and you agree to be in this study, please sign or make your mark below.

Print Name of Subject:_____________________________________________________

________________________________________________ _______________
Signature or Mark of Subject or Legally Authorized Representative     Date

________________________________________________ _______________
Signature of Person Obtaining Consent     Date

________________________________________________            _______________
Witness to Consent if Subject Unable to Read or Write                     Date
(Must be different than the person obtaining consent)

Signed copies of this consent form must be 1) retained on file by the principal investigator, 2) given to the subject and 3) placed in the subject’s medical record (when applicable).

NOT VALID WITHOUT THE CHR
STAMP OF APPROVAL

CHR#:_________________________
VALID FROM_____________ TO_______________

Submit to the CHR Staff Office, Room E2100, Bloomberg School of Public Health.
Some of your blood will be kept in storage and tested after the study ends. Your blood sample will be labeled with a unique identifier (code number) and stored with this code number. Your blood sample will be linked to the other data collected about you in the study. We will not have your name on the blood sample. Your name will be kept in a locked file apart from your blood sample. Future testing may include studies to find out whether certain genetic factors influence how effective early treatment for HIV infection is. Stored blood will not be used for any research that is not related to this study.

You can still be in this study, even if you do not want your blood stored and tested for future studies.

☐ I agree to storage of my blood sample for future testing

☐ I do not agree to storage of my blood sample for future testing. If I do not allow my blood to be stored after the end of the study, I can still be in this study.

If you agree to the storage of your blood now, but change your mind later, you may withdraw your consent at anytime. If you withdraw your consent to store blood, your blood samples will be destroyed. To withdraw your consent for future testing of stored blood please contact Dr. Joseph B. Margolick at (410) 955-1436.

Signature or Mark of Subject or Legally Authorized Representative ___________________________ Date _______________

Signature of Person Obtaining Consent ___________________________ Date _______________

Witness to Consent if Subject Unable to Read or Write (Must be different than the person obtaining consent) ___________________________ Date _______________

Note: Signed copies of this consent form must be: a) retained by the Principal Investigator, b) given to the participant, c) put in the patient’s medical record
Appendix 1

Eligibility Criteria

To enter this study you must:

- Be at least 18 years of age
- Be able to understand what the study is about, and sign the consent form
- Have become infected with HIV in the last 12 months
- Never have taken medicine to treat HIV infection
- Have a viral load greater than 5000
- Have T-cells greater than 250
- Have blood tests see if it would be safe for you to take medicine to treat HIV infection
- Be able to come to study visits and take medication according to the study schedule
- Not be pregnant or breastfeeding
- Not have taken certain medicines (such as cancer chemotherapy or drugs that affect your immune system) within the last 30 days
- Not have a serious medical illness that requires hospitalization.
  You may be able to enter the study 7 days after you complete therapy or become clinically stable
- Not be in jail or prison