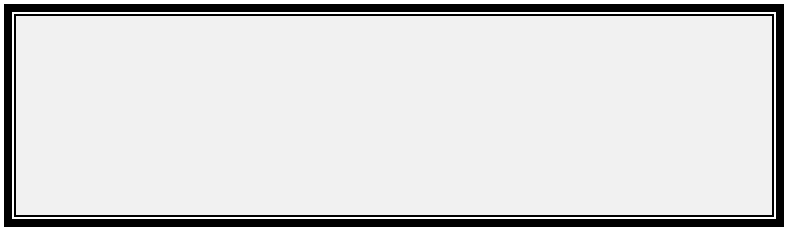
Informed Consent to Participate in Research



1. **Title of Research Study**
   A Phase III Randomized, Multicenter Trial Comparing G-CSF Mobilized Peripheral Blood Stem Cell with Marrow Transplantation from HLA Compatible Unrelated Donors

2. **Principal Investigator Contact Information at Your Institution**
   Name/Title/Phone number/

3. **Contact information for Emergencies after Hours or on Weekends or Holidays**
   Name/Phone number/

4. **Sponsors and Source of Funding or Other Material Support**
   The research in this study is paid for by the National Institutes of Health (NIH) and the National Marrow Donor Program ® (NMDP). The NMDP and the Blood and Marrow Transplant Clinical Trials Network (BMT CTN) will direct the research study. This study will be done at many different medical centers, including [Center Name/Location].

5. **Introduction**
   This is a consent form for a research study. You are being invited to participate in this study because you have a disease that may be treated with a transplant of either bone marrow or peripheral blood stem cells (PBSC). This form is intended to give you information to help you decide if you want to participate in this study. You should read this form and ask any questions you may have before agreeing to be in the study.

   Doctors have been successfully treating blood disorders such as leukemia and myelodysplasia with a transplant of blood stem cells from either the bone marrow or the peripheral blood. The goal of this study is to see if patients receiving a transplant from an unrelated donor have better results using blood stem cells from: 1) bone marrow or 2) peripheral blood. The study may find that patients have similar results with either type of transplant.

   Important results of this study will include:
   - Survival
   - Quality of life
   - Blood counts after transplant
   - Number and severity of infections
   - Graft-versus-host disease (GVHD)
   - Relapse of disease (return of disease)

Other information about the study:

- You will not be paid to be in this study.
- You or your insurance company will pay the bills for your medical treatment.
- You will not be charged for research tests.
- You will face the same risks and benefits as any other bone marrow or peripheral blood stem cell (PBSC) transplant patient.

It is your choice whether or not to participate in this study. You and the medical staff at your transplant center will discuss other treatment options before you make your decision about participating in this study.

6. Purpose of the Study

This study will look at two kinds of blood stem cell transplants, bone marrow and peripheral blood stem cell (PBSC), and their side effects. At this time, doctors use both types of blood stem cells for transplant. Previous studies have compared the survival of patients who received an unrelated donor transplant from bone marrow with patients who received an unrelated donor transplant from PBSCs. In these studies there was no difference in survival between the bone marrow transplant patients and PBSC transplant patients. This may have been because the patients in each group did not have the same characteristics (for example, different diseases, different ages).

In this study, the patient and donor will be randomly assigned (much like the toss of a coin) to either the bone marrow or the PBSC transplant study group. By randomly assigning the patients to receive either a bone marrow or PBSC transplant, the characteristics of each study group should be similar. The primary goal is to see which type of blood stem cell transplant (bone marrow or PBSC) has better survival results. With similar patient characteristics in each study group, researchers should be able to find out if one type of blood stem cell transplant (bone marrow or PBSC) has better survival results for patients, or if both types of blood stem cell transplants have similar survival results.

An important part of this study will look at how well you feel after your transplant. Researchers want to know the effects from each type of stem cell used for the transplant and how long they last.

<u>Good effects might include</u>:

- Quick recovery of blood counts after transplant
- No relapse of disease
- High cure rates
- Few infections
- Able to return to important activities in life

<u>Bad effects might include</u>:

- Slow recovery or no recovery of blood counts after transplant
- Relapse of disease
- Severe graft-versus-host disease (GVHD)
- Serious infections
- Not able to return to important activities in life

The information collected from this study will help doctors and future patients make better treatment choices. About 550 patients will take part in this study at many centers around the country.

7. Study Procedures

If you agree to participate in the study, the transplant process has many steps. A matched donor must be found. Both you and the donor will need to to give permission to participate in this study. A donor could refuse to participate in this study, but continue to be available for your transplant. In that case, you may decide to have a transplant using this donor, but not participate in this study or another donor may be found who does want to participate in this study.

Since this study looks at the results of two different kinds of transplants, bone marrow and peripheral blood stem cell (PBSC), the kind of transplant you will receive will be decided randomly, like a coin toss. Neither you nor your doctor chooses the type of transplant; the type of transplant you will receive is determined by a computer program. Half of the patients in the study will have a bone marrow transplant. The other half will receive a PBSC transplant. Participation in the study means that you are willing to accept either type of transplant.

One part of the study will involve collecting your medical information. Your medical information will be collected for three years. The study coordinators at your center will collect information from your medical record chart every week for 100 days, then at 6 months, 1 year, 2 years, and 3 years.

Another part of the study will ask questions about your physical and emotional health. This information will be collected for five years. A trained interviewer will contact you by telephone before your transplant, then 6 months, 1 year, 2 years and 5 years after your transplant. These interviews will last approximately 15-25 minutes and will be done at a convenient time for you. They will include questions about side effects, health problems and how well you can do things that are important to you. When you are contacted, you may skip any questions you don't want to answer.

As part of the standard transplant procedure, you will need to take many medications and have other medical treatments. The medical staff will explain these during discussion of your medical care.

8. Possible Discomforts and Risks

You will face risks from the transplant itself, and from treatments given before and after the transplant. Your doctor thinks these risks are less than the risk from the disease for which you are receiving a transplant.

The bone marrow and PBSCs from the donor contain blood stem cells, which allow your blood counts (red blood cells, white blood cells, and platelets) to recover. Blood stem cells make all the blood cells in the bone marrow and serve the entire body. It is possible that even after the transplant your bone marrow will not work well enough, and you will be at an increased risk of infections and even death. Infections after transplant can be from bacteria, viruses, parasites, or fungi. Early after transplant, the risk of getting an infection might be less after a PBSC transplant, because the blood counts return faster than with bone marrow. Later, the risk of infections might be increased in PBSC transplants, because graft-versus-host disease (GVHD) might be worse and last longer. Blood counts will be done often to track recovery of the bone marrow. You will get platelets and red cells as needed to keep your counts at a healthy level.

There is a risk that stem cells may not grow after being given to you. This is called graft failure. Graft failure can be fatal unless you have a second transplant. Failure of the donor cells to grow (graft failure) may result from a mismatch with the donor, infection, a reduced effect of pre-transplant drugs on your body, or not enough cells in the product. This risk may be less with PBSCs, since PBSCs contain more blood stem cells than bone marrow.

Graft-versus-host disease (GVHD) is a frequent problem after unrelated donor transplantation. After the cells in the product begin to grow, there is a risk that the donor cells may react against your body. GVHD may show up as a skin rash, or liver or stomach problems. GVHD may cause nausea (feeling sick to your stomach), vomiting (throwing up), lack of appetite, stomach cramps, diarrhea (loose stools), and bleeding of the gut. Chronic GVHD may occur later after transplantation and may involve problems with the eyes, mouth, lips, throat and liver. Early (acute) or late (chronic) GVHD may be bad enough to cause death. GVHD is treated with drugs that weaken the body's defense

system, and thus make you more likely to get an infection. The chance of getting GVHD may be increased with PBSCs, since PBSC transplants contain more donor cells.

Relapse of your disease might occur after transplant, especially in patients with advanced disease. This risk may be decreased by PBSC transplantation.

If one type of transplant does have better results, and you are not randomly assigned to that study group, you may not receive the same benefits as those in the study group with overall better results.

Completion of the quality of life interviews will not cause you any physical discomfort, although it is possible that you will find some of the questions or topics upsetting. If you do, there will be someone available to speak with you. They will be able to refer you to appropriate counselors or other support people.

Refer to Appendix A, B, C or D for additional risks and toxicities toxicities related to the specific transplant conditioning regimen you will receive, the drugs you will receive to help prevent graft-versus-host disease (GVHD) and risks and toxicities related to the transplant procedure itself.

9. Unknown or Unexpected Side Effects

As with any treatment, there may be unknown and/or unexpected side effects from a bone marrow or PBSC transplant. We may learn new things about bone marrow or PBSC transplants that might make you want to stop being in the study. We will let you know if this happens and you can decide if you want to continue in the study.

10. Alternative Treatments Available if You Don't Want to be in the Study

Participation in this study is entirely voluntary. You don't have to be in this study. What you decide will not affect current or future health care you receive at this institution. Before you decide to be in this study, you and the medical staff will discuss other options available to you, including:

- No treatment
- Chemotherapy
- A transplant using your own bone marrow or PBSCs
- A transplant of bone marrow or PBSCs from a relative
- A transplant of cord blood cells
- A bone marrow or PBSC transplant from an unrelated donor without participation in this study

11. Possible Benefits to Participating in the Study

This research study is comparing the treatment results of bone marrow and PBSC transplants. At this time doctors do not know if one type of transplant has better results than the other, or if they both have the same results. If one type of transplant does have better results, and you are randomly assigned to that study group, you may benefit from participating in the study. The knowledge gained from this study may help future patients who need a blood stem cell transplant, but there is no expectation that you will benefit from participating in the study.

As a result of the bone marrow or PBSC transplant your disease may be put in remission or continue in remission.

12. Cost of Participating in the Study

You and/or your insurance company will pay all medical expenses relating to, or arising from transplantation of either bone marrow or PBSC. Research tests described in Section 20 will be paid by the NIH and the NMDP.

For questions about your costs, financial responsibilities, and/or medical insurance coverage for your transplant and this study, please contact /Center/ Financial Counselor at /Number/.

13. Reimbursement for Participating in the Study

You will not be paid for participating in this study.

14. In the Event of Injury While Participating in the Study

If you are injured or become ill while taking part in this study, medical care will be provided at this center. No funds have been set aside to pay you if you are injured. You or your insurance company will be charged for ongoing medical care and/or hospitalization.

Contact your doctor or one of the people listed at the start of this form if you are concerned about a research-related injury.

15. Withdrawing from the Study

You may decide to withdraw at any time, for any reason, without notice from this study that compares bone marrow transplant with PBSC transplant. If you wish, you may withdraw from the study but still receive a blood stem cell transplant. If you withdraw from the study after you have had some or all of the pre-transplant treatments and decide to have no transplant at all, then your blood counts may not return and you could die.

If you decide to withdraw from the study, we ask that you tell [the Principal Investigator] in writing (his/her address is on the front page of this form). If you withdraw, there will be no penalty or loss of benefit to which you are entitled and you will continue to receive medical care.

If you withdraw from the study, the medical staff will continue to tell us about your progress for three years after your transplant. If you do not want this, you must specifically tell your doctor.

If you have any questions about your rights as a study subject, you may contact the Institutional Review Board (IRB) office at /number/.

16. Reasons Your Doctor May Take You off the Study

You can be taken off the study (with or without your consent) for any of these reasons:

- You would be harmed by staying in the study.
- You need treatment not allowed in this study.
- You do not follow directions that are important to participating in the study.
- The study is cancelled.

17. Protection of your Privacy and Confidentiality of Your Research Records

Your participation in this research study will be kept private and confidential. All your medical, demographic (such as race and ethnicity, gender and household income) and quality of life information will be kept private and confidential. *(Name of Transplant Center)* and the organizations listed below will not disclose your participation by any means of communication to any person or organization, except by your written request, or permission, or unless required by federal, state or local laws, or regulatory agencies.

Individuals authorized by the organizations below will have access to your research and medical information for inspections or audits. In agreeing to participate, you consent to such inspections and to the copying of excerpts from these records, if required by these authorized representatives.

Organizations with access to your research and medical information:

- /Institution/
- The National Institutes of Health (NIH)
- Office of Human Research Protection (OHRP)
- The Food and Drug Administration (FDA)
- Institutional Review Boards (IRBs) responsible for this study
- Data and Safety Monitoring Board (DSMB), not part of /Institution/
- The National Marrow Donor Program (NMDP)
- Blood and Marrow Transplant Clinical Trials Network (BMT CTN)
- Quality of Life staff at Center on Outcomes, Research, and Education at Evanston Northwestern Healthcare
- Laboratory staff at Dr. Edmund Waller's laboratory at Emory Unversity, Esoterix, Inc., Dr. Jeffrey Miller's laboratory at the Univerity of Minnesota

Scientific and medical findings resulting from a study may be presented at meetings and published so that the information can be useful to others. You would not be identified in these presentations and publications.

For questions about access to your medical records, please contact /name / at/number/.

18. Expiration Date for Keeping Your Records

Study records will be kept indefinitely by the transplant center for re-analysis and follow-up.

If you have questions about the keeping of your research records or access to your files, please call /name/at /number/.

19. Benefit to Doctors for Your Participation in this Study

Your doctors have no money invested in this study. Presenting research results may help the career of a doctor. Therefore, the doctors running this research study may benefit when the results are presented at scientific meetings or in the scientific press. In addition, the hospital where you will receive your transplant is paid for participating in the study.

20. Blood Samples for Research Purposes

You will be asked to provide blood samples to see if infection-fighting cells are working and to help better understand tissue matching between donors and recipients in this study. You do not have to participate in this part of the study.

If you agree, you will provide blood samples up to 7 times (10-100 mL each time or approximately 1-7 tablespoons) between the time transplant is initiated and two years after (up to a total for all 7 blood draws of 430 mL or approximately 2 cups). The samples will be saved for future testing. The blood

can usually be drawn from your central line at the time of other blood collections. If this is not possible, then it will be drawn directly from a vein.

As a standard part of the transplant procedure you will receive vaccinations for diphtheria, tetanus, Hepatitis B and pneumococcus. The research studies on infection-fighting cells will include studies to look at how well these vaccinations are working. You may still receive the vaccinations as part of your standard medical care even if you decide not to participate in the research on infection-fighting cells.

The doctors conducting this study may choose to do some additional research tests on the blood samples. These tests would only be done if the groups overseeing the safety and protection of subjects participating in this study approved these additional tests. These tests would only be performed on blood samples that were left-over after the tests on infection-fighting cells, vaccinations, and tissue matching were done; no additional blood would be drawn for these tests. This research may include tests to determine and evaluate other factors that affect transplant outcome in this study.

Any of your blood samples drawn for research purposes will be sent to laboratories that have a contract with the NMDP to conduct these research tests. Your blood will be labeled with a unique code that contains no information that could identify you. A link to this code does exist. The link is stored at the Data Coordinating Center for the Blood and Marrow Transplant Clinical Trials Network (BMT CTN). The staff at the laboratory where your blood is being tested does not have a link to this code. Your blood will be stored at these laboratories until the entire sample has been used for the research tests or until the end of the study.

If any of your blood samples are left over after the research studies are completed, these samples will either be destroyed or be sent to the National Heart Lung and Blood Institute (NHLBI) sample repository in Maryland. If your left-over blood samples are sent to the repository, they will be given an anonymous code. These left-over blood samples stored at the repository can never be linked to you. Any research performed on these left-over blood samples must first be approved by an advisory panel at the NHLBI.

You are free to <u>not</u> take part in this research and still participate in the other parts of the study. There will be no change in your care if you choose not to give blood samples for research purposes. Please mark your choice below (check only one box):

- ☐ **I agree to have blood drawn for research purposes.**
- ☐ **I do not agree to have blood drawn for research purposes.**

_____ _____

Signature *Date*

21. Subject's Consent

I have been informed about this study's purpose, procedures, possible benefits and risks. I have been given a chance to ask questions and have had them answered to my satisfaction. I understand that I can ask more questions at any time.

I voluntarily agree to participate in this study.

By signing this consent form, I have not given up any of the legal rights, which I otherwise would have as a subject in a research study.

_____ _____
Signature of Subject *Date*

_____
Print Name of Subject

Certification of Counseling Healthcare Professional

I certify that the nature and purpose, the potential benefits, and possible risks associated with participation in this study have been explained to the above individual and that any questions about this information have been answered.

_____ _____
Counseling Healthcare Professional *Date*

Use of an Interpreter: Complete if the subject is not fluent in English and an interpreter was used to obtain consent:

Print name of interpreter: _____ Date: _____

Signature of interpreter: _____

An oral translation of this document was administered to the donor in _____ (state language) by an individual proficient in English and _____ (state language). See the attached short form addendum for documentation.