APPENDIX B-1

RECIPIENT CONSENT FORM and ATTACHMENTS

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.

Attachment A

Additional Risks and Toxicities Related to the Standard Transplant Procedure
Total Body Irradiation and Cyclophosphamide Conditioning Regimen

There are certain risks related to a bone marrow or peripheral blood stem cell (PBSC) transplant. There are risks from the medications and irradiation therapy you will receive as part of the conditioning for the transplant, and risks related to the transplant itself. Most of these risks and side effects are listed below, but they will vary from person to person. There may be more risks involved with transplantation, and there may be more side effects. Your doctor may give you medications to lessen some of the side-effects.

Risks Related to the Transplant Conditioning Regimen

Cyclophosphamide (Cytoxan): This is a common medication used to treat cancer. This medication kills cancer cells by stopping them from growing. Cyclophosphamide may cause you to have diarrhea (loose stools), nausea (feeling sick to your stomach), vomiting (throwing up), short-term hair loss, short-term bladder problems, and, at times, bleeding from the bladder. A few patients may have bladder damage and bleeding for a longer time. You will be given large amounts of a sterile solution through your central line to protect your bladder. A bladder catheter (thin plastic tube) may be inserted into your bladder, if your physician thinks that it can help you. Cyclophosphamide slows the making of new red blood cells, white blood cells, and platelets. This causes a risk of infection and/or severe bleeding until the transplanted donor cells begin to work in you. You will get blood transfusions as needed. Cyclophosphamide also lowers your defense system. As a result, you may have more infections for several months after transplant. In a small number of patients, cyclophosphamide can damage the heart muscle causing heart failure. Sometimes cyclophosphamide causes abnormal heart function. If this occurs you may have shortness of breath and have fluids build-up in your body. This medication can also cause the lungs to become scarred. If scarring of the lungs occurs it will usually happen three to six months after you receive the medication. Scarring of the lungs can cause you to die. Cyclophosphamide can damage the male (testes) or female (ovaries) sex glands. In men, the number of sperm may be reduced but you would still be able to have intercourse. Women who are still menstruating may have irregular periods or may no longer have any periods. Whether you are a man or woman, this medication will likely greatly decrease your chances of being able to have a child. It is not known whether the use of cyclophosphamide will cause more side effects or problems with your health in the future.

Total Body Irradiation (TBI): TBI may cause you to have diarrhea (loose stools), nausea (feeling sick to your stomach), vomiting (throwing up), and painful swelling of the saliva gland for a few days. You may also experience short-term hair loss. TBI kills both sick and normal marrow, leading to a lack of red blood cells, white blood cells, and platelets. The short-term loss of these blood cells could cause you to become anemic, develop an infection, and/or bleeding. This will continue until the transplanted donor cells begin to work in you. You will get blood transfusions as needed. There is a risk that cataracts (cloudiness) may develop in your eyes. This may mean partial loss of vision, and you may need contact lenses or surgery to remove the cataracts. The TBI dose used will probably result in sterility (not being able to have children.) It is not known whether the use of TBI will cause more side effects or problems with your health in the future.

Risks Related to the Infusion of Bone Marrow or Peripheral Blood Stem Cell (PBSC)

The infusion of bone marrow or PBSC usually has few side effects. Rarely the infusion may cause a headache, chest pain or trouble breathing, a slight fever, or blood in the urine. Very rarely, it may cause an allergic reaction (which shows up as a severe drop in blood pressure and may cause loss of consciousness).

Risks Related to the Medications Used to Help Prevent Graft-versus-host Disease (GVHD)

Cyclosporine or Tacrolimus: These medications are used to try to prevent GVHD. These two medications have similar side effects. The immediate side effects you may experience include nausea (feeling sick to your stomach) or vomiting (throwing up) when the medications are given orally. Other side effects you may experience include high blood pressure (hypertension), shaking of the hands (tremor), increased hair growth and possibly an effect on mental function. If you experience these effects, they generally go away when the dose of the medication is decreased. A few patients have had a seizure while on these medications. You may experience a change of liver or kidney function, in which case the medication dose will be reduced or possibly even withheld. The effect on kidneys seems to increase when other medications, which might cause kidney problems, are given at the same time, especially antibiotics. Occasionally, the kidney damage caused may require the use of an artificial kidney machine (hemodialysis).

Some patients when given cyclosporine through a vein to treat GVHD experience a painful sensation in their hands or feet or both. The pain decreases or goes away when the GVHD improves or when the cyclosporine is given by mouth instead of through a vein.

Some patients given tacrolimus develop diabetes and must take insulin while taking tacrolimus.

Methotrexate: This is also a medication used to try to prevent GVHD. Methotrexate causes damage to cells, and therefore can affect many different tissues of your body. It may cause or can worsen the mouth sores or inflammation of the mouth which you may have already developed from the procedures and medications used to prepare you for the transplant. Methotrexate may slow down the recovery of blood cells after transplantation. Methotrexate can cause kidney damage. If your kidneys are already damaged for other reasons, it can worsen kidney function. If kidney damage does occur, the methotrexate dose may be reduced or the medication may not be given at all.

Cyclosporine, Tacrolimus, Methotrexate and Steriods: These medications interfere with the body's defense system (the immune system). This may cause you to have more infections (especially viral infections and pneumonia) for several months after transplant.

If other agents are used for GVHD prophylaxis, then analogous paragraphs describing risk of those agents must be added to your version of the consent form.

Risks Related to the Transplant Procedure

The following risks are not specifically related to any one medication or the transplanted donor cells, but they are risks that are a part of the transplant procedure.

Bleeding: Platelets help your blood to clot. Your platelets will be low until the new bone marrow grows and, as a result, bleeding may occur. This can be minor bleeding, such as nosebleeds or bruising, but

more serious, life-threatening bleeding in the lungs and brain can occur if the platelet count remains low. Usually, there is success in preventing major bleeding problems with transfusions of platelets. However, some patients may not respond well to transfused platelets and may be at serious risk for bleeding.

Veno-Occlusive Disease (VOD): This can occur as a result of high dose chemotherapy, irradiation therapy, or both. VOD causes severe damage to the liver. Symptoms include jaundice (yellowing of the skin and eyes), weight gain, and extra fluid build-up in the abdominal cavity and other parts of the body. It can often be managed successfully, and completely resolve. However, complications can arise that may be fatal.

Mouth Sores and Diarrhea: The large doses of medicines and irradiation cause irritation in the lining of the mouth and intestines. This can result in painful mouth sores and diarrhea. If you have severe mouth sores you will be given medicine to help control the pain. If your mouth sores are severe you may not be able to eat normally until the sores are healed. Mouth sores get better when the white blood count starts to rise, and engraftment occurs.

Capillary Leak Syndrome: This may occur as a result of chemotherapy and irradiation therapy. The blood vessels may become 'leaky' and fluid enters the abdominal cavity, lungs, and other tissues. You may gain water weight and not go to the bathroom as often as you normally do. Capillary leak syndrome can be difficult to manage if extra fluid enters the lungs and causes difficulty breathing. You may die if there is continued fluid collection in the lungs.

Unexpected Organ Damage and Other Side Effects: It is possible you may experience unexpected, life-threatening heart, lung, kidney, or liver damage as a result of the transplant. Occasionally, the high doses of chemotherapy and radiation cause severe lung damage that cannot always be treated. If this happens, you may need to use oxygen or even a respirator. The lung damage may get worse and be life-threatening. Rarely, multi-organ failure (such as lung and kidney failure) may occur, which is often fatal.

Late Effects: You may experience side effects that occur several months to many years after your transplant. You may experience poor function of the thyroid gland, requiring you to take thyroid medication. As a result of irradiation, cataracts may occur earlier in life compared to a person who had not had a transplant. If you develop cataracts (cloudiness in the eyes) they may require treatment. It is rare, but your kidneys could be affected, causing anemia (low red blood cell count) or high blood pressure. There is also a risk you may develop a second cancer as a result of the chemotherapy, irradiation and/or underlying disease. If secondary cancers occur they generally do not occur until 10 to 15 years after the transplant. The long-term effects upon heart, lung, and brain are unknown.

Fluid Build-up: You will receive intravenous fluids during the transplant process and you may have difficulty eliminating this fluid. Furosemide is a medication that is often given to help eliminate this excess fluid. This medication may cause hearing loss and loss of body chemicals such as potassium and sodium.

Attachment B

Additional Risks and Toxicities Related to the Standard Transpant Procedure
Busulfan and Cyclophosphamide Conditioning Regimen

There are certain risks related to a bone marrow or peripheral blood stem cell (PBSC) transplant. There are risks from the medications you will receive as part of the conditioning for the transplant, and risks related to the transplant itself. Most of these risks and side effects are listed below, but they will vary from person to person. There may be more risks involved with transplantation, and there may be more side effects. Your doctor may give you medications to lessen some of the side-effects.

Risks Related to the Transplant Conditioning Regimen

Cyclophosphamide (Cytoxan): This is a common medication used to treat cancer. This medication kills cancer cells by stopping them from growing. Cyclophosphamide may cause you to have diarrhea (loose stools), nausea (feeling sick to your stomach), vomiting (throwing up), short-term hair loss, short-term bladder problems, and, at times, bleeding from the bladder. A few patients may have bladder damage and bleeding for a longer time. You will be given large amounts of a sterile solution through your central line to protect your bladder. A bladder catheter (thin plastic tube) may be inserted into your bladder, if your physician thinks that it can help you. Cyclophosphamide slows the making of new red blood cells, white blood cells, and platelets. This causes a risk of infection and/or severe bleeding until the transplanted donor cells begin to work in you. You will get blood transfusions as needed. Cyclophosphamide also lowers your defense system. As a result you may have more infections for several months after transplant. In a small number of patients, cyclophosphamide can damage the heart muscle causing heart failure. Sometimes cyclophosphamide causes abnormal heart function. If this occurs you may have shortness of breath and have fluids build-up in your body. This medication can also cause the lungs to become scarred. If scarring of the lungs occurs it will usually happen three to six months after you receive the medication. Scarring of the lungs can cause you to die. Cyclophosphamide can damage the male (testes) or female (ovaries) sex glands. In men, the number of sperm may be reduced but you would still be able to have intercourse. Women who are still menstruating may have irregular periods or may no longer have any periods. Whether you are a man or woman, this medication will likely greatly decrease your chances of being able to have a child. It is not known whether the use of cyclophosphamide will cause more side effects or problems with your health in the future.

Busulfan: This medication disrupts the growth of cancer cells and destroys them. While taking busulfan you most likely will have diarrhea (loose stools), nausea (feeling sick to your stomach), vomiting (throwing up), lower white blood cell count that increases your risk of infection, lower platelet count that increases your risk of bleeding, hair loss, stopping of menstrual periods in women, temporary reduced or no sperm production in men. Less likely side effects that you may experiene are fatigue, sores in the mouth or on the lips, fever, rash, loss of appetite, changes in color of the skin, seizure. Rare side effects that you may experience are damage to your lungs, which may cause you to cough, be short of breath and have trouble breathing. It is rare, but busulfan can also cause changes in your liver function.

Risks Related to the Infusion of Bone Marrow or Peripheral Blood Stem Cell (PBSC)

The infusion of bone marrow or PBSC usually has few side effects. Rarely the infusion may cause a headache, chest pain or trouble breathing, a slight fever, or blood in the urine. Very rarely, it may cause

an allergic reaction (which shows up as a severe drop in blood pressure and may cause loss of consciousness).

Risks Related to the Medications Used to Help Prevent Graft-Versus-Host Disease (GVHD)

Cyclosporine or Tacrolimus: These medications are used to try to prevent GVHD. These two medications have similar side effects. The immediate side effects you may experience include nausea (feeling sick to your stomach) or vomiting (throwing up) when the medications are given orally. Other side effects you may experience include high blood pressure (hypertension), shaking of the hands (tremor), increased hair growth and possibly an effect on mental function. If you experience these effects they generally go away when the dose of the medication is decreased. A few patients have had a seizure while taking these medications. You may experience a change of liver or kidney function, in which case the medication dose will be reduced or possibly even withheld. The effect on kidneys seems to increase when other medications, which might cause kidney problems, are given at the same time, especially antibiotics. Occasionally, the kidney damage caused may require the use of an artificial kidney machine (hemodialysis).

Some patients when given cyclosporine through a vein to treat GVHD experience a painful sensation in their hands or feet or both. The pain decreases or goes away when the GVHD improves or when the cyclosporine is given by mouth instead of through a vein.

Some patients given tacrolimus develop diabetes and must take insulin while taking tacrolimus.

Methotrexate: This is also a medication used to try to prevent GVHD. Methotrexate causes damage to cells, and therefore can affect many different tissues of your body. It may cause or can worsen the mouth sores or inflammation of the mouth which you may have already developed from the procedures and medications used to prepare you for the transplant. Methotrexate may slow down the recovery of blood cells after transplantation. Methotrexate can cause kidney damage. If your kidneys are already damaged for other reasons, it can worsen kidney function. If kidney damage does occur, the methotrexate dose may be reduced or the medication may not be given at all.

Cyclosporine, Tacrolimus, Methotrexate and Steroids: These medications interfere with the body's defense system (the immune system). This may cause you to have more infections (especially viral infections and pneumonia) for several months after transplant.

If other agents are used for GVHD prophylaxis, then analogous paragraphs describing risk of those agents must be added to your version of the consent form.

Risks Related to the Transplant Procedure

The following risks are not specifically related to any one medication or the transplanted donor cells, but they are risks that are a part of the transplant procedure.

Bleeding: Platelets help your blood to clot. Your platelets will be low until the new bone marrow grows and, as a result, bleeding may occur. This can be minor bleeding, such as nosebleeds or bruising, but more serious, life-threatening bleeding in the lungs and brain can occur if the platelet count remains low. Usually, there is success in preventing major bleeding problems with transfusions of platelets. However, some patients may not respond well to transfused platelets and may be at serious risk for bleeding.

Veno-Occlusive Disease (VOD): This can occur as a result of high dose chemotherapy. VOD causes severe damage to the liver. Symptoms include jaundice (yellowing of the skin and eyes), weight gain, and extra fluid build-up in the abdominal cavity and other parts of the body. It can often be managed successfully, and completely resolve. However, complications can arise that may be fatal.

Mouth Sores and Diarrhea: The large doses of medicines cause irritation in the lining of the mouth and intestines. This can result in painful mouth sores and diarrhea. If you have severe mouth sores you will be given medicine to help control the pain. If your mouth sores are severe you may not be able to eat normally until the sores are healed. Mouth sores get better when the white blood count starts to rise, and engraftment occurs.

Capillary Leak Syndrome: This may occur as a result of chemotherapy. The blood vessels may become 'leaky' and fluid enters the abdominal cavity, lungs, and other tissues. You may gain water weight and not go to the bathroom as often as you normally do. Capillary leak syndrome can be difficult to manage if extra fluid enters the lungs and causes difficulty breathing. You may die if there is continued fluid collection in the lungs.

Unexpected Organ Damage and Other Side Effects: It is possible you may experience unexpected, life-threatening heart, lung, kidney, or liver damage as a result of the transplant. Occasionally, the high doses of chemotherapy cause severe lung damage that can not always be treated. If this happens, you may need to use oxygen or even a respirator. The lung damage may get worse and be life-threatening. Rarely, multi-organ failure (such as lung and kidney failure) may occur, which is often fatal.

Late Effects: You may experience side effects that occur several months to many years after your transplant. You may experience poor function of the thyroid gland, requiring you to take thyroid medication. It is rare, but your kidneys could be affected, causing anemia (low red blood cell count) or high blood pressure. There is also a risk you may develop a second cancer as a result of the chemotherapy and/or underlying disease. If secondary cancers occur they generally do not occur until 10 to 15 years after the transplant. The long-term effects upon heart, lung, and brain are unknown.

Fluid Build-up: You will receive intravenous fluids during the transplant process and you may have difficulty eliminating this fluid. Furosemide is a medication that is often given to help eliminate this excess fluid. This medication may cause hearing loss and loss of body chemicals such as potassium and sodium.

Attachment C

Additional Risks and Toxicities Related to the Standard Transplant Procedure
Fludarabine and Melphalan Conditioning Regimen

There are certain risks related to a bone marrow or peripheral blood stem cell (PBSC) transplant. There are risks from the medications you will receive as part of the conditioning for the transplant, and risks related to the transplant itself. Most of these risks and side effects are listed below, but they will vary from person to person. There may be more risks involved with transplantation, and there may be more side effects. Your doctor may give you medications to lessen some of the side effects.

Risks Related to the Transplant Conditioning Regimen

Fludarabine: This is a medication used to treat cancer. It is used in stem cell transplants to reduce the risk of rejecting the donor's transplanted cells. Likely side effects you may experience are low white blood cell count with increased risk of infection, low platelet count with increased risk of bleeding, feeling tired or sleepy, and anemia (low red blood cell count). Rare side effects you may experience include confusion or coma, trouble seeing or problems with your eyes, trouble breathing, diarrhea (loose stools), nausea (feeling sick to your stomach), vomiting (throwing up), pneumonia, agitation, numbness and tingling of the fingertips and toes, and kidney problems.

Melphalan: This medication disrupts the growth of cancer cells and destroys them. Side effects you most likely will experience include nausea (feeling sick to your stomach), hair loss, and low white blood cell count, which may lead to infection. Less likely side effects you may experience include diarrhea (loose stools), mouth ulcers, and low platelet count with increased risk of bleeding. It is rare, but you may experience a severe allergic reaction. Symptoms of a severe allergic reaction include itching, hives (bumps on your skin), flushing (redness), wheezing, chest tightness, skin rashes, fever, chills, muscle stiffening, severe breathing problems, and loss of appetite.

Risks Related to the Infusion of Bone Marrow or Peripheral Blood Stem Cell (PBSC)

The infusion of bone marrow or PBSC usually has few side effects. Rarely the infusion may cause a headache, chest pain or trouble breathing, a slight fever, or blood in the urine. Very rarely, it may cause an allergic reaction (which shows up as a severe drop in blood pressure and may cause loss of consciousness).

Risks Related to the Medications Used to Help Prevent Graft-Versus-Host Disease (GVHD)

Cyclosporine or Tacrolimus: These medications are used to try to prevent GVHD. These two medications have similar side effects. The immediate side effects you may experience may include nausea (feeling sick to your stomach) or vomiting (throwing up) when the medications are given orally. Other side effects you may experience include high blood pressure (hypertension), shaking of the hands (tremor), increased hair growth and possibly an effect on mental function. If you experience these effects they generally go away when the dose of the medication decreased. A few patients have had a seizure while taking these medications. You may experience a change of liver or kidney function, in which case the medication dose will be reduced or possibly withheld. The effect on kidneys seems to increase when other medications that might cause kidney problems are given at the same time, especially antibiotics.

Occasionally, the kidney damage caused may require the use of an artificial kidney machine (hemodialysis).

Some patients when given cyclosporine through a vein to treat GVHD experience a painful sensation in their hands or feet or both. The pain decreases or goes away when the GVHD improves or when the cyclosporine is given by-mouth instead of through a vein.

Some patients given tacrolimus develop diabetes and must take insulin while taking tacrolimus.

Methotrexate: This is a medication used to try to prevent GVHD. Methotrexate causes damage to cells, and therefore can affect many different tissues of your body. It may cause or can worsen the mouth sores or inflammation of the mouth which you may have already developed from the procedures and medications used to prepare ou for the transplant. Methotrexate may slow down the recovery of blood cells after transplantation. Methotrexate can cause kidney damage. If your kidneys are already damaged for other reasons, it can worsen kidney function. If kidney damage does occur, the methotrexate dose may be reduced or the medication may not be given at all.

Cyclosporine, Tacrolimus, Methotrexate, and Steroids: These medications interfere with the body's defense system (the immune system). This may cause you to have more infections (especially viral infections and pneumonia) for several months after transplant.

If other agents are used for GVHD prophylaxis, then analogous paragraphs describing risk of those agents must be added to your version of the consent form.

Risks Related to the Transplant Procedure

The following risks are not specifically related to any one medication or the transplanted donor cells, but they are risks that are a part of the transplant procedure.

Bleeding: Platelets help your blood to clot. Your platelets will be low until the new bone marrow grows and as a result bleeding may occur. This can be minor bleeding, such as nosebleeds or bruising, but more serious, life-threatening bleeding in the lungs and brain can occur if the platelet count remains low. Usually, there is success in preventing major bleeding problems with transfusions of platelets. However, some patients may not respond well to transfused platelets, and may be at serious risk for bleeding.

Veno-Occlusive Disease (VOD): This can occur as a result of high dose chemotherapy. VOD causes severe damage to the liver. Symptoms include jaundice (yellowing of the skin and eyes), weight gain, and extra fluid build-up in the abdominal cavity and other parts of the body. It may often be managed successfully, and completely resolve. However, complications can arise that can be fatal.

Mouth Sores and Diarrhea: The large doses of medicines cause irritation in the lining of the mouth and intestines. This can result in painful mouth sores and diarrhea. If you have severe mouth sores you will be given medicine to help control the pain. If your mouth sores are severe you may not be able to eat normally until they are healed. Mouth sores get better when the white blood count starts to rise, and engraftment occurs.

Capillary Leak Syndrome: This may occur as a result of chemotherapy. The blood vessels may become 'leaky' and fluid enters the abdominal cavity, lungs, and other tissues. You may gain water weight and not go to the bathroom as often as you normally do. Capillary leak syndrome can be difficult to manage

if extra fluid enters the lungs and causes difficulty breathing. You may die if there is continued fluid collection in the lungs.

Unexpected Organ Damage and Other Side Effects: It is possible you may experience unexpected, life-threatening heart, lung, kidney, or liver damage as a result of this the transplant. Occasionally, the high doses of chemotherapy cause severe lung damage that can not always be treated. If this happens, you may need to use oxygen or even a respirator. The lung damage may get worse and be life-threatening. Rarely, multi-organ failure (such as lung and kidney failure) may occur, which is often fatal.

Late Effects: You may experience side effects that occur several months to many years after your transplant. You may experience poor function of the thyroid gland, requiring you to take thyroid medication. It is rare, but your kidneys could be affected, causing anemia (low red blood cell count) or high blood pressure. There is also a risk you may develop a second cancer as a result of the chemotherapy and/or underlying disease. If secondary cancers occur they generally do not occur until 10 to 15 years after the transplant. The long-term effects upon heart, lung, and brain are unknown.

Fluid Build-up: You will receive intravenous fluids during the transplant process and you may have difficulty eliminating all of this fluid. Furosemide is a medication that is often given to help eliminate this excess fluid. This medication may cause hearing loss and loss of body chemicals such as potassium and sodium.

Attachment D

Additional Risks and Toxicities Related to the Standard Transplant Procedure
Fludarabine and Busulfan Conditioning Regimen

There are certain risks related to a bone marrow or peripheral blood stem cell (PBSC) transplant. There are risks from the medications you will receive as part of the conditioning for the transplant, and risks related to the transplant itself. Most of these risks and side effects are listed below, but they will vary from person to person. There may be more risks involved with transplantation, and there may be more side effects. Your doctor may give you medications to lessen some of the side effects.

Risks Related to the Transplant Conditioning Regimen

Fludarabine: This is a medication used to treat cancer. It is used in stem cell transplants to reduce the risk of rejecting the donor's transplanted cells. Likely side effects you may experience are low white blood cell count with increased risk of infection, low platelet count with increased risk of bleeding, feeling tired or sleepy, and anemia (low red blood cell count). Rare side effects you may experience include confusion or coma, trouble seeing or problems with your eyes, trouble breathing, diarrhea (loose stools), nausea (feeling sick to your stomach), vomiting (throwing up), pneumonia, agitation, numbness and tingling of the fingertips and toes, and kidney problems.

Busulfan: This medication disrupts the growth of cancer cells and destroys them. While taking busulfan you most likely will have diarrhea (loose stools), nausea (feeling sick to your stomach), vomiting (throwing up), lower white blood cell count that increases your risk of infection, lower platelet count that increases your risk of bleeding, hair loss, stopping of menstrual periods in women, temporary reduced or no sperm production in men. Less likely side effects that you may experience are fatigue, sores in the mouth or on the lips, fever, rash, loss of appetite, changes in color of the skin, seizure. Rare side effects that you may experience are damage to your lungs, which may cause you to cough, be short of breath and have trouble breathing. It is rare, but busulfan can also cause changes in your liver function.

Antithymocyte Globulin (ATG): This medication is given pre-transplant with the conditioning regimen medications to try and prevent both acute and chronic graft-versus-host disease. While taking ATG you most likely will have, a fever and chills, a lower white blood cell count that increases your risk of infection, a lower platelet count that increases your risk of bleeding, and a skin rash. Less likely side effects you may experience are fatigue, diarrhea, vomiting, muscle aches and headaches. Rare side effects that you may experience are changes in your blood pressures (either higher or lower blood pressure), rapid heart beat, be short of breath and have trouble breathing, chest pain and retention of fluids.

Risks Related to the Infusion of Bone Marrow or Peripheral Blood Stem Cells (PBSC)

The infusion of bone marrow or PBSC usually has few side effects. Rarely the infusion may cause a headache, chest pain or trouble breathing, a slight fever, or blood in the urine. Very rarely, it may cause an allergic reaction (which shows up as a severe drop in blood pressure and may cause loss of consciousness).

Risks Related to the Medications Used to Help Prevent Graft versus Host Disease (GVHD)

Cyclosporine or Tacrolimus: These medications are used to try to prevent GVHD. These two medications have similar side effects. The immediate side effects you may experience include nausea (feeling sick to your stomach) or vomiting (throwing up) when the medications are given orally. Other side effects you may experience include high blood pressure (hypertension), shaking of the hands (tremor), increased hair growth and possibly an effect on mental function. If you experience these effects, they generally go away when the dose of the medication is decreased. A few patients have had a seizure while on these medications. You may experience a change of liver or kidney function, in which case the medication dose will be reduced or possibly even withheld. The effect on kidneys seems to increase when other medications, which might cause kidney problems, are given at the same time, especially antibiotics. Occasionally, the kidney damage caused may require the use of an artificial kidney machine (hemodialysis).

Some patients when given cyclosporine through a vein to treat GVHD experience a painful sensation in their hands or feet or both. The pain decreases or goes away when the GVHD improves or when the cyclosporine is given by mouth instead of through a vein.

Some patients given tacrolimus develop diabetes and must take insulin while taking tacrolimus.

Methotrexate: This is also a medication used to try to prevent GVHD. Methotrexate causes damage to cells, and therefore can affect many different tissues of your body. It may cause or can worsen the mouth sores or inflammation of the mouth which you may have already developed from the procedures and medications used to prepare you for the transplant. Methotrexate may slow down the recovery of blood cells after transplantation. Methotrexate can cause kidney damage. If your kidneys are already damaged for other reasons, it can worsen kidney function. If kidney damage does occur, the methotrexate dose may be reduced or the medication may not be given at all.

Cyclosporine, Tacrolimus, Methotrexate and Steroids: These medications interfere with the body's defense system (the immune system). This may cause you to have more infections (especially viral infections and pneumonia) for several months after transplant.

If other agents are used for GVHD prophylaxis, then analogous paragraphs describing risk of those agents must be added to your version of the consent form.

Risks Related to the Transplant Procedure

The following risks are not specifically related to any one medication or the transplanted donor cells, but they are risks that are a part of the transplant procedure.

Bleeding: Platelets help your blood to clot. Your platelets will be low until the new bone marrow grows and, as a result, bleeding may occur. This can be minor bleeding, such as nosebleeds or bruising, but more serious, life-threatening bleeding in the lungs and brain can occur if the platelet count remains low. Usually, there is success in preventing major bleeding problems with transfusions of platelets. However, some patients may not respond well to transfused platelets and may be at serious risk for bleeding.

Veno-Occlusive Disease (VOD): This can occur as a result of high dose chemotherapy, irradiation therapy, or both. VOD causes severe damage to the liver. Symptoms include jaundice (yellowing of the skin and eyes), weight gain, and extra fluid build-up in the abdominal cavity and other parts of the body.

It can often be managed successfully, and completely resolve. However, complications can arise that may be fatal.

Mouth Sores and Diarrhea: The large doses of medicines and irradiation cause irritation in the lining of the mouth and intestines. This can result in painful mouth sores and diarrhea. If you have severe mouth sores you will be given medicine to help control the pain. If your mouth sores are severe you may not be able to eat normally until the sores are healed. Mouth sores get better when the white blood count starts to rise, and engraftment occurs.

Capillary Leak Syndrome: This may occur as a result of chemotherapy and irradiation therapy. The blood vessels may become 'leaky' and fluid enters the abdominal cavity, lungs, and other tissues. You may gain water weight and not go to the bathroom as often as you normally do. Capillary leak syndrome can be difficult to manage if extra fluid enters the lungs and causes difficulty breathing. You may die if there is continued fluid collection in the lungs.

Unexpected Organ Damage and Other Side Effects: It is possible you may experience unexpected, life-threatening heart, lung, kidney, or liver damage as a result of the transplant. Occasionally, the high doses of chemotherapy and radiation cause severe lung damage that cannot always be treated. If this happens, you may need to use oxygen or even a respirator. The lung damage may get worse and be life-threatening. Rarely, multi-organ failure (such as lung and kidney failure) may occur, which is often fatal.

Late Effects: You may experience side effects that occur several months to many years after your transplant. You may experience poor function of the thyroid gland, requiring you to take thyroid medication. It is rare, but your kidneys could be affected, causing anemia (low red blood cell count) or high blood pressure. There is also a risk you may develop a second cancer as a result of the chemotherapy, irradiation and/or underlying disease. If secondary cancers occur they generally do not occur until 10 to 15 years after the transplant. The long-term effects upon heart, lung, and brain are unknown.

Fluid Build-up: You will receive intravenous fluids during the transplant process and you may have difficulty eliminating this fluid. Furosemide is a medication that is often given to help eliminate this excess fluid. This medication may cause hearing loss and loss of body chemicals such as potassium and sodium.

Legal Guardian 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 Child's 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. Your child is being invited to participate in this study because he/she has 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 your child to participate in this study. You should read this form and ask any questions you may have before allowing your child to participate 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:

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

You and your child have a choice whether or not to participate in this study. The medical staff at your child's transplant center will discuss other treatment options before you make a decision about allowing your child to participate 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 and 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 patients recover after transplant. Researchers want to know what the effects are from each type of blood stem cells 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 allow your child to participate in this study, the transplant process has many steps. A matched donor must be found. You will need to give permission for your child to participate in the study and the donor will also need to give permission to participate in this study. A donor could refuse to participate in this study, but continue to be available for your child's transplant**.** In that case, you may

decide that your child will have a transplant using this donor, but not participate in this study, or another donor who does want to participate in this study may be found.

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 your child will receive will be decided randomly, like a coin toss. Neither you, nor your child's doctor, choose the type of transplant; the type of transplant your child 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 for your child.

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

If your child is 16 or 17 years old, another part of the study will ask questions about his/her physical and emotional health. This information will be collected for five years. A trained interviewer will contact your child by telephone before his/her transplant, then 6 months, 1 year, 2 years and 5 years after the transplant. These interviews will last approximately 15-25 minutes and will be done at a convenient time for your child. They will include questions about side effects, health problems and how well your child can do things that are important to him/her. When your child is contacted, your child may skip any questions he/she doesn't want to answer.

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

8. Possible Discomforts and Risks

Your child will face risks from the transplant itself and from treatments given before and after the transplant. Your child's doctor thinks these risks are less than the risk from the disease for which your child is receiving a transplant.

The bone marrow and PBSCs from the donor contain blood stem cells, which allow your child's 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 child's bone marrow will not work well enough and he/she 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. Your child will get platelets and red cells as needed to keep his/her counts at a healthy level.

There is a risk that stem cells may not grow after being given to your child. This is called graft failure. Graft failure can be fatal unless your child has a second transplant. Failure of the donor cells to grow (graft failure) may result from a mismatch with the donor, infections, a reduced effect of pre-transplant medications on your child's 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

child's 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 makes your child 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 child's 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 your child is not randomly assigned to that study group, your child may not receive the same benefits as those children in the study group with overall better results.

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

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

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 or your child want to stop being in the study. We will let you know if this happens and you can decide if you want to continue to allow your child to be in the study.

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

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

- No treatment
- Chemotherapy
- A transplant using your child's 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 your child is randomly assigned to that study group, he/she 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 your child will benefit from participating in this study.

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

12. Cost of Participating in the Study

You and/or your child's 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 child's transplant and this study, please contact /Center/ Financial Counselor at /Number/.

13. Reimbursement for Participating in the Study

You or your child will not be paid for participating in this study.

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

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

Contact your child's 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 your child 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 your child from the study but he/she may still receive a blood stem cell transplant. If you decide to withdraw your child from the study after your child has had some or all of the pre-transplant treatments and decide to have no transplant at all, then your child's blood counts may not return and he/she could die.

If you decide to withdraw your child 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 your child, there will be no penalty or loss of benefit to which your child is entitled, and he/she will continue to receive medical care.

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

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

16. Reasons Your Child's Doctor May Take Your Child off the Study

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

- Your child would be harmed by staying in the study.
- Your child needs treatment not allowed in this study.
- Your child does not follow directions that are important to participating in the study.
- The study is cancelled.

17. Protection of Your Child's Privacy and Confidentiality of Your Child's Research Records

Your child's participation in this research study will be kept private and confidential. All your child's 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 child's 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 child's research and medical information for inspections or audits. In allowing your child to participate, you consent to such inspections and to the copying of excerpts from your child's records, if required by these authorized representatives.

Organizations with access to your child's 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., and 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. Your child would not be identified in these presentations and publications.

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

18. Expiration Date for Keeping Your Child's 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 child's research records or access to your child's files, please call /name/ at /number/.

19. Benefit to Doctors for Your Child's Participation in the Study

Your child's 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 your child will receive his/her transplant is paid for participating in the study.

20. Blood Samples for Research Purposes

You will be asked to allow your child 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 allow your child to participate in this part of the study.

If you agree, your child 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 amount of blood drawn will never be more than what is safe for your child to provide. The blood can usually be drawn from your child's 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 your child 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. Your child may still receive the vaccinations as part of his/her standard medical care even if your child does not 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 child's blood samples drawn for research purposes will be sent to laboratories that have a contract with the NMDP to conduct these research tests. Your child's blood will be labeled with a unique code that contains no information that could identify him/her. 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 child's blood is being tested does not have a link to this code. Your child's blood will be stored at these laboratories until all the sample has been used for the research tests or until the end of the study.

If any of your child's 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 child's 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 your child. 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> allow your child to take part in this research and still allow your child to participate in the other parts of the study. There will be no change in your child's care if you choose not to allow your child to give blood samples for research purposes. Please mark your choice below (check only one box):

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

_____ _____
Signature of Parent/Legal Guardian *Date*

_____ _____
Signature of Parent/Legal Guardian *Date*

The signatures of both parents (or legal guardians) are required.

21. Parental/Legal Guardian Consent
The signatures of both parents (or legal guardians) are required.

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 allow my child to participate in this study.

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

_____ _____
Signature of Parent/Legal Guardian *Date*

_____
Print Name of Parent/Legal Guardian

_____ _____
Signature of Parent/Legal Guardian *Date*

_____
Print Name of Parent/Legal Guardian

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.

Attachment A

Additional Risks and Toxicities Related to the Standard Transplant Procedure
Total Body Radiation and Cyclophosphamide Conditioning Regimen

There are certain risks related to a bone marrow or peripheral blood stem cell (PBSC) transplant. There are risks from the medications and irradiation therapy your child will receive as part of the conditioning for the transplant and risks related to the transplant itself. Most of these risks and side effects are listed below, but they will vary from person to person. There may be more risks involved with transplantation, and there may be more side effects. Your child's doctor may give your child medications to lessen some of the side effects.

Risks Related to the Transplant Conditioning Regimen

Cyclophosphamide (Cytoxan): This is a common medication used to treat cancer. This medication kills cancer cells by stopping them from growing. Cyclophosphamide may cause your child to have diarrhea (loose stools), nausea (feeling sick to your stomach), vomiting (throwing up), short-term hair loss, short-term bladder problems, and, at times, bleeding from the bladder. A few patients may have bladder damage and bleeding for a longer time. Your child will be given large amounts of a sterile solution through his/her central line to protect the bladder. A bladder catheter (thin plastic tube) may be inserted into your child's bladder, if your child's physician thinks that it can help him/her. Cyclophosphamide slows the making of new red blood cells, white blood cells, and platelets. This causes a risk of infection and/or severe bleeding until the transplanted donor cells begin to work in your child. Your child will get blood transfusions as needed. Cyclophosphamide also lowers the defense system. As a result your child may have more infections for several months after transplant. In a small number of patients, cyclophosphamide can damage the heart muscle causing heart failure. Sometimes cyclophosphamide causes abnormal heart function. If this occurs your child may have shortness of breath and have fluids build-up in his/her body. This medication can also cause the lungs to become scarred. If scarring of the lungs occurs it will usually happen three to six months after your child receives the medication. Scarring of the lungs can cause your child to die. Cyclophosphamide can adversely affect the production of hormones responsible for the onset and completion of puberty and the number and function of eggs (girls) and sperm (boys) leading to decreased fertility and even sterility. The onset of puberty can be delayed in your child and your child's ultimate height can be decreased. Since it is not possible to predict in a specific child the extent of these effects, it is important that your child has continuing, careful follow-up after the transplant. It is not known whether the use of cyclophosphamide will cause more side effects or problems with your child's health in the future.

Total Body Irradiation (TBI): TBI may cause your child to have diarrhea (loose stools), nausea (feeling sick to your stomach), vomiting (throwing up), and painful swelling of the saliva glands for a few days. Your child may also experience short-term hair loss. TBI kills both sick and normal marrow, leading to a lack of red blood cells, white blood cells, and platelets. The short-term loss of these blood cells could cause your child to become anemic, develop an infection, and/or bleeding. This will continue until the transplanted donor cells begin to work in your child. Your child will get blood transfusions as needed. There is a risk that cataracts (cloudiness) may develop in your child's eyes. This may mean partial loss of vision, and your child may need contact lenses or surgery to remove the cataracts. TBI can adversely affect the production of hormones responsible for the onset and completion of puberty and the number and function of eggs (girls) and sperm (boys) leading to decreased fertility and even sterility. The onset of puberty can be delayed in your child and your child's ultimate height can be decreased. Since it is not possible to predict in a specific child the extent of these effects, it is important that your child has

continuing, careful follow-up after the transplant. It is not known whether the use of TBI will cause more side effects or problems with your child's health in the future.

Risks Related to the Infusion of Bone Marrow or Peripheral Blood Stem Cells (PBSC)

The infusion of bone marrow or PBSC usually has few side effects. Rarely the infusion may cause a headache, chest pain or trouble breathing, a slight fever, or blood in the urine. Very rarely, it may cause an allergic reaction (which shows up as a severe drop in blood pressure and may cause loss of consciousness).

Risks Related to the Medications Used to Help Prevent Graft-Versus-Host Disease (GVHD)

Cyclosporine or Tacrolimus: These medications are used to try to prevent GVHD. These two medications have similar side effects. The immediate side effects your child may experience include nausea (feeling sick to your stomach) or vomiting (throwing up) when the medications are given orally. Other side effects your child may experience include high blood pressure (hypertension), shaking of the hands (tremor), increased hair growth and possibly an effect on mental function. If your child experiences these effects they generally go away when the dose of the medication is decreased. A few patients have had a seizure while taking these medications. Your child may experience a change of liver or kidney function, in which case the medication dose will be reduced or possibly even withheld. The effect on kidneys seems to increase when other medications, which might cause kidney problems, are given at the same time, especially antibiotics. Occasionally, the kidney damage caused may require the use of an artificial kidney machine (hemodialysis).

Some patients when given cyclosporine through a vein to treat GVHD, experience a painful sensation in their hands or feet or both. The pain decreases or goes away when the GVHD improves or when the cyclosporine is given by mouth instead of through a vein.

Some patients given tacrolimus develop diabetes and must take insulin while taking tacrolimus.

Methotrexate: This is also a medication used to try to prevent GVHD. Methotrexate causes damage to cells, and therefore can affect many different tissues of your child's body. It may cause or can worsen the mouth sores or inflammation of the mouth which your child may have already developed from the procedures and medications used to prepare him/her for the transplant. Methotrexate may slow down the recovery of blood cells after transplantation. Methotrexate can cause kidney damage. If your child's kidneys are already damaged for other reasons, it can worsen kidney function. If kidney damage does occur, the methotrexate dose may be reduced or the medication may not be given at all.

Cyclosporine, Tacrolimus, Methotrexate, and Steroids: These medications interfere with the body's defense system (the immune system). This may cause your child to have more infections (especially viral infections and pneumonia) for several months after transplant.

If other agents are used for GVHD prophylaxis, then analogous paragraphs describing risk of those agents must be added to your version of the consent form.

Risks Related to the Transplant Procedure

The following risks are not specifically related to any one medication or the transplanted donor cells, but they are risks that are a part of the transplant procedure.

Bleeding: Platelets help the blood to clot. Your child's platelets will be low until the new bone marrow grows and, as a result, bleeding may occur. This can be minor bleeding, such as nosebleeds or bruising, but more serious, life-threatening bleeding in the lungs and brain can occur if the platelet count remains low. Usually, there is success in preventing major bleeding problems with transfusions of platelets. However, some patients may not respond well to transfused platelets and may be at serious risk for bleeding.

Veno-Occlusive Disease (VOD): This can occur as a result of high dose chemotherapy, irradiation therapy, or both. VOD causes severe damage to the liver. Symptoms include jaundice (yellowing of the skin and eyes), weight gain, and extra fluid build-up in the abdominal cavity and other parts of the body. It can often be managed successfully, and completely resolve. However, complications can arise that may be fatal.

Mouth Sores and Diarrhea: The large doses of medicines and irradiation cause irritation in the lining of the mouth and intestines. This can result in painful mouth sores and diarrhea. If your child has severe mouth sores he/she will be given medicine to help control the pain. If your child's mouth sores are severe, he/she may not be able to eat normally until the sores are healed. Mouth sores get better when the white blood count starts to rise, and engraftment occurs.

Capillary Leak Syndrome: This may occur as a result of chemotherapy and irradiation therapy. The blood vessels may become 'leaky' and fluid enters the abdominal cavity, lungs, and other tissues. Your child may gain water weight and not go to the bathroom as often as he/she normally does. Capillary leak syndrome can be difficult to manage if extra fluid enters the lungs and causes difficulty breathing. Your child may die if there is continued fluid collection in the lungs.

Unexpected Organ Damage and Other Side Effects: It is possible your child may experience unexpected, life-threatening heart, lung, kidney, or liver damage as a result of the transplant. Occasionally, the high doses of chemotherapy and irradiation cause severe lung damage that cannot always be treated. If this happens, your child may need to use oxygen or even a respirator. The lung damage may get worse and be life-threatening. Rarely, multi-organ failure (such as lung and kidney failure) may occur, which is often fatal.

Late Effects: Your child may experience side effects that occur several months to many years after the transplant. Your child may experience poor function of the thyroid gland, requiring him/her to take thyroid medication. As a result of irradiation, cataracts (cloudiness of the eyes) may occur earlier in life as compared to a person who had not had a transplant. If your child develops cataracts they may require treatment. It is rare, but your child's kidneys could be affected, causing anemia (low red blood cell count) or high blood pressure. There is also a risk your child may develop a second cancer as a result of the chemotherapy, irradiation and/or underlying disease. If secondary cancers occur they generally do not occur until 10 to 15 years after the transplant. The long-term effects upon heart, lung, and brain are unknown.

Fluid Build-up: Your child will receive intravenous fluids during the transplant process and he/she may have difficulty eliminating this fluid. Furosemide is a medication that is often given to help eliminate this excess fluid. This medication may cause hearing loss and loss of body chemicals such as potassium and sodium.

Attachment B

Additional Risks and Toxicities Related to the Standard Transplant Procedure
Busulfan and Cyclophosphamide Conditioning Regimen

There are certain risks related to a bone marrow or peripheral blood stem cell (PBSC) transplant. There are risks from the medications your child will receive as part of the conditioning for the transplant, and risks related to the transplant itself. Most of these risks and side effects are listed below, but they will vary from person to person. There may be more risks involved with transplantation, and there may be more side effects. Your child's doctor may give your child medications to lessen some of the side effects.

Risks Related to the Transplant Conditioning Regimen

Cyclophosphamide (Cytoxan): This is a common medication used to treat cancer. This medication kills cancer cells by stopping them from growing. Cyclophosphamide may cause your child to have diarrhea (loose stools), nausea (feeling sick to your stomach), vomiting (throwing up), short-term hair loss, short-term bladder problems, and, at times, bleeding from the bladder. A few patients may have bladder damage and bleeding for a longer time. Your child will be given large amounts of a sterile solution through the central line to protect his/her bladder. A bladder catheter (thin plastic tube) may be inserted into your child's bladder, if your child's physician thinks that it can help him/her. Cyclophosphamide slows the making of new red blood cells, white blood cells, and platelets. This causes a risk of infection and/or severe bleeding until the transplanted donor cells begin to work in your child. Your child will get blood transfusions as needed. Cyclophosphamide also lowers the defense system. As a result your child may have more infections for several months after transplant. I n a small number of patients, cyclophosphamide can damage the heart muscle causing heart failure. Sometimes cyclophosphamide causes abnormal heart function. If this occurs your child may have shortness of breath and have fluids build-up in his/her body. This medication can also cause the lungs to become scarred. If scarring of the lungs occurs it will usually happen three to six months after your child receives the medication. Scarring of the lungs can cause your child to die. Cyclophosphamide can adversely affect the production of hormones responsible for the onset and completion of puberty and the number and function of eggs (girls) and sperm (boys) leading to decreased fertility and even sterility. The onset of puberty can be delayed in your child and your child's ultimate height can be decreased. Since it is not possible to predict in a specific child the extent of these effects, it is important that your child has continuing careful follow-up after the transplant. It is not known whether the use of cyclophosphamide will cause more side effects or problems with your child's health in the future.

Busulfan: This medication disrupts the growth of cancer cells and destroys them. While taking busulfan your child most likely will have diarrhea (loose stools), nausea (feeling sick to your stomach), vomiting (throwing up), lower white blood cell count that increases the risk of infection, lower platelet count that increases the risk of bleeding, hair loss, stopping of menstrual periods in girls who have reached puberty, temporary reduced or no sperm production in boys who have reached puberty. Less likely side effects that your child may experience are fatigue, sores in the mouth or on the lips, fever, rash, loss of appetite, changes in color of the skin, seizure. Rare side effects that your child may experience are damage to the lungs, which may cause him/her to cough, be short of breath, and have trouble breathing. It is rare, but busulfan can also cause changes in your child's liver function.

Risks Related to the Infusion of Bone Marrow or Peripheral Blood Stem Cells (PBSC)

The infusion of bone marrow or PBSC usually has few side effects. Rarely the infusion may cause a headache, chest pain or trouble breathing, a slight fever, or blood in the urine. Very rarely, it may cause an allergic reaction (which shows up as a severe drop in blood pressure and may cause loss of consciousness).

Risks Related to the Medications Used to Help Prevent Graft-Versus-Host Disease (GVHD)

Cyclosporine or Tacrolimus: These medications are used to try to prevent GVHD. These two medications have similar side effects. The immediate side effects your child may experience include nausea (feeling sick to your stomach) or vomiting (throwing up) when the medications are given orally. Other side effects your child may experience include high blood pressure (hypertension), shaking of the hands (tremor), increased hair growth and possibly an effect on mental function. If your child experiences these effects they generally go away when the dose of the medication is decreased. A few patients have had a seizure while taking these medications. Your child may experience a change of liver or kidney function, in which case the medication dose will be reduced or possibly even withheld. The effect on kidneys seems to increase when other medications, which might cause kidney problems, are given at the same time, especially antibiotics. Occasionally, the kidney damage caused may require the use of an artificial kidney machine (hemodialysis).

Some patients when given cyclosporine through a vein to treat GVHD, experience a painful sensation in their hands or feet or both. The pain decreases or goes when the GVHD improves or when the cyclosporine is given by mouth instead of through a vein.

Some patients given tacrolimus develop diabetes and must take insulin while taking tacrolimus.

Methotrexate: This is also a medication used to try to prevent GVHD. Methotrexate causes damage to cells, and therefore can affect many different tissues of your child's body. It may cause or can worsen the mouth sores or inflammation of the mouth which your child may have already developed from the procedures and medications used to prepare him/her for the transplant. Methotrexate may slow down the recovery of blood cells after transplantation. Methotrexate can cause kidney damage. If your child's kidney is already damaged for other reasons, it can worsen kidney function. If kidney damage does occur, the methotrexate dose may be reduced or the medication may not be given at all.

Cyclosporine, Tacrolimus, Methotrexate, and Steroids: These medications interfere with the body's defense system (the immune system). This may cause your child to have more infections (especially viral infections and pneumonia) for several months after transplant.

If other agents are used for GVHD prophylaxis, then analogous paragraphs describing risk of those agents must be added to your version of the consent form.

Risks Related to the Transplant Procedure

The following risks are not specifically related to any one drug or the transplanted donor cells, but they are risks that are a part of the transplant procedure.

Bleeding: Platelets help the blood to clot. Your child's platelets will be low until the new bone marrow grows and, as a result, bleeding may occur. This can be minor bleeding, such as nosebleeds or bruising,

but more serious, life-threatening bleeding in the lungs and brain can occur if the platelet count remains low. Usually, there is success in preventing major bleeding problems with transfusions of platelets. However, some patients may not respond well to transfused platelets and may be at serious risk for bleeding.

Veno-Occlusive Disease (VOD): This can occur as a result of high dose chemotherapy. VOD causes severe damage to the liver. Symptoms include jaundice (yellowing of the skin and eyes), weight gain, and extra fluid build-up in the abdominal cavity and other parts of the body. It can often be managed successfully, and completely resolve. However, complications can arise that may be fatal.

Mouth Sores and Diarrhea: The large doses of medicines cause irritation in the lining of the mouth and intestines. This can result in painful mouth sores and diarrhea. If your child has severe mouth sores he/she will be given medicine to help control the pain. If your child's mouth sores are severe, he/she may not be able to eat normally until the sores are healed. Mouth sores get better when the white blood count starts to rise, and engraftment occurs.

Capillary Leak Syndrome: This may occur as a result of chemotherapy. The blood vessels may become 'leaky' and fluid enters the abdominal cavity, lungs, and other tissues. Your child may gain water weight and not go to the bathroom as often as she/she normally does. Capillary leak syndrome can be difficult to manage if extra fluid enters the lungs and causes difficulty breathing. Your child may die if there is continued fluid collection in the lungs.

Unexpected Organ Damage and Other Side Effects: It is possible your child may experience unexpected, life-threatening heart, lung, kidney, or liver damage as a result of the transplant. Occasionally, the high doses of chemotherapy cause severe lung damage that can not always be treated. If this happens, your child may need to use oxygen or even a respirator. The lung damage may get worse and be life-threatening. Rarely, multi-organ failure (such as lung and kidney failure) may occur, which is often fatal.

Late Effects: Your child may experience side effects that occur several months to many years after the transplant. Your child may experience poor function of the thyroid gland, requiring him/her to take thyroid medication. It is rare, but your child's kidneys could be affected, causing anemia (low red blood cell count) or high blood pressure. There is also a risk your child may develop a second cancer as a result of the chemotherapy and/or underlying disease. If secondary cancers occur they generally do not occur until 10 to 15 years after the transplant. The long-term effects upon heart, lung, and brain are unknown.

Fluid Build-up: Your child will receive intravenous fluids during the transplant process and he/she may have difficulty eliminating this fluid. Furosemide is a medication that is often given to help eliminate this excess fluid. This medication may cause hearing loss and loss of body chemicals such as potassium and sodium.

Attachment C

Additional Risks and Toxicities Related to the Standard Transplant Procedure
Fludarabine and Melphalan Conditioning Regimen

There are certain risks related to a bone marrow or peripheral blood stem cell PBSC) transplant. There are risks from the medications your child will receive as part of the conditioning for the transplant and risks related to the transplant itself. Most of these risks and side effects are listed below, but they will vary from person to person. There may be more risks involved with transplantation, and there may be more side effects. Your child's doctor may give your child medications to lessen some of the side effects.

Risks Related to the Transplant Conditioning Regimen

Fludarabine: This is a medication used to treat cancer. It is used in stem cell transplants to reduce the risk of rejecting the donor's transplanted cells. Likely side effects your child may experience are low white blood cell count with increased risk of infection, low platelet count with increased risk of bleeding, feeling tired or sleepy, and anemia (low red blood cell count). Rare side effects your child may experience include confusion or coma, trouble seeing or problems with your child's eyes, trouble breathing, diarrhea (loose stools), nausea (feeling sick to your stomach), vomiting (throwing up), pneumonia, agitation, numbness and tingling of the fingertips and toes, and kidney problems.

Melphalan: This medication disrupts the growth of cancer cells and destroys them. Side effects your child most likely will experience include nausea (feeling sick to stomach), hair loss, and low white blood cell count, which may lead to infection. Less likely side effects your child may experience include diarrhea (loose stools), mouth ulcers, and low platelet count with increased risk of bleeding. It is rare, but your child may experience a severe allergic reaction. Symptoms of a severe allergic reaction include itching, hives (bumps on the skin), flushing (redness), wheezing, chest tightness, skin rashes, fever, chills, muscle stiffening, severe breathing problems, and loss of appetite.

Risks Related to the Infusion of Bone Marrow or Peripheral Blood Stem Cells (PBSC)

The infusion of bone marrow or PBSC usually has few side effects. Rarely the infusion may cause a headache, chest pain or trouble breathing, a slight fever, or blood in the urine. Very rarely, it may cause an allergic reaction (which shows up as a severe drop in blood pressure and may cause loss of consciousness).

Risks Related to the Medications Used to Help Prevent Graft-Versus-Host Disease (GVHD)

Cyclosporine or Tacrolimus: These medications are used to try to prevent GVHD. These two medications have similar side effects. The immediate side effects your child may experience include nausea (feeling sick to your stomach) or vomiting (throwing up) when the medications are given orally. Other side effects your child may experience include high blood pressure (hypertension), shaking of the hands (tremor), increased hair growth and possibly an effect on mental function. If your child experiences these effects, they generally go away when the dose of the medication is decreased. A few patients have had a seizure while taking these medications. Your child may experience a change of liver or kidney function, in which case the medication dose will be reduced or possibly even withheld. The effect on kidneys seems to increase when other medications, which might cause kidney problems, are

given at the same time, especially antibiotics. Occasionally, the kidney damage caused may require the use of an artificial kidney machine (hemodialysis).

Some patients when given cyclosporine through a vein to treat GVHD, experience a painful sensation in their hands or feet or both. The pain decreases or goes away when the GVHD improves or when the cyclosporine is given by mouth instead of through a vein.

Some patients given tacrolimus develop diabetes and must take insulin while taking tacrolimus.

Methotrexate: This is also a medication used to try to prevent GVHD. Methotrexate causes damage to cells, and therefore can affect many different tissues of your body. It may cause or can worsen the mouth sores or inflammation of the mouth which your child may have already developed from the procedures and medications used to prepare him/her for the transplant. Methotrexate may slow down the recovery of blood cells after transplantation. Methotrexate can cause kidney damage. If your child's kidneys are already damaged for other reasons, it can worsen kidney function. If kidney damage does occur, the methotrexate dose may be reduced or the medication may not be given at all.

Cyclosporine, Tacrolimus, Methotrexate, and Steroids: These medications interfere with the body's defense system (the immune system). This may cause your child to have more infections (especially viral infections and pneumonia) for several months after transplant.

If other agents are used for GVHD prophylaxis, then analogous paragraphs describing risk of those agents must be added to your version of the consent form.

Risks Related to the Transplant Procedure

The following risks are not specifically related to any one medication or the transplanted donor cells, but they are risks that are a part of the transplant procedure.

Bleeding: Platelets help the blood to clot. Your child's platelets will be low until the new bone marrow grows and, as a result, bleeding may occur. This can be minor bleeding, such as nosebleeds or bruising, but more serious, life-threatening bleeding in the lungs and brain can occur if the platelet count remains low. Usually, there is success in preventing major bleeding problems with transfusions of platelets. However, some patients may not respond well to transfused platelets and may be at serious risk for bleeding.

Veno-Occlusive Disease (VOD): This can occur as a result of high dose chemotherapy. VOD causes severe damage to the liver. Symptoms include jaundice (yellowing of the skin and eyes), weight gain, and extra fluid build-up in the abdominal cavity and other parts of the body. It can often be managed successfully, and completely resolve. However, complications can arise that may be fatal.

Mouth Sores and Diarrhea: The large doses of medicines cause irritation in the lining of the mouth and intestines. This can result in painful mouth sores and diarrhea. If your child has severe mouth sores he/she will be given medicine to help control the pain. If your child's mouth sores are severe, he/she may not be able to eat normally until the sores are healed. Mouth sores get better when the white blood count starts to rise, and engraftment occurs.

Capillary Leak Syndrome: This may occur as a result of chemotherapy. The blood vessels may become 'leaky' and fluid enters the abdominal cavity, lungs, and other tissues. Your child may gain water weight and not go to the bathroom as often as he/she normally does. Capillary leak syndrome can be difficult to

manage if extra fluid enters the lungs and causes difficulty breathing. Your child may die if there is continued fluid collection in the lungs.

Unexpected Organ Damage and Other Side Effects: It is possible your child may experience unexpected, life-threatening heart, lung, kidney, or liver damage as a result of the transplant. Occasionally, the high doses of chemotherapy cause severe lung damage that can not always be treated. If this happens, your child may need to use oxygen or even a respirator. The lung damage may get worse and be life-threatening. Rarely, multi-organ failure (such as lung and kidney failure) may occur, which is often fatal.

Late Effects: Your child may experience side effects that occur several months to many years after the transplant. Your child may experience poor function of the thyroid gland, requiring him/her to take thyroid medication. It is rare, but your child's kidneys could be affected, causing anemia (low red blood cell count) or high blood pressure. There is also a risk your child may develop a second cancer as a result of the chemotherapy and/or underlying disease. If secondary cancers occur they generally do not occur until 10 to 15 years after the transplant. The long-term effects upon heart, lung, and brain are unknown.

Fluid Build-up: Your child will receive intravenous fluids during the transplant process and he/she may have difficulty eliminating all of this fluid. Furosemide is a medication that is often given to help eliminate this excess fluid. This medication may cause hearing loss and loss of body chemicals such as potassium and sodium.

Attachment D

Additional Risks and Toxicities Related to the Standard Transplant Procedure
Fludarabine and Busulfan Conditioning Regimen

There are certain risks related to a bone marrow or peripheral blood stem cell (PBSC) transplant. There are risks from the medications your child will receive as part of the conditioning for the transplant, and risks related to the transplant itself. Most of these risks and side effects are listed below, but they will vary from person to person. There may be more risks involved with transplantation, and there may be more side effects. Your child's doctor may give your child medications to lessen some of the side effects.

Risks Related to the Transplant Conditioning Regimen

Fludarabine: This is a medication used to treat cancer. It is used in stem cell transplants to reduce the risk of rejecting the donor's transplanted cells. Likely side effects your child may experience are low white blood cell count with increased risk of infection, low platelet count with increased risk of bleeding, feeling tired or sleepy, and anemia (low red blood cell count). Rare side effects your child may experience include confusion or coma, trouble seeing or problems with your child's eyes, trouble breathing, diarrhea (loose stools), nausea (feeling sick to your stomach), vomiting (throwing up), pneumonia, agitation, numbness and tingling of the fingertips and toes, and kidney problems.

Busulfan: This medication disrupts the growth of cancer cells and destroys them. While taking busulfan your child most likely will have diarrhea (loose stools), nausea (feeling sick to your stomach), vomiting (throwing up), lower white blood cell count that increases the risk of infection, lower platelet count that increases the risk of bleeding, hair loss, stopping of menstrual periods in girls who have reached puberty, temporary reduced or no sperm production in boys who have reached puberty. Less likely side effects that your child may experience are fatigue, sores in the mouth or on the lips, fever, rash, loss of appetite, changes in color of the skin, seizure. Rare side effects that your child may experience are damage to the lungs, which may cause him/her to cough, be short of breath, and have trouble breathing. It is rare, but busulfan can also cause changes in your child's liver function.

Antithymocyte Globulin (ATG): This medication is given pre-transplant with the conditioning regimen medications to try and prevent both acute and chronic graft-versus-host disease. While taking ATG your child will most likely will have, a fever and chills, a lower white blood cell count that increases your child's risk of infection, a lower platelet count that increases your child's risk of bleeding, and a skin rash. Less likely side effects your child may experience are fatigue, diarrhea, vomiting, muscle aches and headaches. Rare side effects that your child may experience are changes in your blood pressures (either higher or lower blood pressure), rapid heart beat, be short of breath and have trouble breathing, chest pain and retention of fluids.

Risks Related to the Infusion of Bone Marrow or Peripheral Blood Stem Cells (PBSC)

The infusion of bone marrow or PBSC usually has few side effects. Rarely the infusion may cause a headache, chest pain or trouble breathing, a slight fever, or blood in the urine. Very rarely, it may cause an allergic reaction (which shows up as a severe drop in blood pressure and may cause loss of consciousness).

Risks Related to the Medications Used to Help Prevent Graft-Versus-Host Disease (GVHD)

Cyclosporine or Tacrolimus: These medications are used to try to prevent GVHD. These two medications have similar side effects. The immediate side effects your child may experience include nausea (feeling sick to your stomach) or vomiting (throwing up) when the medications are given orally. Other side effects your child may experience include high blood pressure (hypertension), shaking of the hands (tremor), increased hair growth and possibly an effect on mental function. If your child experiences these effects they generally go away when the dose of the medication is decreased. A few patients have had a seizure while taking these medications. Your child may experience a change of liver or kidney function, in which case the medication dose will be reduced or possibly even withheld. The effect on kidneys seems to increase when other medications, which might cause kidney problems, are given at the same time, especially antibiotics. Occasionally, the kidney damage caused may require the use of an artificial kidney machine (hemodialysis).

Some patients when given cyclosporine through a vein to treat GVHD, experience a painful sensation in their hands or feet or both. The pain decreases or goes when the GVHD improves or when the cyclosporine is given by mouth instead of through a vein.

Some patients given tacrolimus develop diabetes and must take insulin while taking tacrolimus.

Methotrexate: This is also a medication used to try to prevent GVHD. Methotrexate causes damage to cells, and therefore can affect many different tissues of your child's body. It may cause or can worsen the mouth sores or inflammation of the mouth which your child may have already developed from the procedures and medications used to prepare him/her for the transplant. Methotrexate may slow down the recovery of blood cells after transplantation. Methotrexate can cause kidney damage. If your child's kidney is already damaged for other reasons, it can worsen kidney function. If kidney damage does occur, the methotrexate dose may be reduced or the medication may not be given at all.

Cyclosporine, Tacrolimus, Methotrexate, and Steroids: These medications interfere with the body's defense system (the immune system). This may cause your child to have more infections (especially viral infections and pneumonia) for several months after transplant.

If other agents are used for GVHD prophylaxis, then analogous paragraphs describing risk of those agents must be added to your version of the consent form.

Risks Related to the Transplant Procedure

The following risks are not specifically related to any one drug or the transplanted donor cells, but they are risks that are a part of the transplant procedure.

Bleeding: Platelets help the blood to clot. Your child's platelets will be low until the new bone marrow grows and, as a result, bleeding may occur. This can be minor bleeding, such as nosebleeds or bruising, but more serious, life-threatening bleeding in the lungs and brain can occur if the platelet count remains low. Usually, there is success in preventing major bleeding problems with transfusions of platelets. However, some patients may not respond well to transfused platelets and may be at serious risk for bleeding.

Veno-Occlusive Disease (VOD): This can occur as a result of high dose chemotherapy. VOD causes severe damage to the liver. Symptoms include jaundice (yellowing of the skin and eyes), weight gain,

and extra fluid build-up in the abdominal cavity and other parts of the body. It can often be managed successfully, and completely resolve. However, complications can arise that may be fatal.

Mouth Sores and Diarrhea: The large doses of medicines cause irritation in the lining of the mouth and intestines. This can result in painful mouth sores and diarrhea. If your child has severe mouth sores he/she will be given medicine to help control the pain. If your child's mouth sores are severe, he/she may not be able to eat normally until the sores are healed. Mouth sores get better when the white blood count starts to rise, and engraftment occurs.

Capillary Leak Syndrome: This may occur as a result of chemotherapy. The blood vessels may become 'leaky' and fluid enters the abdominal cavity, lungs, and other tissues. Your child may gain water weight and not go to the bathroom as often as she/she normally does. Capillary leak syndrome can be difficult to manage if extra fluid enters the lungs and causes difficulty breathing. Your child may die if there is continued fluid collection in the lungs.

Unexpected Organ Damage and Other Side Effects: It is possible your child may experience unexpected, life-threatening heart, lung, kidney, or liver damage as a result of the transplant. Occasionally, the high doses of chemotherapy cause severe lung damage that cannot always be treated. If this happens, your child may need to use oxygen or even a respirator. The lung damage may get worse and be life-threatening. Rarely, multi-organ failure (such as lung and kidney failure) may occur, which is often fatal.

Late Effects: Your child may experience side effects that occur several months to many years after the transplant. Your child may experience poor function of the thyroid gland, requiring him/her to take thyroid medication. It is rare, but your child's kidneys could be affected, causing anemia (low red blood cell count) or high blood pressure. There is also a risk your child may develop a second cancer as a result of the chemotherapy and/or underlying disease. If secondary cancers occur they generally do not occur until 10 to 15 years after the transplant. The long-term effects upon heart, lung, and brain are unknown.

Fluid Build-up: Your child will receive intravenous fluids during the transplant process and he/she may have difficulty eliminating this fluid. Furosemide is a medication that is often given to help eliminate this excess fluid. This medication may cause hearing loss and loss of body chemicals such as potassium and sodium.

APPENDIX B-2

DONOR CONSENT FORM

NATIONAL MARROW DONOR PROGRAM® (NMDP)
A PHASE III RANDOMIZED, MULTICENTER TRIAL COMPARING G-CSF MOBILIZED PERIPHERAL BLOOD STEM CELLS WITH MARROW TRANSPLANTATION FROM HLA COMPATIBLE UNRELATED DONORS

DONOR/SUBJECT RESEARCH CONSENT FORM

Would you be willing to take part in a research study?
Because you have been matched with a recipient in seeking a blood stem cell transplant, you are being asked to take part in a clinical trial (a type of research study). This research study is sponsored by the NMDP and the Blood and Marrow Clinical Trials Network (BMT CTN). In this clinical trial the blood-forming cells will be collected from either the donor's bone marrow or the donor's bloodstream. This research study will only include people who choose to be in it.

This form contains key facts about the study and what you will be asked to do if you take part. Please read it in detail and take your time to decide. You might want to view the PBSC vs. Marrow Randomized Clinical Trial Donor Consent video as well (also offered as a CD-ROM). If you do not want to take part in this study, you may still be asked to donate for this recipient.

If you have any questions, please ask your Donor Center Coordinator or the Donor Center Medical Director before you make your final choice. If you agree to take part, you will be given a copy of this consent form for your records.

1. Why is this study being done?
The National Marrow Donor Program® (NMDP) uses bone marrow and blood-forming cells from the bloodstream for transplantation. In the past, blood-forming cells were always taken from the bone marrow. Now we know that a drug called "filgrastim" can increase the number of blood-forming cells in the bloodstream so much that these cells can be collected from the bloodstream of donors and used for transplant. When these blood-forming cells are collected from the bloodstream they are called peripheral blood stem cells (PBSC).

When the NMDP compared recipients who received bone marrow with recipients who received PBSCs, there was no difference in survival between the two groups. But because the recipients in each group did not have the same characteristics (age, disease type and so on) more research is needed.

This study will randomly assign recipients and donors into the two groups (bone marrow or PBSC). This makes it fairer to compare the two groups.

The NMDP and the BMT CTN hope what they learn from this study will help doctors and future recipients and donors make the best choice for the type of blood-forming cells to use for transplant; bone marrow or PBSC. If you would like to know more about why this study is needed, read Attachment A.

This study has two main goals:

1. To see if recipients given blood-forming cells from a donor's bone marrow do better or worse than recipients given PBSCs.
2. To compare three things about donors who donate bone marrow to those who donate PBSCs:
   - What differences (if any) are there in physical side effects that donors feel?
   - What differences are there in the time it takes donors to recover?
   - How does the quality of life differ for the two types of donors? For instance: how does a donor feel emotionally, how does donation affect a donor's daily life, and what does the donor feel about the donation process?

2. What will happen if I take part in this research study?

If you agree to take part in this research study, your donation will be different in these three ways:

1. How you donate – from your bone marrow or your bloodstream – will be chosen at random. A computer will make this choice.
2. You will be asked to give four extra blood samples for research purposes.
3. You will be asked to answer questions about how you feel emotionally after the donation.

Your safety is important. After you join the study, your health will be checked just like any donor. To protect both you and the recipient, you will have:

- A complete check-up.
- Standard blood tests.
- Blood tests for diseases like hepatitis, West Nile virus and HIV.
- A check for sickle hemoglobin (hemoglobin S).
- If you are a woman, a test to see if you are pregnant.

These tests will help to make sure that donating is safe for both you and the recipient getting the donation. (If you have more questions about why the blood tests are needed, see Attachment B.) All donors will have these tests. You will have these tests before you know if you will donate bone marrow or PBSCs. You must be able to donate both ways – from your bone marrow or your bloodstream – to go forward in this study. If you are able to donate only one way and cannot go forward in this study, you may still be asked to donate for this recipient.

Either as part of your complete check-up or as part of some other scheduled blood draw, 9 teaspoons of blood will be drawn from a vein in your arm for research studies. Your blood will be tested for antibodies specific to germs that cause infection, for example, Hepatitis B. The antibody levels in your blood may be compared against the antibody levels in the recipient's blood after the transplant. These samples will also be used to better understand tissue matching between donors and recipients.

If you are able to go forward in the study, you will be chosen at random to donate either from your bone marrow or your bloodstream. This means that the way you donate will be picked by chance. A computer program will make the choice. You cannot choose how you will donate. You will have an equal chance of giving blood-forming cells from bone marrow or from your bloodstream. Your donation itself will be just the same as if you were not taking part in the study.

If you are chosen to donate bone marrow:

1. Getting Ready to Donate Bone Marrow

   You may be asked to donate blood for your own use (this is called "autologous" blood donation). Depending on how much bone marrow you are asked to donate, you may need to have one to three units (each unit is about a pint or about two cups) of your blood drawn and stored before the donation. You will be asked to sign a separate consent form each time you give a unit of blood. If your blood counts are low after your marrow donation, your stored blood will be given back to you by transfusion.

   The doctors at the transplant center where the recipient is being treated may also ask for a sample of your blood before the transplant. The blood will be used at the transplant center for tests needed in treating the recipient. For instance, DNA from your blood may be stored to help see which blood cells growing in the recipient after the transplant come from your cells and which come from the recipient's cells. You will not be asked to give more than about 20 teaspoons of blood. The blood will be drawn from a vein in your arm. This blood cannot be used for research studies without further consent from you.

2. Donating Bone Marrow

   Bone marrow is collected in an operating room in a hospital. You will be given either general anesthesia or spinal anesthesia. Before the bone marrow donation, you will meet with a doctor to discuss the type of anesthesia that will be used. (This consent form is not for the anesthesia or the actual bone marrow donation. At the hospital you will be asked to sign another consent form for the anesthesia and the bone marrow donation.)

   The amount of bone marrow you will be asked to donate depends on the size of the recipient. For safety reasons, no more than two teaspoons of bone marrow per pound of your body weight will be removed. For instance: if you weigh 150 pounds, no more than 6 cups of bone marrow would be taken.

   You will lie on your stomach for the donation. Your bone marrow will be taken out of your pelvic bone (iliac crest). The doctor taking the bone marrow will make at least two, and maybe more, very small cuts in the skin of your back that covers the pelvic bones. Hollow needles will be placed through these cuts and into the bone. After a needle is put in the marrow space of the bone, a syringe will be attached to the needle and the marrow will be drawn out. Once the bone marrow is taken, the anesthetic will be allowed to wear off and you will be returned to your hospital room.

   Your donated bone marrow may be tested to find out the number and types of cells, to make sure that it is sterile, and to learn other things that may be important to the transplant.

How much time will it take to donate bone marrow?

A list of visits and calls is given in the following table (an X marks what will happen on each visit/call):

Visit/Call	Risks Assessed	Unit of Blood Drawn and Stored	Bone Marrow Donated	Blood Drawn	Quality of Life Assessed by Phone
Screening check-up	X			X	
1st Quality of Life contact					X
Pre-donation appointment 1[a]		X		X	
Pre-donation appointment 2[a]		X			
Pre-donation appointment 3[a]		X			
Bone marrow donation	X		X	X	
2 days after donation (call)	X				X
1 week after donation[b] (call)	X				X
1 month after donation	X			X	
6 months after donation	X			X	X
1 year after donation	X			X	X
2 years after donation	X			X	
3 years after donation (study ends)	X			X	
Yearly visits after donation as part of the NMDP's routine donor follow up	X			X	

[a] The number of autologous blood units you give depends on how much bone marrow will be taken.
[b] Calls will continue weekly until complete healing from donation is reported.

What are the possible risks of donating bone marrow?

Caution: You should not take aspirin or aspirin-containing drugs for two weeks before your donation, or for soreness after it, without a doctor's approval.

GIVING A SAMPLE OF BLOOD	
Risks	*Very small, may include:* • Bruising where the needle was put in. • Fainting. • More rarely, infection where the needle was put in.
DONATING BONE MARROW	
Risks	*From the anesthetic:* For a few hours after your bone marrow has been taken, you may feel groggy and sick from the anesthetic. You will not be allowed to eat food or to get out of bed until you are wide awake and all the anesthetic has worn off. Even after the anesthetic has worn off, you may still be sick and faint for a period of time. *From the collection:* You should expect to feel some pain from the collection of the bone marrow. Most donors go through soreness in their lower back, like a back strain, that lasts for a few weeks. You may find it hard to sit in a chair for long periods of time or to climb stairs. You will most likely be less active than normal for the first two weeks after your donation. There are certain risks with donating bone marrow. Serious problems from bone marrow collection are rare but could occur due to an unexpected reaction to the anesthetic or trouble with the process of taking the bone marrow. *Possible risks with anesthetics include:* • High fever. • Allergic reaction. • Low blood pressure and a slowed heart rate. • Not able to pass urine for a brief time (spinal anesthesia). • Headache (spinal anesthesia). *Possible risks from donation include:* • Infection where the skin was cut to collect your bone marrow (requires antibiotic treatment). • Pain or numbness in a leg. • Bleeding where the skin was cut. • More severe pain than normal. • Bone, nerve or other tissue damage (requires more medical treatment or physical therapy). Life-threatening problems are extremely rare. But you should know, that as with any surgery, there is a risk of death.

Additional Risks
Donating can cause intense feelings, especially if the transplant does not succeed. These feelings may range from stress during the process to great joy or the blues after the donation. By donating for this recipient, you are doing all you can to help them. You cannot control the success of the transplant, or whether the recipient lives or dies. You should not feel personally responsible for the outcome.

You may be asked to donate again for the recipient if the donated cells do not grow in the recipient or if the recipient's disease is not cured. If you are asked to donate again, you are free to say no.

If you are chosen to donate PBSCs:

1. Getting Ready to Donate PBSCs

   The drug filgrastim has been shown to increase the number of blood-forming cells in the bloodstream. You will get a shot of filgrastim under your skin once a day for five days. Before each shot, you will be asked about any symptoms you may have. You will have blood samples (1½ to 3 teaspoons) taken from a vein in your arm before your shots on Day 1 and on Day 5. These samples are used to see how the drug affects your blood cell counts.

   The doctors at the transplant center where the recipient is being treated may also ask for a sample of your blood before the transplant. The blood will be used at the transplant center for tests needed in treating the recipient. For instance, DNA from your blood may be stored to help see which blood cells growing in the recipient after the transplant come from your cells and which come from the recipient's cells. You will not be asked to give more than about 20 teaspoons of blood. The blood will be drawn from a vein in your arm. This blood cannot be used for research studies without further consent from you.

2. Donating PBSCs

   PBSCs are donated in a hospital or blood center. Before you donate, a needle will be placed in a vein in each of your arms. Blood is removed through the needle in one arm and passed through a special machine called a blood cell separator. This process is called "apheresis." The machine collects your PBSCs, and the rest of your blood is given back through the needle in your other arm. You will make one or two PBSC donations, depending on the size of the recipient. During each donation you will need to lie fairly still in a recliner chair for four to six hours.

   With each donation, 2 teaspoons of blood will be taken at the start and at the end of the process to measure your blood cell counts. Your donation may be tested to find out the number and types of cells, to make sure that it is sterile, and to learn other things that may be important to the transplant.

Needing a Central Line
Sometimes, a donor's arm veins are not big enough for the needles used in the apheresis process. In the NMDP's experience, this happens in about 18% of women and 3% of men. If your veins are too small, you may be asked to have a special blood-drawing tube called a "central line" placed in a larger vein in your body. The choice to use a central line may be made at your complete check-up (when your veins will be checked) or it could be made on the day you donate.

Placing a central line requires a surgical procedure under local anesthesia. A doctor does this in a hospital. In this case, your collection will also take place in the hospital and, if you donate over two days, you will need to stay in the hospital the night between donations.

If a central line is recommended in your case, you will be asked to sign a separate consent form that explains the risks of central line placement. You are free to say no to having a central line placed. If you choose to not have the central line placement, you may be asked to donate bone marrow instead.

How much time will it take to donate PBSCs?

A list of visits and calls is given in the following table (an X marks what will happen on each visit/call):

Visit/Call	Risks Assessed	Filgrastim Shot Given	PBSCs Donated	Blood Drawn	Quality of Life Assessed by Phone
Screening check-up	X			X	
1st Quality of Life contact					X
Preparation, Day 1	X	X		X	
Preparation, Day 2	X	X			
Preparation, Day 3	X	X			
Preparation, Day 4	X	X			X
First donation, Day 5	X	X	X	X	
Second donation[a]	X		X	X	
2 days after donation (call)	X				X
1 week after donation[b] (call)	X				X
1 month after donation	X			X	
6 months after donation	X			X	X
1 year after donation	X			X	X
2 years after donation	X			X	
3 years after donation (study ends)	X			X	
Yearly visits after donation as part of the NMDP's routine donor follow up	X			X	

[a] If needed, based on size of the recipient.
[b] Calls will continue weekly until complete healing from donation is reported.

What are the possible risks of donating PBSCs?

Cautions: You should not take aspirin or drugs with aspirin in them while getting filgrastim and for two weeks after PBSC donation without a doctor's approval. During the PBSC donation, your platelet count may be lower because platelets are collected with the PBSCs. Taking aspirin when your platelet count is lower may increase your chance of bleeding.

You should not take filgrastim if you are pregnant. You should not become pregnant while taking filgrastim and for 48 hours after the last shot. This drug could cause serious problems for an unborn child.

The following table lists side effects and risks for receiving filgrastim and donating PBSCs.

GIVING A SAMPLE OF BLOOD	
Risks	*Some people have:* • Bruising where the needle was put in. • Fainting. *Very few people have:* • An infection where the needle was put in.

GETTING SHOTS OF FILGRASTIM	
Risks	*Most people have:* • Pain from the shot. • High white blood cell count. White blood cell counts usually return to normal levels within a few days to a few weeks after you stop receiving filgrastim. • Aching pain in bones while getting the filgrastim. The aching bone pain is usually relieved by acetaminophen (Tylenol™) or ibuprofen (Motrin™, Advil™). If you have pain that is not relieved by these drugs, you should contact the Donor Center Coordinator, _____ at ( ) _____, and the dose of filgrastim may be reduced. *Some people have:* • Headaches. • Muscle aches. • Being tired. • Nausea and vomiting. • Trouble sleeping. *Very few people have:* • Allergy symptoms: – rapid heart rate. – Dizziness. – shortness of breath. – itching or rash. All symptoms usually go away within two or three days after stopping filgrastim. • Lowered platelet count. Filgrastim may cause your platelet count to be lower than normal. Platelets help stop bleeding. Two out of 1400 NMDP donors had very low platelet counts that needed to be watched closely. Although one donor went into the hospital for this, neither had symptoms from the low platelet count and both got well.

GETTING SHOTS OF FILGRASTIM (cont'd)	
	Your platelet count will be measured on Day 5, before the first PBSC donation. You will be told if your platelet count is less than 80% of the lower limit of normal. In this case, depending on the true value of your platelet count, a doctor will talk with you about other options, such as to: – Monitor your platelet count during the PBSCs donation. – Shorten the donation process. – Delay the donation for a day. – Cancel the PBSCs donation. – Ask you to consider a bone marrow donation. – Ask you to consider some other course of action that is okay with you. • There is a small (about 1 in 1,200) risk of being hospitalized for observation of side effects from the filgrastim (for example bone pain, nausea). • There is a small (about 1 in 10,000) risk of pain and bleeding from the spleen. The NMDP is aware of four non-NMDP donors who had pain and bleeding from the spleen while getting filgrastim. In two cases the spleen was taken out by surgery. All four got well. Symptoms of bleeding from the spleen are pain in the upper left side just below the rib cage**. If you feel pain in this area you should contact your Donor Center right away, as this can be a risk.** • Based on limited long-term data from healthy people who have received filgrastim, no long-term risks have been found so far. Normal individuals are at risk for developing cancer, including leukemia, lymphoma or other blood diseases throughout their life time. It is unknown whether filgrastim increases or decreases an individuals risk of developing cancer. The data being collected during follow-up will help establish if there are any positive or negative long-term effects from receiving filgrastim. **If you think you are having any serious or unexpected symptoms, contact the Donor Center right away at ( ) _____.**

DONATING PBSCs	
Risks	*Most people have:* • Pain and bruising where the needles are put into the arms. • Lowered platelet count. In addition to collecting PBSCs, the blood cell separator also collects platelets. Platelets help stop bleeding. If your platelet count after the first donation is too low, the second donation may be cancelled. Platelet counts usually return to normal levels within two to four weeks after collection of PBSCs. *Some people have:* • Lightheadedness. • Nausea. • Numbness and tingling. To prevent clotting, your blood will be mixed in the machine with a liquid called an "anticoagulant" during the PBSC collection. When the blood is returned to you, the anticoagulant can cause numbness and tingling of the fingertips or around the mouth. If you feel numbness and tingling, you must tell the nurse running the machine. These symptoms are easily treated with calcium, but if not treated could progress to muscle cramps. *Very few people:* • Faint due to short-term low blood pressure. • Experience chills during the process. • Experience severe bleeding in the arm. • Have a loss of blood from a breakdown of the blood cell separator machine. If the machine does breakdown you could lose about 1½ cups of blood. This is unlikely to cause you harm. • There is a small (about 1 in 1,200) risk of being hospitalized for observation of side effects from the donation (for example lightheadedness, nausea).

Additional Risks
Donating for a recipient can cause strong feelings, especially if the transplant does not succeed. These feelings may range from stress during the process to great joy or feeling sad after the donation. By donating for this recipient, you are doing all you can to help them. You cannot control the success of the transplant, or whether the recipient lives or dies. You should not feel personally responsible for the outcome.

You may be asked to donate again for the recipient if the donated cells do not grow in the recipient or if the recipient's disease is not cured. If you are asked to donate again, you are free to say no.

After You Donate Either Bone Marrow or PBSCs

After your donation, you will be called on the phone and asked questions about how you are feeling physically. These calls will start two days after the donation and will be made each week until you feel you are back to normal. You will be called again at one month, six months and then yearly after that.

You will also be asked to give a small blood sample (1½ teaspoons) at one month and six months after your donation, and then yearly after that. These samples will be used to measure your blood cell counts and to see how you are healing from the donation.

Quality of Life Surveys

To see how donation has affected your life, and how you have dealt with it, this study also asks questions about the quality of your life.

If you can answer the following three questions with a "yes," you will be called and asked questions about your quality of life.

- Do you read or speak English?
- Do you have access to a phone?
- Are you able to complete a survey?

You can ask to have a written copy of the questions sent to you before you are called. The people calling will arrange a time that works for you. The calls will take 30 minutes or less and will happen on this schedule:

- Within four weeks before your donation.
- On Day 4 of filgrastim injections *(only for PBSC donors)*.
- At two days after your donation.
- Every week after your donation until you have reported that you are fully well again for four weeks in a row.
- At six months after your donation.
- At one year after the donation.

The questions you will be asked include:

- How are you recovering physically?
- How well are you doing emotionally?
- How has the donation affected your everyday activities?
- How do you feel about the donation experience?
- What is your age, gender, race, marital status, work status, and what level of schooling have you had?

What are the possible side effects and risks of answering questions?

ANSWERING QUESTIONS FOR THE QUALITY OF LIFE STUDY

There are no physical side effects or risks to being in the quality of life part of the study. It will take at least three extra hours of your time over one year. Some people may feel awkward answering questions about themselves, but you may skip any questions that bother you.

3. What do I do if I am injured in this study?

The risk of serious injury to donors participating in this study is thought to be small. If you are injured, treatment (to include first aid, emergency treatment and other needed care) will be on hand for you. The NMDP will pay for this treatment. Please call your Donor Center Coordinator right away at ( ) _____ if you are injured.

In the case of an injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

4. Do I have to agree to be in this study?

No, it is up to you if you want to participate in this study. If you decline to participate, the NMDP will not remove you from the Registry unless you ask for this to be done. Your decision to decline participation will not change your relationship with your Donor Center or the NMDP. There will not be any penalty or loss of benefits. Your decision to decline participation will not affect your right or access to health care or any other service that you are entitled to receive at your Donor Center.

5. Are there alternatives to being in this study?

Yes. If you decide you do not want to take part in this study, you may be asked to donate either bone marrow or PBSCs for the recipient without participating in this study. In that case, the type of donation will not be decided randomly.

6. How long will I be in this study?

As part of your normal donor follow-up, each year you will be asked to give a blood sample and answer some questions about how you are feeling physically. This information will be shared with the study for three years. You will be called with questions about your quality of life for one year.

You will be informed of any new finding which may affect your decision to continue your participation in this research study.

7. Can I stop being in this study?

Yes, you may stop taking part in this study at any time. If you want to withdraw, you are asked to tell your Donor Center Coordinator. Your choice to stop will not change your relationship with your Donor Center or the NMDP. There will not be any penalty or loss of benefits. Your choice to stop will not affect your right or access to health care or any other service that you are entitled to receive at your Donor Center.

If you choose to stop before you donate bone marrow or PBSCs: It is important you know that if you decline to donate after the intended recipient begins to get treatment to get ready for the transplant, he or she will most likely die. If you have any questions about this statement, please contact your Donor Center Medical Director.

8. Will it cost me money to be in this study?

No. There is no cost to you for the check-ups, donating the cells or the surveys.

9. Will I be paid to be in this study?
No. You will not be given any payment for being in this study.

10. Are there rewards to being in this study?
You will not receive direct payment or reward for being in this study. But, this study may help future recipients in need of transplants, as well as future donors.

11. How does the NMDP use donor data?
As part of your participation in this study, your demographic and health information will be entered into the NMDP Research Database. The NMDP collects some data on all donors. This helps the NMDP make sure it is doing the best job it can and learn how to improve where needed.

By signing this consent form, you allow _____ (Donor Center) to give the NMDP your demographic information (for instance: gender, age and ethnic background) and health information that was taken as part of the donation process (for instance: results from infectious disease testing and the physical exam and information on healing from the donation). This information will be used by the NMDP to evaluate operation of the Registry, to report to its funding agencies, and to conduct research. In addition, people doing studies approved by the NMDP may use this information for research.

This authorization does not have an expiration date. You have the right to cancel this authorization at any time by notifying the NMDP in writing that you are canceling the authorization. The address for the NMDP is 3001 Broadway Street NE, Suite 500, Minneapolis, MN 55413. If you cancel this authorization, any identifiable health information will be removed from the NMDP Research Database. If you cancel your authorization, this will not affect your right or access to healthcare or any other services you are entitled to receive at _____ (Donor Center).

12. Will my health information and surveys be kept private?
We will do our best to make sure that the personal information in your health record is kept private. We cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Groups that may look at and/or copy health records for research, quality assurance and data analysis include:

- The NMDP
- The BMT CTN
- The NMDP Institutional Review Board (IRB)
- The National Institutes of Health (NIH) and other government agencies, like the Food & Drug Administration (FDA), involved in keeping research safe for people.

Steps used to keep your data private are:

- To label your data with a nine-digit identification (ID) number instead of your name. This ID number is chosen at random and does not contain any identifying information about you.
- To limit who sees your data.
- To keep your data in locked files.
- To destroy all papers when they are thrown away (for instance, by shredding).
- To use special, protected computer systems.

13. Who can I contact with questions or concerns about this study?
The doctors for this study are:
Dr. _____ _____ ( ) _____
(Donor Center Medical Director)

Dr. John Miller (800) 526-7809
(NMDP Medical Director)

For questions about your rights while taking part in this study, please contact Roberta King, Institutional Review Board (IRB) Administrator, at (800) 526-7809.

14. Donor/Participant's Signature (NMDP DID:_____)
I have been given a copy of all 18 pages of this form. I have read it, or it has been read to me. I understand this information and have had my questions answered. I agree to take part in this study.

_____ _____
Donor/Participant's Signature *Date*

_____
Donor/Participant's Name Printed

Certification of Counseling Healthcare Professional

I certify that the nature and purpose, the potential benefits, and possible risks associated with participation in this research 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.*

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

_____ _____
Interpreter's Signature Date

ATTACHMENT A

WHY IS THIS STUDY NEEDED?

The main goal of this study is to find out if there are differences in the outcomes of unrelated donor transplants based on whether blood-forming cells are taken from the bloodstream (PBSCs) or from the bone marrow.

Blood-forming cells are needed for transplantation. The greatest number of blood-forming cells are found in the bone marrow, while only a few blood-forming cells are normally found in the blood. In the past, blood-forming cells were always taken from the bone marrow. However, it is now known that a drug called "filgrastim" can increase the number of blood-forming cells in the blood so much that transplants can be performed using these cells taken from the blood.

When the NMDP compared the past survival of recipients who received an unrelated donor marrow transplant with recipients who received an unrelated donor PBSC transplant, there was no difference in survival between the two groups. This may have been because the recipients in each group did not have the same characteristics (different ages, different disease stages).

In this study, the donor and recipient will be randomly assigned (much like the toss of a coin) to either the PBSC group or the bone marrow group. By randomly assigning the recipients to receive either PBSCs or bone marrow, the characteristics of the recipients in each group should be similar. This makes it fairer to compare the two groups. With similar types of recipients in each group, the study should be able to find out if recipients who receive one type of donation do better after transplant than recipients who receive the other type of donation, or if recipients in both groups have similar results from their transplant.

There are also goals of this study specifically related to the donor. These goals are: 1) to examine any difference in the physical side effects PBSC donors and bone marrow donors have; 2) to examine any difference in the time it takes donors to recover from PBSC donation and marrow donation; and 3) to examine any difference in quality of life issues between the two types of donations, such as how the donation affects donors emotionally, how the donation affects the daily activities of donors, and how the donors feel about the donation experience.

ATTACHMENT B

WHY DO I NEED THESE BLOOD TESTS?

Standard Blood Tests
Tests are done on your blood to make sure it is safe for you to donate PBSCs or bone marrow. Any increased risk might mean that you would not be allowed to donate, or that only one of the two methods of donating would be advisable for you. These tests also protect the recipient getting your donation.

Blood Tests for Diseases
Your blood will be tested for infectious diseases including HIV, Hepatitis and West Nile Virus.

If your check-up or blood tests reveal anything that is not normal, you will be told. The NMDP or your Donor Center may also be required by law to notify your state public health agency if you test positive for Hepatitis B, Hepatitis C, the virus that causes AIDS (HIV) or other infectious diseases.

Check for Sickle Hemoglobin
Your blood will be tested for sickle hemoglobin. This test may result in genetic information that is new to you. There have been reports of severe reactions to filgrastim in persons with sickle cell disease. If your blood test is positive for sickle hemoglobin, you will not be able to participate in this study. However, you may still be asked to donate bone marrow for this recipient.

Pregnancy Test
If you are a woman of childbearing years, you will be required to take a pregnancy test. You must not donate bone marrow if you are pregnant. You must not take filgrastim if you are pregnant. This medication could cause serious problems for an unborn child. You must make sure that you do not get pregnant while taking filgrastim and for 48 hours after the last shot.

Extra Blood Samples for Research in this Study
Your blood will be tested for antibodies specific to germs that cause infection, for example, Hepatitis B. The antibody levels in your blood may be compared against the antibody levels in the recipient's blood after the transplant.

These samples are also used to better understand tissue matching between donors and recipients.

ATTACHMENT C

DEFINITIONS

Anesthesia is the giving of a drug or drugs designed to relieve pain and/or cause loss of consciousness.

Apheresis is a process where a machine divides blood into its separate parts. Blood is removed from one arm of the donor, passed through the machine, which separates out the needed type of cell(s), and returns the remaining blood to the donor. Over time, the donor's body naturally replaces the blood cells that are removed.

A **Central Line** is a sterile tube put into one of the larger veins, usually in the groin area (femoral vein), the neck area (internal jugular) or just below the collarbone (subclavian vein).

Demographic Information are facts about the part of the country where you live; what sex, race and age you are, and what ethnic group(s) you belong to. These facts help people study the health data. It does not include your name.

Filgrastim is a drug that causes the bone marrow to produce more blood forming cells than usual. When these cells go into the bloodstream they are often called peripheral blood stem cells (PBSC). They can be collected from the bloodstream. Filgrastim is also called "G-CSF" and marketed in the U.S. as Neupogen®. Filgrastim has been approved by the Food & Drug Administration (FDA) to collect PBSCs from recipients getting transplants of their own cells. It is also approved to treat recipients with cancer getting chemotherapy, for recipients getting bone marrow transplants and for recipients with diseases causing very low white blood counts.

An **Institutional Review Board (IRB)** is a group of people who review research methods and results to protect your rights and safety.

PBSC are "peripheral blood stem cells." This is another term for the blood forming cells circulating in your bloodstream that can be taken by a machine.

Platelets are special blood cells that help you stop bleeding by making clots.

Blood forming cells are cells found in the bone marrow and bloodstream that rebuild your blood, bone marrow and the immune system.

A **Syringe** is used to inject or withdraw a fluid. It has a hollow needle to break the skin and fluid is either injected into the body through the needle or fluids such as blood are withdrawn from the body.
A **Teaspoon** is a common unit of measurement. One teaspoon is equal to about five milliliters. There are three teaspoons in a tablespoon, 48 teaspoons in a cup.

APPENDIX B-3

ASSENT TO PARTICIPATE FORMS

Assent to Participate in Research (Ages 7 to 11 years old)

1. **Title of Research Study**
   A Phase III Randomized, Multicenter Trial Comparing G-CSF Mobilized Peripheral Blood Stem Cells 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/

You are being invited to be in a research project. This research project is about deciding which kinds of donor cells work better for transplants. Donor cells can come from bone marrow or blood. Your doctors want to learn whether it is better to use bone marrow or blood for other children who need a transplant in the future.

You should talk to your parents about this research project. If you have questions, ask your parents or your doctor.

You have a disease in your blood cells and the disease makes you sick. To help you get better, the doctors will give you strong medicines to make the bad blood cells go away.

The medicines may make you throw up, lose your hair and have mouth sores.

After these strong medicines, you will get a transplant of new cells from a donor who is a person you do not know. The cells will come from the donor's bone marrow or from the donor's blood. The cells should make new and healthy blood in your body.

Your parents, doctors, and nurses will explain what happens with the transplant. You should ask them about anything you do not understand. They will answer your questions.

You don't have to be in this research project. Your doctors and nurses will not be mad at you if you don't want to be in the research project. If you decide you don't want to be in this research project, you may still receive a transplant for your disease.

Sign your name on the line below if you want to be in this research project. You can keep a copy of this form at home.

_____ _____
Minor's Signature *Date*

_____ _____
Print Name of Minor *Age of Minor*

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 assent:

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.

Assent to Participate in Research (Ages 12 to 17 years old)

1. **Title of Research Study**
   A Phase III Randomized, Multicenter Trial Comparing G-CSF Mobilized Peripheral Blood Stem Cell versus 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. **Invitation to Participate in a Research Study**
   You are being invited to join a research study because you have a disease that may be treated with a transplant of bone marrow or blood cells from a healthy person not related to you. This form gives you information to help you decide if you want to be in this study. You should read this form and ask any questions you have before agreeing to be in the study.

   It is your choice whether or not to join this study. The medical staff at your transplant center will tell you about other treatment options before you make your decision about joining this study. If you do not join this study, you may still have a transplant for your disease.

5. **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. If you join this study, the type of cells used for your transplant will be picked by a computer program. The goal of this study is to see which type of blood stem cell transplant (bone marrow or PBSC) has better results.

   An important part of this study will look at how patients recover after transplants. Researchers want to know what the effects are from each type of blood 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 (return) 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 (return) of disease
   - Severe graft-versus-host disease (GVHD)
   - Serious infections
   - Not able to return to important activities in life

6. Study Procedures

If you agree to join this study, the donor will also need to agree to join the study. A donor could decide not to join this study, but still agree to give you cells for your transplant. If that happens, you can still have your transplant without being in this study, or another donor who does want to join this study may be found.

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. Saying yes to joining 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.

If you are 16 or 17 years old, 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 telephone 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 as part of your transplant. Your doctors will explain these during discussion of your medical care. Even if you decide not to join this research study, you will still need to take medications and have other medical treatments as part of your transplant.

7. Possible Discomforts and Risks of Being in the Research Study

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. 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 the blood stem cells may not grow after being given to you. This is called graft failure. This risk may be less with PBSCs, since PBSCs contain more blood stem cells than bone marrow.

Graft-versus-host disease (GVHD) is a common problem after unrelated donor transplantation. After the cells in the product start to grow, there is a risk that the donor cells might react against your body. GVHD it can show up as a skin rash, or liver or stomach problems, like feeling sick to your stomach, throwing up, not feeling hungry, stomach cramps, diarrhea, and bleeding of the gut. Chronic GVHD may occur later after transplantation and can cause problems with the eyes, mouth, lips, throat and liver. You will get medicines to help prevent GVHD, but sometimes people get it anyway. If you do,

there are other medicines used to help treat it. The chance of getting GVHD might be more with PBSCs, because PBSC transplants have 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.

If you are 16 or 17 years old, you will complete quality of life interviews. These 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.

8. Possible Risks and Discomforts from the Standard Transplant Procedure

As part of the standard transplant procedures, you will face risks from the transplant itself and from treatments given before and after the transplant. These risks are no different than the risks you would face if you had a transplant but did not join the study. Your doctor thinks these risks are less than the risk from the disease for which you are receiving a transplant.

Your organs may be damaged by the chemotherapy or irradiation given to you to prepare you for the transplant, or by other medications given to you after the transplant. We expect these risks to be the same whether you receive bone marrow or PBSCs. If you want more information about additional risks and the drugs that will be used for your conditioning regimen, it is available for you.

As part of a standard transplant procedure you may develop an infection after the transplant. The new cells from the donor may not grow in you (graft failure). You may develop graft-versus-host disease (GVHD). Your disease could relapse.

When the bone marrow or PBSC are given to you through the catheter, there are usually few side effects. Sometimes people may have a headache, chest pain or trouble breathing, a slight fever, or blood in the urine. Very rarely, it may cause an allergic reaction.

9. Alternatives Treatments Available if You Don't Want to be in the Study

Participation in this study is entirely voluntary. You don't have to join this study. What you and your family decide will not affect current or future health care you receive at this institution. If you are not in this study, you might have a transplant with marrow or blood stem cells anyway.

10. 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.

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

11. Withdrawing From the Study

You can decide to leave the study at any time, for any reason, without notice. If you want you can withdraw from the study but still get a blood stem cell transplant. If you leave 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.

12. Protection of Your Privacy and Confidentiality of Your Research Records

Your participation in this research study, and your medical and quality of life information, will be kept private and confidential.

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

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

13. Blood Samples for Research Purposes

You will be asked to give 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.

In addition, part of this study will look at if vaccinations after transplantation can help prevent infection. You will get vaccinations for diphtheria, tetanus, Hepatitis B and pneumococcus. Blood will be drawn for medical tests to see if the vaccinations are working. If you do not agree to give blood samples for research, your doctor may still recommend vaccinations as part of your medical treatment.

The doctors conducting this study may choose to do some additional research tests on the blood samples.

You don't have to be in this research. If you don't want to give blood samples for research you can still be in the other parts of the study. Your care will not be changed if you decide not to give these 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*

14. Minor's Assent

I have been told about this study's purpose, procedures, possible benefits and risks. I have been given a chance to ask questions and they have been 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 Minor *Date*

_____
Print Name of Minor

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.