APPENDIX B-2

RELATED DONOR INFORMED CONSENT

Related Donor Informed Consent to Participate in Research

This is an informed consent document for a research study that your family member is participating in. This document will inform you about the details of this study, which will involve manipulation of your donated cells before they are given to your family member.

Your family member has a blood cancer and will be treated with a stem cell transplant under a research study. The goal of this study is to compare 2 different combinations of treatment plans to a standard transplant procedure. The objective is to see whether one or both of these treatment plans are better at reducing the occurrence of chronic graft versus host disease (GVHD), a life-threatening complication of transplant. The treatment plan that your family member was randomized to requires manipulation of your cells through a device that removes certain types of cells that can cause this complication.

This informed consent document will explain important information about the study. There is no additional requirement from you beyond the procedure of stem cell collection to which you have already agreed. The cells you donate will be manipulated using a cell selection system that is part of the research study. Therefore, you need to be informed about this process and consent that your cells can be manipulated according to the procedures in the study. It is important to know that:

- You will not be paid to be in this study.
- You, your medical insurance company, or the patient's medical insurance company will pay for all medical bills for your treatment and the cell manipulation procedure.

Before you decide on consenting and signing this document, please read the information below. Feel free to ask questions to understand your rights. The consent process is voluntary and will not interfere with your donation and the recipient's transplant.

1. Title of Research Study

A Randomized, Multi-Center, Phase III Trial of Calcineurin Inhibitor-Free Interventions for Prevention of Graft-versus-Host Disease

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 National Institutes of Health (NIH), through the Blood and Marrow Transplant Clinical Trials Network (BMT CTN), are providing staff support and money for this research study. The BMT CTN and the NIH will make decisions about how to manage the study. Miltenyi Biotec, a company that produces the cell selection system used to process the stem cells before giving them to patients, is also a contributor to this study and they are providing supplies and money. This research study is also registered with the US Food and Drug Administration (FDA) which is overseeing the investigational device that is part of the cell selection system that will be used to remove T cells from your stem cell donation, called stem cell manipulation, prior to transplantation.

5. What will be different for you as a donor of peripheral blood stem cells if you choose to participate in this study?

Participation in this study by signing this document will not change any aspect of the stem cell donation that you have agreed to already. By signing this document, you acknowledge that your family member is participating in a research study and that you consent that the cells you donate can be manipulated in an investigational device.

6. What is the purpose of this study?

The purpose of this study is to compare two different combinations of treatment plans to a standard transplant procedure in order to see whether one or both of them are better at reducing the occurrence and severity of chronic GVHD. The research portion of this study involves manipulation of your stem cell product by removing T-cells, which cause chronic GVHD.

7. What will be done if you take part in this research study?

By signing this document, you consent that, after your donation, your cells will be manipulated by removing certain cells that can cause chronic GVHD in the recipient. The manipulation is performed by the investigational device. The way that you donate stem cells will not be changed with your participation in the study.

T-Cell Depletion (CD34+ Selection)

The blood cells collected from you as part of the donation process will have large numbers of T cells, along with other cells, including your blood stem cells. The process of removing these T cells is called T-cell depletion and there are several ways that this can be done. In this study, they are being removed through a process called negative selection. The device used to do this is called CliniMACS and is produced by Miltenyi Biotec. The procedure involves labeling the stem cells, also called CD34+ cells, with an antibody attached to a magnetic substance. The CliniMACS tubing set has columns that will bind only the CD34+ cells allowing all the other cells, including the T cells, to pass through. After the selection is done, the stem cell product will have mainly CD34+ cells, or stem cells, and will be depleted of T cells. The CliniMACS device has been extensively used in transplantation and has been proven to be safe. However, it remains an investigational device. This means it is not yet approved by the FDA for routine use. The FDA has granted approval for the use of this device and the CD34 reagent in this study and the study investigators are required to tell the FDA all information related to what happens with study participants. The CliniMACS CD34 Reagent System was approved as a

humanitarian device and authorized by U.S. Federal law for use in the treatment of patients with acute myeloid leukemia (AML) in first complete remission. The effectiveness of the device for this use has not been demonstrated.

8. Will you provide blood samples for research?

You will not be asked to provide extra blood samples for this research study.

9. What are the possible discomforts and risks?

T-cell Depletion: The process of manipulation occurs after your donation is completed. The amount of cells requested for collection from you is not larger than what is routinely requested for a transplant. However, the amount of cells donated needs to be above a certain number and some donors may need an extra day of donation in order to achieve this number of cells. Results from earlier studies using the same cell manipulation procedures found that 36% of the time, only 1 collection was needed; 45% of the time, 2 collections were needed; and 7% of the time, a third collection was needed.

Breach of Confidentiality: Medical records are considered confidential. These records are kept in a secured area accessible to people involved in the conduct of the study. You will not be identified by name in any publication or presentation of the results of this study. All data entered into a computer will be coded. No data that may be linked to you will be entered on any network computer that could allow access to confidential information. The master list will be stored off-line and available only to the principal investigator and his or her designee(s). Although we will make every effort possible to maintain confidentiality, there is however, a slight risk of loss of confidentiality.

10. As with any treatment, there may be yet unknown and/or unexpected side effects from donating peripheral blood stem cells.

Donating blood stem cells is routinely done and is not considered research. Unanticipated side effects may occur that have not been previously reported. If you have any unusual symptoms, you should report them immediately to your doctor.

In an attempt to avoid side effects, your doctor will examine you and obtain laboratory tests (blood tests, chest x-ray, etc.) to determine the effects of the donation and alter the drug doses if necessary.

11. What other alternatives are available if you do not want to be in this study?

Your participation is voluntary and you may choose not to participate in this research study or withdraw your consent at any time. Your choice will not at any time affect the commitment of your health care providers to provide care to you or to your family member. There will be no penalty or loss of benefits to which you or your family member are otherwise entitled. Alternatives to participating in this research include donating your blood stem cells to your family member for a transplant that is not part of this research study.

12. What are the possible benefits to you?

You will not benefit directly from participating in this research. You may receive indirect benefit from knowing that you may be helping your family member or other donors and patients in the future.

13. What are the possible benefits to others?

You may be helping other patients get better treatment in the future.

14. If you choose to take part in this study, will it cost you anything?

Normally the insurance company of the patient covers the medical expenses associated with collecting your blood stem cells and the T-cell depletion procedure. This will be reviewed with the patient's insurance company prior to collecting your stem cells. Neither you (the donor) nor your insurance company will be charged for the T-cell depletion of the peripheral blood stem cell graft.

15. Will you be paid for taking part in this research study?

No.

16. How can you withdraw from this research study?

If you change your mind after you have provided consent, you can still decline participation in the study prior to the stem cell manipulation. Please contact the person who discussed this document with you and request to be withdrawn from the study. The stem cell manipulation will occur within 24 to 36 hours from your donation.

17. How will your privacy and the confidentiality of your research records be protected?

The centers and doctors in charge of this study will keep your personal information as private as possible. They will do their best to see that it is shared only when required by state or federal law or the terms of this consent. The research study that your family member is participating in will not be collecting any information about you as the donor.

Information that does not include personally identifiable information about this clinical trial has been or will be submitted, at the appropriate and required time, to the government-operated clinical trial registry data bank, which contains registration, results, and other information about registered clinical trials. This data bank can be accessed by you and the general public at www.ClinicalTrials.gov. Federal law requires clinical trial information for certain clinical trials to be submitted to the data bank.

18. How will the researcher(s) benefit from you being in this study?

The researchers have no money invested in this study. But, in general, presenting research results helps the career of a scientist. Therefore, the Principal Investigator may benefit if the results of this study are presented at scientific meetings or in the scientific press. In addition, the Principal Investigator is being paid a small amount to cover the costs of the study.

19. HIPAA[1] authorization to use and disclose individual health information for research purposes

a. Purpose: As a research participant, I authorize the Principal Investigator and the researcher's staff to use and disclose my individual health information for the purpose of conducting the research study entitled *A Randomized, Multi-Center, Phase III Trial of Calcineurin Inhibitor-Free Interventions for Prevention of Graft-versus-Host Disease.*

b. Individual Health Information to be Used or Disclosed: My individual health information that may be used or disclosed to conduct this research includes: demographic information (e.g., age, date of birth, sex, weight), medical history (e.g., diagnosis, complications with prior treatment) and physical examination findings.

c. Parties Who May Disclose My Individual Health Information: The researcher and the researcher's staff may obtain my individual health information from (*list hospitals, clinics or providers from which health care information can be requested*).

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d. Parties Who May Receive or Use My Individual Health Information: The individual health information disclosed by parties listed in item "c." above and information disclosed by me during the course of the research may be received and used by the following parties:

- Principal Investigator and the researcher's staff
- Dr. Marcelo Pasquini, Study Chairperson at Medical College of Wisconsin
- Dr. Miguel Perales, Study Chairperson at Memorial Sloan-Kettering Cancer Center
- Dr. Leo Luznik, Study Chairperson at Johns Hopkins University
- National Heart, Lung and Blood Institute (NHLBI) and National Cancer Institute (NCI), both of the National Institutes of Health (NIH), study sponsors
- Blood and Marrow Transplant Clinical Trials Network Data and Coordinating Center (BMT CTN DCC), including the Center for International Blood and Marrow Transplant Research (CIBMTR), the National Marrow Donor Program (NMDP), and the EMMES Corporation
- The BMT CTN Data and Safety Monitoring Board (DSMB)
- U.S. government agencies that are responsible for overseeing research such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP)

[1] HIPAA is the Health Insurance Portability and Accountability Act of 1996, a federal law related to privacy of health information.

- U.S. government agencies that are responsible for overseeing public health concerns such as the Centers for Disease Control (CDC) and federal, state and local health departments
- Miltenyi Biotec, makers of the device that removes cells that are associated with the development of GHVD (used in the treatment group that your family member was randomized to)

e. Right to Refuse to Sign this Authorization: I do not have to sign this Authorization. If I decide not to sign the Authorization, I will not be allowed to participate in this study or receive any research-related treatment that is provided through the study. However, my decision not to sign this authorization will not affect any other treatment, payment, or enrollment in health plans or eligibility for benefits.

f. Right to Revoke: I can change my mind and withdraw this authorization at any time by sending a written notice to the Principal Investigator to inform the researcher of my decision. If I withdraw this authorization, the researcher may only use and disclose the protected health information already collected for this research study. No further health information about me will be collected by or disclosed to the researcher for this study.

g. Potential for Re-disclosure: My individual health information disclosed under this authorization may be subject to re-disclosure outside the research study and no longer protected. Examples include potential disclosures for law enforcement purposes, mandated reporting or abuse or neglect, judicial proceedings, health oversight activities and public health measures.

h. This authorization does not have an expiration date.

20. Donor's Consent

I have been informed of 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 Donor Date

_____
Print Name of Donor

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.

_____ _____
Signature of Counseling Healthcare Professional Date

_____
Print Name of Counseling Healthcare Professional

Related Donor Informed Assent to Participate in Research

This is a form for a research study. This form is to help you decide if you want to participate in this study.

Purpose of the Research Study
Your brother or sister has blood cancer and is being treated with a transplant of peripheral blood stem cells from a matched family member donor in a research study.

The goal of this study is to compare 2 different treatment plans to a standard transplant procedure. The objective is to see whether one or both of these treatment plans are better at reducing the rate of a serious complication called chronic graft versus host disease (GVHD). The treatment plan that your brother or sister was assigned to requires putting your donated cells through a device that removes certain types of cells that cause this complication before the cells are transplanted to your brother or sister.

You are being asked to be in the study because you are a match for your brother or sister and can donate peripheral blood stem cells to them. Your doctor or another person on the study team will explain to you what you must do if you are going to donate peripheral blood stem cells for your brother or sister. The team will also follow you closely to see if you are having any side effects while donating peripheral blood stem cells on the study.

If you have any questions, ask your doctors and make sure you understand their answers. Your parents (or a guardian) are also asked for their permission for you to join this treatment study.

I agree to donate blood stem cells in this study.

_____ _____
Signature of Donor Date

_____
Print Name of Donor

_____ _____
Signature of Doctor Date

_____
Print Name of Doctor