****

**National Marrow Donor Program®**

**Institutional Review Board**

Guidance for Completing

Initial Application for Bio-Medical Studies

Human Research Protection Program

CIBMTR Minneapolis

National Marrow Donor Program/Be The Match

500 N 5th St, Minneapolis, MN 55401-1206

Email IRBstaff@nmdp.org

TABLE OF CONTENTS

Introduction 3

Project Identification 3

Question 2

Investigator Information 3

Question 3

Question 4

Question 6

Question 7

Funding 4

Question 8 A, B

Summary of Activities 4

Question 9

Question 9A, B

Participant population 4-6

Question 10A, B, E

Question 11, A, C, D, F

Question 12

Research Category 6-8

Question 13

Question 14

Question 15, B, E, H

Question 17

Question 18

Compensation 8

Question 26

Oversight and monitoring 8-9

Question 27

Question 28

Question 29

Question 30

Question 31

Question 32

Question 33

International Research 9

Introduction

This document is intended to provide additional guidance for correctly completing the Initial Application for Bio-Medical Studies. Only questions that are often times missed, answered incorrectly, or misinterpreted are further explained in this document. Other questions of the application are self-explanatory.

Any questions about the initial application submission should be directed to the NMDP Institutional Review Board (IRB) staff at IRBstaff@nmdp.org or contact Julia Tkachenko at 763-406-5890 or jtkachen@nmdp.org.

Project Identification

**2. Single or Multi-Institutional Study (list all participating sites)**

A Multi-Institutional Study is conducted at more than one facility (e.g., hospital or clinic). The NMDP IRB Office must receive the local IRB approval letters from participating sites prior to those sites requesting NMDP/Be The Match donors on the study.

Investigator Information

**3. Principal Investigator Information**

The Principal Investigator (PI) is responsible for reporting requirements to the NMDP IRB. If the study is a multi-institutional study, the PI named in the IRB application is responsible for submitting the subsequent continuing review applications to the NMDP IRB, which shall include aggregate data from all participating sites.

**4. Co-Investigator Information**

Co-Investigators are individuals other than the PI who are also conducting the scientific portion of the study.

If there is an extensive list of Co-Investigators, it may be submitted under a separate cover.

**6. Institutional Official**

This is the person listed as the Signatory Official on your institution’s Federalwide Assurance (FWA) with the Office of Human Research Protections (OHRP).

If the study is an NMDP, CIBMTR, or BMT CTN study, the Institutional Official named in the application should be the NMDP’s Institutional Official. Otherwise, refer to your own Institutional Official as stated above.

**7. Institution’s Federalwide Assurance (FWA) Number**

FWA is a document filed with the Department of Health and Human Services (DHHS) stating that the institution will comply with DHHS protection of human subjects regulations. The institution’s IRB office should know this number.

Funding

**8A. Indicate the funding source(s)**

The funding source is an agency intending to provide funding (usually in the form of grants) for your research. This includes grants from federal or private agencies, contract from a pharmaceutical company or other entity, or a sub-contract from another university or research organization.

**8B. Provide the following information for each sponsor**

The sponsor is the company, institution, individual donor, or government agency responsible for initiation, management or financing of a research study.

Summary of Activities

**9. Summary of Study: Use lay language that can be understood by the general public.**

The summary of the study should be written as if you were trying to give an overview of your research to someone with no more than a high school education. Any technical terms need to be defined in simple language. All abbreviations should be spelled out the first time they are used or defined in lay terms.

**9A. What are the research questions (hypothesis)?**

Describe the problem(s) of interest and how it will be studied. How will the research advance scientific knowledge and/ or human health? What is the current standard of care, if any?

**9B. What research methods will be used?**

It is not necessary to include a complete description of the study design in this portion of the submission. Give a general sense of the strategy and/or techniques involved.

Participant population

**10A. What is the total number of recipients to be enrolled at all participating centers?**

The number of recipients to be enrolled must be corroborated in the study protocol.

**10B. What is the anticipated rate of accrual?**

The number of recipients anticipated to be enrolled per year.

Note: If annual accrual at the time of continuing review is less than 25% of the projected annual accrual rate, you will be asked to provide rationale for keeping the study open.

**10E. If the study includes children (defined as less than 18 years, with no exception for emancipated minors), one of the following criteria for risk/benefit assessment must be met according to federal regulations (45CFR46, subpart D)**

Section 404 of the regulations allows the IRB to approve research if the IRB finds that the risks of the research are no more than minimal.

Minimal Risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests (45 CFR 46.102(i)).

Section 405 of the regulations allows the IRB to approve research if the IRB finds that:

more than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual subject or by a monitoring procedure that is likely to contribute to the subject’s well-being;

the risk is justified by the anticipated benefit to the subjects; and,

the relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches

Section 406 allows the IRB to approve research if the IRB finds that:

more than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is not likely to contribute to the well being of the child;

the risk represents a minor increase over minimal risk;

the intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social or educational situations; and,

the intervention or procedure is likely to yield generalizable knowledge about the subjects’ disorder or condition which is of vital importance for the understanding or amelioration of the subjects’ disorder or condition.

**11. Does the study include donors?**

A donor is a person donating any Hematopoietic Cell Product, or a product related to that donation, for either transplant into a recipient or for laboratory research.

If the study includes Be The Match® Registry members that are not involved in the search and donation process for specific recipients, information about how those Registry members will be involved in the study should be explained in this section. (Replace “donors” with “Registry members” in Q11A through Q11D.)

**11A. Does the protocol include any donor-focused research questions.**

Unrelated donors are considered research subjects if:

1. Obtaining NMDP donor data specifically for research purposes. OR

2. Obtaining NMDP donor material (e.g., cells) for research purposes, and donor data will be generated from the material (e.g., blood drawn for laboratory research). OR

3. Using an investigational device supported by an FDA IDE on an NMDP donor or on an NMDP donor’s specimen (marrow, peripheral blood stem cells or other tissue). OR

4. Giving an NMDP donor an investigational drug.

**11C. Will there be more donors than recipients on the study and if so, explain why.**

An example of this is when donors are requested on the study at Confirmatory Typing (CT). The transplant center may be testing several NMDP unrelated donors to find the best potential HLA match for one recipient enrolled on the study.

**11D. Does this study involve NMDP unrelated donors?**

If you answer “Yes” to this question, you also need to answer the two bullet points.

The first bullet point asks *What is the expected number of NMDP unrelated donors needed to consent to this study?* The NMDP IRB defines donor enrollment as having consented to the study, regardless whether or not the donor goes on to provide the material or data needed for the study. If NMDP unrelated donors need to be screened outside of the NMDP Standard Donor Eligibility Determination process in order to determine their eligibility for the study, then the donor must sign a screening consent. An example of this might be additional blood needed from the donor for EBV testing. Donors who sign this screening consent for the study must be considered enrolled on the study and counted towards accrual.

**11F. What is the preferred stem cell source?**

If the study is being conducted in conjunction with a donor stem cell donation for a recipient, indicate the preferred stem cell source from the NMDP donor.

**12. If the donor declines to participate in the research study, but agrees to donate the hematopoietic cell product, will you proceed with the donor’s HC donation, or will you search for an alternate donor?**

If the identified hematopoietic cell donor declines participation in the research study, state whether this donor will still be asked to donate the hematopoietic cell product or if another donor will be chosen.

Research Category

**13. Does the study include manipulation of donor cells using an investigational medical device that is under an IDE with the FDA?**

An investigational device is a medical device which is the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device. Unless exempt from the IDE regulations, an investigational device must be categorized as either “significant risk” (SR) or “non-significant risk” (NSR). The determination that a device presents a non-significant or significant risk is initially made by the sponsor. The proposed study is then submitted either to FDA (for SR studies) or to an IRB (for NSR studies).

Please note that **IND** protocols for cell processing devices do not need to be submitted to the NMDP IRB as long as there are no other protocol activities that would define the donor as a research subject. Only cell processing devices under **IDE** must be submitted to the NMDP IRB for review.

(NOTE: IND protocols for cell processing devices that do not include other protocol activities that would define the donor as a research subject, but **do** include other protocol activities where the donor is supporting research activities must be submitted to NMDP’s Scientific Merit and Donor Safety Committee (SMDS). Refer to the SMDS Application.)

**14. Does the study include an investigational new drug (IND) application with the FDA?**

When using a drug for research, consider if the drug is FDA approved for the purposed use. If not, the use of the drug for research needs a special FDA authorization. For more information, consult the FDA website at

<http://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/investigationalnewdrugindapplication/default.htm>

Though FDA does not issue approval letters, please submit relevant documentation including the initial submission receipt confirmation and a record of verbal approval, if available.

**15. Will donor material be used for laboratory research?**

Donor material may include blood samples, bone marrow, PBSC product, leukapheresis product, cheek cells collected with buccal swabs, etc.

**15B. Describe how the donor material will be used.**

Describe how donor material (e.g., a portion of the stem cells, or cells from a blood sample or leukapheresis donation) will be used in this study.

**15E. At what time point(s) will the material be donated?**

These are the stages during the search and donation process when the donors could participate in research:

At the time of the Confirmatory Typing (CT) request. The CT testing is performed on a fresh blood sample from the donor to verify compatibility with the patient. An additional sample may be requested during this time for research purposes.

At the time of the workup request. Transplant centers have the option to request blood samples from the donor to be collected and received prior to donation (known as “pre-collects”). Individual transplant centers may designate when they want the samples collected (e.g., at the time of the information session, three weeks prior to donation, prior to filgrastim injections, etc.). An additional sample may be requested during this time for research purposes.

At the time of donation. An additional blood sample may be drawn for research purposes on the day of the marrow or PBSC donation.

Post donation. Donors may provide a product (e.g., blood, leukapheresis, marrow, or PBSC) for research purposes after their primary stem cell donation. This is known as a subsequent donation request.

**15H. Will cell lines be prepared using donor material and used for laboratory research?**

If cell lines will be prepared from donor material and **used for laboratory research** (regardless of whether or not the cell lines will also be used for patient treatment), you must answer 15Hi through 15Hviii.

**17. Will donors need to be screened outside of the NMDP Standard Donor Eligibility Determination Process?**

**NMDP Standard Donor Eligibility Determination**

Federal regulations went into effect May 2005, which require that all hematopoietic stem cell donors whose product will be infused into a recipient must be evaluated to determine their potential for transmitting a relevant communicable disease. This determination is made through health history screening, review of medical records, physical assessment and testing for specified infectious diseases, all according to FDA requirements.

**Infectious Disease Tests Required for Stem Cell Donors:**

* Hepatitis B
* Hepatitis C
* Human T-Lymphotropic Virus I/II
* Human Immunodeficiency Virus (HIV 1/ 2)
* Syphilis
* Cytomegalovirus (CMV)
* West Nile Virus
* Chagas

**18. Will participating in this research study increase the donor’s chance of being asked to donate cells a second time for the recipient (e.g., do the research aspects of this study put the recipient at greater risk than normal for primary or secondary graft failure)?**

If you answer ‘yes’, estimate the percent of risk above the normal risk for requesting a second donation from the donor.

Examples of recipients at a higher risk of experiencing graft failure may be those receiving HLA-mismatched grafts or those receiving reduced-intensity conditioning regimens.

Compensation

**26. Will you give study participants gifts, payments, compensation, reimbursement, or services without charge for their participation?**

Consider reimbursement versus inducement:

Reimbursement is meant to directly offset the direct, out-of-pocket costs that a subject incurs as a result of participating in the study. For example, in some studies subjects will end up paying for things like gas, parking, child care, or food in order to make the appointments that are required for the research procedures.

Inducement is a payment that is meant to motivate the subject to participate in the study for financial gain. Such payments may be considered undue influence on the subject to participate in a research study.

Oversight and monitoring

**27. IRB/ERB Review**

Please note, if the local IRB approval is not available at the time of NMDP IRB review, the study will not be approved by the NMDP IRB for enrollment of NMDP donors until the local IRB approval is obtained.

For multisite studies, provide local IRB approval letters from each site.

**28. Has the study undergone review by a scientific review committee?**

A Scientific Review Committee (SRC) ensures that the scientific question being asked within a protocol is relevant, and that the design of the protocol is appropriate to answer that question.

Submit a summary of SRC evaluation and recommendations, if applicable.

**29. Has the study been peer-reviewed for scientific merit?**

Peer review is a process conducted by scientific and technical experts who provide an independent assessment of the scientific merit of the research being reviewed. A review for scientific merit is required for studies that receive funding from the Department of the Navy.

**30. Human Subject Protection Training**

An institution holding OHRP-approved Federalwide Assurance (FWA) is responsible for ensuring that its investigators conducting human subjects research understand and act in accordance with the requirements of the DHHS regulations for protection of human subjects.

**31. Stopping Rules**

Stopping rules are designed to monitor the safety of a research study. They allow the study to be terminated based on the number of negative or harmful outcomes in study participants, as defined in the study protocol.

An explanation of stopping rules should be written in simple language that can be understood by someone with no more than a high school education

**32. Has a Data Safety Monitoring Board (DSMB), or other committee, been assigned to monitor this study?**

The DSMB committee should be composed of statisticians and clinical investigators not directly involved with the study responsible for reviewing study progress and outcomes. The DSMB committee may decide to close the study based on the number of adverse events and stopping rules.

Your DSMB may be known by a different name, (e.g., data safety monitoring committee, etc.) If such a committee has been assigned to monitor the study, submit the data and safety monitoring plan along with the IRB application.

**33. Is the study listed on www.ClinicalTrials.gov?**

ClinicalTrials.gov is a web-based resource that provides patients, their family members, health care professionals, researchers, and the public with easy access to information on publicly and privately supported clinical studies on a wide range of diseases and conditions. Certain studies are required by the FDA to be registered on ClinicalTrials.gov.

For information about registering your study on ClinicalTrials.gov go to <http://www.clinicaltrials.gov/ct2/manage-recs/how-register>

International Research

When designing your international research, you may reference “The International Compilation of Human Research Standards” on the Department of Health and Human Services website at <http://www.hhs.gov/ohrp/international/intlcompilation/intlcompilation.html>