POLICY

POLICY STATEMENT

The National Marrow Donor Program® (NMDP) Institutional Review Board (IRB) evaluates the proposed number of subjects when it reviews the risks and benefits of the proposed research. This evaluation is based on 1) the number of subjects exposed to the research risk weighed against the potential research benefit and 2) whether the number of proposed subjects is sufficient, but not excessive, to answer the research question. The IRB grants approval for a specific number of subjects and the number cannot be increased without prior IRB approval. It is the investigator's responsibility to ensure that the number of subjects enrolled on the protocol does not exceed the number that was approved by the IRB.

BUSINESS SECTION/DEPARTMENT

Center for International Blood and Marrow Transplant Research (CIBMTR)

PURPOSE

The purpose of this policy is to define what constitutes enrolled subjects in regards to research reviewed by the NMDP IRB and who is responsible for tracking the number of enrolled subjects on a research protocol.

SCOPE

The policy pertains to all research projects reviewed and approved by the NMDP IRB.

RELATED DOCUMENTS

Not applicable

DEFINITIONS

Enrolled subjects: Individuals who have given consent to participate in the research. Enrolled subjects are the same as accrued subjects.

Over-enrollment: The number of subjects enrolled in the research is greater than the number approved by the IRB at the time of initial approval or subsequent amendment.

Screened subjects: Individuals who have given informed consent and participated in screening procedures to determine their eligibility for the study. Informed consent is only required as part of the screening process if data are collected about the individual that

are specific to the research protocol, i.e., not collected as part of routine medical care or some other routine process. If the screening process requires informed consent, individuals who have given informed consent to participate in the screening procedures should be counted as enrolled subjects.

Screen failures: Individuals who participate only in screening procedures and are deemed ineligible for the study. If the screening process requires informed consent, individuals who have given informed consent to participate in the screening procedures should be counted as enrolled subjects, even if they are deemed ineligible for the study.

Withdrawals: Individuals who have given informed consent but who withdrew from the study or were withdrawn from the study either before or after having participated in some study procedures. Individuals who withdraw from a study after providing informed consent count towards enrollment.

RESPONSIBILITIES

CIBMTR: Establish and maintain policy

IRB staff are responsible for managing the IRB approval process.

Principal Investigators are responsible for tracking subject enrollment on their research studies, reporting enrollment numbers to the NMDP IRB, and requesting an increase in the number of subjects if necessary.

REQUIREMENTS

Increasing the Number of Approved Subjects

Investigators may request an increase in the number of subjects at any time by completing an *NMDP IRB Request for Study Amendment* application, or at the time of the continuing review they may request that the number of subjects be increased. If the IRB approves the request, the number of subjects enrolled may be increased. Federal regulations do not allow IRBs to give retroactive approval for changes made a to a research project. Therefore, the number of subjects must not be increased until approval has been granted.

Enrollment of NMDP Unrelated Donors on Recipient-Focused Transplant Center Sponsored Protocols

The NMDP IRB reviews a number of transplant center sponsored protocols that are recipient-focused but include research activities that involve the recipient's donor. For these research protocols where the donor is considered a research subject on their recipient's research protocol, there will be an approved enrollment number for recipients and an approved enrollment number for donors. The investigator at the transplant center is responsible for ensuring that both recipient enrollment and donor enrollment does not exceed the approved number.

1. The IRB at the transplant center sponsoring the research is responsible for approving the number of recipient subjects.
2. The NMDP IRB is responsible for approving the number of unrelated donor subjects when transplants are facilitated by the NMDP. The NMDP IRB may consider the following scenarios when determining the number of unrelated donors approved for the protocol:
    a. If there is a one-to-one relationship between the number of recipients and number of donors participating on the protocol, the NMDP prefers that the IRB choose to base the number of donors approved on the number of recipients approved by the transplant center IRB. In this case the approved donor enrollment number by the NMDP IRB will be stated as "Number of donors enrolled is not to exceed the number of enrolled recipients approved by the transplant center IRB." If the protocol enrolls both related and unrelated donors, then the combined number of related and unrelated donors must not exceed the total number of recipients enrolled. The NMDP IRB does not require an amendment to the initial approval to increase the number of donors as long as there is a valid IRB approval at the transplant center to increase the number of recipients. The approved increase in the number of recipients must be reported at the time of the NMDP IRB continuing review, along with documentation of the transplant center IRB approval. Alternatively, the IRB may exercise its option to approve a specific number of donors and require that the investigator obtain approval from the NMDP IRB for any increase in the number of donors enrolled.
    b. If there is not a one-to-one relationship between recipients enrolled and donors enrolled, then the NMDP IRB application must clearly state the number of donors to be enrolled and the rationale for different enrollment numbers for donors and recipients. The NMDP IRB will be responsible for approving the initial number of enrolled donors. Any increase in the number of donors enrolled must also be approved by the NMDP IRB prior to enrolling donors beyond the initially approved number.

Over-enrollment of Subjects

Over-enrollment is considered non-compliance with the conditions of IRB approval and, as such, must be reported to the NMDP IRB Office as soon as the over-enrollment is discovered, including reporting of donor over-enrollment on transplant center sponsored protocols. Following standard procedures outlined in *NMDP SOP SOO213 IRB Managing Non-compliance*, IRB staff will determine if the over-enrollment is minor, serious, or continuing non-compliance. Depending on the outcome of the non-compliance investigation, a corrective or preventive action plan may be required and other consequences, such as not allowing use of the data from the over-enrolled subjects, or reporting to federal agencies, may occur.

REFERENCES

1. Code of Federal Regulations (CFR) Title 45, Part 46.103(b)(4) – Protection of Human Subjects, Assuring compliance with this policy
2. Office of Human Research Protections (OHRP), "Guidance on IRB Continuing Review of Research," November 10, 2010

REVISION HISTORY

Revision	Brief Description of Revision
P00094 rev 1	Version 3.0 of this policy – approved by NMDP IRB on May 21, 2015

ADDENDA

Not applicable