Is the Unrelated Donor a Human Research Subject or a Third Party in Research?

ALGORITHM

A donor who donates for a recipient on a research protocol isn't automatically a research subject. Thus the need for this algorithm. Before proceeding, determine which activities on the protocol are research activities and which are standard therapeutic activities.

Is the activity research?

A systematic investigation that is clearly formulated in an experimental protocol and designed to develop or contribute to generalizable knowledge. This includes clinical investigations for which the investigator holds an Investigational Device Exemption (IDE) or an Investigational New Drug Application (IND).
45 CFR 46.102(d)
21 CFR 50.3(c)

no →

Activity is not research.

Donor is not a research subject.

→ 

yes ↓

Activity is research.

Is the donor a research subject?

Does the activity involve…

1) Obtaining NMDP donor data specifically for research purposes? **OR**
2) Obtaining NMDP donor material (e.g., cells) specifically for research purposes? **OR**
3) Using an investigational device on an NMDP donor's specimen (marrow, peripheral blood stem cells or other tissue)? **OR**
4) Giving an NMDP donor an investigational drug or device?

If you answered "yes" to any of these, then the donor is a research subject.
45 CFR 46.102(f)(1), (2)
21 CFR 812.3(p)
21 CFR 56.111(e)

NOTE 1

no →

Donor is not a research subject.

Is the donor a third party in research?

Does the research activity in which the patient is involved put the donor at greater risk for a second donation or donating for a futile transplant?

NOTE 2

no →

Donor is not a third party in research.

Patient research does not impact donor. NMDP does not need to be informed of patient's research activity.

→ 

yes ↓

Donor is a third party in research.

Donor must be allowed to weigh his/her risks against the benefit to the patient.

ACTION:
Inform NMDP IRB Office of the patient's research activity.

yes ↓

Donor is a research subject.

Activity is research involving donors as human subjects.
45 CFR 46.101(a)(1)

ACTION:
Submit NMDP IRB Application

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ALGORITHM ANALYSIS WORKSHEET

Transplant center name: _____

Transplant center number: _____

Person completing this form: _____

Email: _____ Phone #: _____

Study title: _____

_____

Protocol #: _____

Principal Investigator: _____

Please use the algorithm to determine whether or not the unrelated donor is a research subject or a third party in research.

CONCLUSION

1) What is the research activity? _____

_____

2) Based on the protocol's research activities, is the NMDP donor a research subject on this protocol?

_____ yes (Complete NMDP IRB application.)
_____ no

Please justify "no" answer: _____
_____

3) Based on the protocol's research activities, is the NMDP donor a third party in research on this protocol?

_____ yes (Inform NMDP IRB Office of patient's research activity.)
_____ no

Please justify "no" answer: _____
_____

Regardless of the conclusion, please submit this algorithm analysis to your local IRB with the rest of your IRB application materials or continuing review materials.

For questions regarding the algorithm, please contact Roberta King, Director, NMDP Research Operations at (612) 627-5807 or rking@nmdp.org.

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ALGORITHM NOTES

Note 1

Examples for which this question would be answered "yes":

1. The product will be experimentally manipulated.
2. Individually identifiable donor data (may be coded but link exists at donor center) collected explicitly for research purposes will be included in the research. This does not include standard data provided to all transplant centers as part of the donor selection process (e.g., gender, age, race, weight, HLA typing, standard infectious disease marker, etc.) or results from clinical tests performed at the transplant center, (e.g., chimerism tests). Examples of donor data collected for research purposes are survey or interview questions (e.g., survey asking questions regarding donor's allergy history, etc.) or data obtained from the donor's donation medical record that are not routinely provided to the center performing the transplant (e.g., donor family history data or lab values for CBC and differential, etc.).
3. The donor will be asked to provide blood, marrow, PBSC or other tissue samples for laboratory research studies (not for clinical care purposes).
4. The donor will be asked to provide blood or marrow to develop cellular therapies for the recipient (e.g., donor cell lines are being created to treat or prevent specific viral infections, stem cells are being used to treat damaged tissues such as heart attacks, etc.).
5. The stem cell collection is specifically altered by the research protocol (e.g., additional stem cell products are requested, altered method for collecting the product, etc.).
6. Transplant efficacy has not been established in peer reviewed literature (e.g., transplant for solid tumors, autoimmune disorders, etc.).

Note 2

Examples for which this question would be answered "yes":

1. The patient's research activity puts them at greater risk of graft failure and therefore puts the donor at greater risk of a second donation. Transplant protocols that include a novel conditioning regimen could fall into this category.
2. The research focuses on sub-populations of patients with a disease where transplant efficacy has been established, but that particular sub-population is normally not eligible for transplant. Generally these research protocols involve experimental methods or drugs to reduce transplant related mortality or further eradicate advanced disease. Protocols such as these put the donor at greater risk of donating for a futile transplant. Transplant protocols for elderly patients or for patients with existing co-morbidities or extremely advanced diseases may fall into this category.

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REGULATORY DEFINITIONS

Office of Human Research Protections (OHRP)

OHRP definition of research [45 CFR 46.102(d)]

Research means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.

OHRP definition of human subject [45 CFR 46.102(f)(1), (2)]

Human subject means a living individual about whom an investigator (whether professional or student) conducting research obtains

(1) Data through intervention or interaction with the individual, or
(2) Identifiable private information.

Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. *Interaction* includes communication or interpersonal contact between investigator and subject. *Private information* includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

Food and Drug Administration (FDA)

FDA definition of clinical investigation [21 CFR 50.3(c)]

Clinical investigation means any experiment that involves a test article and one or more human subjects; and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i), 507(d), or 520(g) of the act; or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that are subject to the provisions of part 58 of this chapter, regarding non-clinical laboratory studies.

FDA definition of human subject [21 CFR 56.111(e)]

Human subject means an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient.

FDA definition of human subject from the medical device regulations [21 CFR 812.3(p)]

Subject means a human who participates in an investigation either as an individual on whom or on whose specimen an investigational device is used or as a control. A subject may be in normal health or may have a medical condition or disease.