JDRF SCIENTIFIC GUIDELINES
Updated July 2011

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1.0 INTRODUCTION

All applications—regardless of award mechanism—related to (1) clinical research involving ongoing patient contact, (2) islet transplantation in humans, or (3) use of human embryos or fetal tissue must conform to JDRF guidelines and policies, listed below. **Applications that are not consistent with these guidelines will be administratively triaged without review.**

JDRF supports human subject research that seeks to translate basic research discoveries to cure, prevent and/or reverse Type 1 diabetes and its complications. Applicants should follow general guidelines for research applications and should include the information requested below about the human subject study design, safety monitoring, and ethical requirements regarding human subject research participation.

2.0 HUMAN SUBJECT RESEARCH GUIDELINES

Human Subject Application Requirements

All applications involving human subject research should address study design as stated below.

NOTE: All templates referenced below are available with the application on proposalCENTRAL

Human Subject Protocol Synopsis Requirement

All applications that propose human subject studies must include a Protocol Synopsis. Use of the JDRF Protocol Synopsis template is not required; however, at a minimum, all information requested on the template must be included within your study synopsis.

Human Subject Research Plan

All applications that propose research with human subjects must include a Human Subject Research Plan (HSRP). All eight items in the HSRP template must be addressed and the HSRP should not exceed three pages. Please refer to the following instructions for completing the HSRP:

1. **Criteria for subject inclusion/exclusion, especially those pertinent to subject protection:** Describe the proposed involvement of study subjects, including patients and healthy control subjects, stating their anticipated number, age range, gender, ethnic/racial background, and health status. Identify criteria for inclusion or exclusion of any subpopulation, including children and adolescents.

2. **Potential benefits and risks to subjects, plans to minimize risks, and knowledge to be gained from the study:**

For each proposed intervention and proposed subject group, describe the following:

- The potential direct and indirect benefits to the individual subject and/or group of subjects.
- The potential risks (physical, psychological, social, legal, or other) to all study subjects, including the likelihood and seriousness of each risk.
- Potential risks to pregnant women and fetuses.

For research involving children and adolescents:

- Classify the level of each intervention and each subject group according to the categories in the U.S. Department of Health and Human Subjects Federal Regulations (45CFR46 Subpart D) (see Appendix A).
- Describe the planned procedures for protecting against or minimizing potential risks and assess their likely effectiveness.
- Discuss the importance of the potential benefit to society through knowledge to be gained as a result of the proposed research. Discuss why the risks to subjects are reasonable in relation to the importance of the knowledge to be gained from the study results.

3. **Monitoring study subject safety:**

Discuss plans for ensuring necessary medical or professional intervention in the event of adverse effects for subjects.

4. **Sources of research material and confidentiality protections:**

Identify sources of research materials obtained from individually identifiable living human subjects in the form of specimens, records, or data. Indicate whether these materials or information will be obtained specifically for research and how the materials or information will be used.
Address planned measures to protect the confidentiality of study subjects and subject materials and information generated by the study.

5. Costs, incentives, and remuneration for study subjects:
Describe any potential costs for study subjects and any incentives or remuneration that study subjects will receive by participating in the study, including compensation for injury incurred as a result of study participation.

For research studies that propose remuneration for participation of minors, state whether the remuneration is offered to the parents or their minor children.

6. Research subject informed consent process:
Describe the process for obtaining subject informed consent, including the circumstances under which consent will be sought and obtained, who will seek it, the nature of the information to be provided to prospective subjects, and the method of documenting consent. Recognize that consent is an interactive process and that a signed form is merely evidence that the interaction took place.
Assent of minors: For research studies involving children and adolescents, discuss plans for obtaining assent of minors.

When available, submission of a *draft* patient information and consent (assent) document is strongly recommended.

Guidelines for the informed consent document are provided in Appendix B below.

7. Potential conflicts of interest, including investigator plans to inform study subjects about any perceived conflicts:
State whether study personnel responsible for the design, conduct, or reporting of the research have an economic interest in, or act as an officer or a director of any outside entity whose financial interests would reasonably appear to be affected by the research.
Include plans to inform study subjects about any perceived conflicts of interest.

8. Investigator expertise and education in the protection of human research subjects:
For all key personnel, describe their education on the protection of human research subjects.

Submission of the FDA-IND letter, where applicable, will be required prior to initiation of funding.

Documents Required for Clinical Grant Review
The following documents will be required for submission to the JDRF Clinical Grant Review Committee. Note that some of these documents are part of the current application (HSRP, documentation of human subjects training of key grant personnel):

- IRB(or ethics committee)-ready protocol
- IRB (or ethics committee)-ready informed consent document
- JDRF Human Subject Research Plan

Please note that IRB/Ethics Committee approval ***is not required*** for the Committee meeting to take place. It is strongly recommended that you seek IRB/Ethics Committee approval ***after*** the meeting has taken place.

NOTE: All templates referenced above are available with the application on proposalCENTRAL

Good Clinical Practice Guideline Requirement for JDRF-Funded Human Subject Grants
All JDRF Human Subject Grants are expected to adhere to the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines Consolidated Guidance (ICH-E6).

Any request to deviate from GCP should be made in writing during initial grant submission.

Standard of Care Requirements for JDRF-Funded Human Subject Grants
All JDRF Human Subject Grants are expected to adhere to Current Standards of Care for treatment of diabetes. Acceptable standards include American Diabetes Association (ADA), American Association of Clinical Endocrinologists (AACE), International Society for Pediatric and Adolescent Diabetes (ISPAD), and European Association for the Study of Diabetes (EASD).

JDRF may, at its discretion, reference other treatment guidelines appropriate to the protocol being reviewed.

Any request to deviate from these requirements should be made in writing during initial grant submission.

General Information Regarding Protocol Review

All human subject grants undergo a review by the JDRF Clinical Grant Review Committee. Funding for human subject grants will not be awarded until the protocol review process is completed.

The Committee conducts statistical and ethics reviews of the JDRF Human Subject Research Plan and the IRB-ready protocol and informed consent document. It is strongly recommended that you speak with the JDRF Program Director or delegate *prior to* finalizing your study documents.

Documents Required Prior to Funding Release

Prior to funding, the following information will be **required**:

- Documentation of IRB review and approval (or international local ethics board equivalent)
- Sample human subject (patient) information and informed consent documents
- Documentation for human research subject education of key study personnel
- Copy of the FDA-IND letter (or country-equivalent), where applicable
- HSRP and CRP
- Protocol Synopsis
- Study Protocol

Note that JDRF will require annual confirmation of the review of funded human subject investigation research.

3.0 HUMAN ISLET TRANSPLANTATION

Background

JDRF is committed to the goal of accomplishing successful human islet transplantation in diabetes. Through its islet isolation and distribution facilities and centers for clinical islet transplantation as well as partnerships with NIH to support islet transplantation, JDRF has made and will continue to make a major commitment to this line of investigation.

In the past two years, significant advances in islet transplantation have occurred, particularly the recently reported successful Edmonton protocol. These advances have expanded the potential scientific and clinical opportunities in islet transplantation. This document is intended to outline JDRF guidelines concerning future research support in this area.

Independent Research Support from JDRF

JDRF will continue to support cutting edge research that will lead to successful human islet transplantation and therefore encourages applications that propose new, innovative ideas and that focus on unanswered questions. Areas of interest include, but are not limited to: 1) improving islet isolation, survival and stability; 2) determining whether islets can be stored and/or shipped to other sites; 3) evaluating short term anti-inflammatory therapies as a means of improving early engraftment; 4) evaluating alternative sites for transplantation; 5) evaluating effects of in vitro islet manipulations; 6) development of new, innovative and safe clinical protocols.

Establishment of New Programs

Although JDRF recognizes the desirability of establishing new programs for human islet transplantation worldwide, investigators are encouraged, when possible, to seek alternative sources of funds to initiate these efforts before applying to JDRF for funding. JDRF welcomes applications for expansion or extension of existing efforts. In general, investigators should provide evidence of competence by successfully performing several islet transplants using "standard" protocols. This "entry-level" criterion has been established in order to expedite the translation of research to clinical practice. Source of pancreata should also be addressed in the application.

Immune Tolerance Network

JDRF is committed to supporting the work of the Immune Tolerance Network (ITN). Investigators interested in pursuing tolerance protocols for islet transplantation are encouraged to also submit their applications to the ITN. However, JDRF recognizes that the ITN may not be able to accommodate all ideas or groups and, therefore, JDRF will accept research applications for tolerance induction. Applicants are encouraged to take advantage of the wealth of information available through the ITN concerning clinical islet transplantation in preparing applications to JDRF.

Review Procedures

JDRF will follow its usual review procedures and applications will be independently evaluated either through our current review group or through an ad hoc review panel.

Letters of Intent

Investigators proposing studies with budgets in excess of USD 1 million over three years must submit letters of intent to JDF. Letters of intent should include the following information:

1) Project title

2) Name, affiliation, address, phone and fax numbers and email address of the principal investigator
3) Identities of other key personnel and participating institutions and a description of their roles in the project
4) Goals, hypothesis to be tested and specific aims of the study
5) Brief description of the scientific rationale of the proposed study
6) Source of islets for transplantation and availability of pancreata
7) Evidence of competence in human islet transplantation using “standard” protocols
8) Estimated budget

The letter of intent should not exceed four pages and should be submitted via proposalCENTRAL.

Applicants will be notified within (6) weeks whether to submit a full application and proposal.

Contacts

Questions regarding JDRF’s policy on human islet transplantation or letters of intent should be directed to:

Albert Hwa Ph.D.
212-479-7663
ahwa@jdrf.org

OR

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212-479-7682
jgreenstein@jdrf.org

4.0 HUMAN EMBRYOS IN STEM CELL RESEARCH
Updated February 2003

Purpose of Policy
The purpose of JDRF's Policy Statement for the Use of Human Embryos in Stem Cell Research is to be clear regarding research to derive human embryonic stem (hES) cells.

Statement of Policy
JDRF funds research for the derivation of hES from excess embryos created by in vitro fertilization (IVF) for reproductive purposes. This includes stored embryos that are no longer needed for reproductive purposes and embryos determined to be clinically unsuitable for uterine implantation.

Applicants who propose research to derive hES cells from excess human embryos should address within the research application:

a) The source of embryos
b) The basic procedures of the protocol for the derivation of hES, including embryo screening protocols
c) A plan for obtaining donor informed consent for the research use of embryos; submission of draft patient information and consent documents is required
d) A statement as to why the use of human embryos is necessary to conduct the research
e) In addition to review by the review committee, all applications that propose the derivation and/or use of human pluripotent stem cells will be subject to review by a JDRF oversight panel to ensure that the ethical issues addressed in the guidelines are fully met. Prior to the initiation of funding of approved applications, JDRF will require:
    a) Documentation of approval by an institutional review board (IRB) or the international local ethics review committee equivalent to ensure that appropriate protections are in place and will be followed.
    b) Sample patient information and informed consent forms
    c) Documentation of required regulatory approvals (e.g., national and/or local licensing agencies)
    d) Assurance of the sponsoring institution that the research is in accord with local laws and regulations
    e) Warrant that any research tools (for example cell lines, genetic arrays) derived from the research will be available internationally to other academic groups without restrictive material transfer agreements

Requirements
Conditions for Stem Cell Research Using Excess Human Embryos
To ensure the ethical conduct of such research, it should satisfy the following conditions:

a) There should be clear separation between the decision to create embryos for reproductive purposes and the decision to donate excess embryos for stem cell research.
b) The research consent process should allow for timely, fully informed, and voluntary consent from the persons for whom the embryos were created for reproductive purposes.
c) There should be no financial inducements, monetary or otherwise, for the donation of embryos for research.
d) The attending fertility physician treating the potential embryo donors should make all clinical treatment decisions independent of and uninfluenced by any potential research

use of excess embryos. The attending fertility physician and the researcher proposing to use embryos for human stem cell research should not be one and the same.

e) A clinical embryo screening protocol should be in place. This protocol should utilize and specify defined criteria, and the implementation of those criteria should not be influenced by the potential research use of embryos.
f) Embryos used for research should not be maintained intact in culture beyond 14 days post-fertilization, the internationally accepted time limit.

Required Elements of Informed Consent for Stem Cell Research Use of Excess Embryos

Informed consent for the use of excess embryos for human stem cell research should include the following:

a) A statement that only embryos that are unsuitable for or in excess of clinical use will be used in research
b) A statement that the embryos will be used to derive human pluripotent stem cells for research
c) A statement that embryos donated will not be transferred to any woman's uterus and will not survive the human pluripotent stem cell derivation process
d) A statement that the research is not intended to provide direct medical benefit to the donor
e) A statement that research donation is voluntary and that a decision to consent or refuse to participate in research will not affect the quality of clinical care
f) A statement as to whether information that could identify the donors of the embryos, directly or indirectly through identifiers linked to the donors, will be removed prior to the derivation or the use of human pluripotent stem cells
g) A statement that derived cells/and or cell lines may be kept for many years and may be shared with multiple researchers at multiple research institutions
h) A disclosure of the possibility that the results of the research on the human pluripotent stem cells may have commercial potential, and a statement that the donor will not receive financial or any other benefits from any such future commercial development
i) A statement that human pluripotent stem cells derived from the research may be used for human transplantation research and that the donation is made without any restriction or direction regarding the individual(s) who may be the recipients(s) of transplantation of the cells derived from the embryo
j) An individual should be identified who can be consulted for independent advice on the research donation of embryos

Contacts

Questions regarding JDRF's policy on human embryos in stem cell research should be directed to:

Adrianne Wong, Ph.D.
212-479-7642
awong@jdrf.org

5.0 HUMAN FETAL TISSUE IN RESEARCH
Updated February 2003

Purpose of Policy
The purpose of the JDRF Policy Statement for the Use of Human Fetal Tissue in Research is to be clear regarding research using human cadaveric fetal tissue and embryonic germ cells derived from human cadaveric fetal tissue.

Statement of Policy
JDRF's long-standing position has been to support research using human fetal material that conforms to state and federal statutory and regulatory requirements. Consistent with these requirements, JDRF requires that for all research using human cadaveric fetal tissue, the decision to donate fetal tissue for research should occur independent of and subsequent to the decision to terminate a pregnancy and that there should be no inducements, financial or otherwise, for the research donation.

Applicants who propose research using human fetal tissue should address within the research application:

1. The source of fetal tissue
2. The basic procedures of the research protocol using fetal tissue
3. A plan for obtaining donor informed consent for the research use of human fetal tissue; submission of draft patient information and consent documents is required
4. A statement as to why this source of tissue is necessary to conduct the research

Prior to the initiation of funding of approved applications, JDRF will require:

1. Documentation of approval by an institutional review board (IRB) or the international local ethics review committee equivalent to ensure that appropriate protections are in place and will be followed
2. Sample patient information and informed consent forms
3. Assurance of the sponsoring institution that the research is in accord with local laws and regulations
4. Warrant that any research tools (for example cell lines, genetic arrays) derived from the research will be available internationally to other academic groups without restrictive material transfer agreements

Requirements
Required Elements of Informed Consent for Research Use of Human Fetal Tissue

Informed consent for the use of fetal tissue for research should include the following:

a) A statement that fetal tissue obtained from an elective termination of pregnancy may be used for research
b) A statement that the research is not intended to provide medical benefit to the donor
c) A statement that the research donation is voluntary and that a decision to consent or refuse to participate in research will not affect the quality of clinical care
d) A statement that the donor will not receive financial or any other benefits from the research or any future commercial products
e) In cases where the research will derive cell lines, a statement as to whether information that could identify the tissue donor, directly or indirectly through identifiers linked to the donor, will be removed prior to the derivation or use of the cell lines
f) In cases where the fetal tissue or derived cell lines may be used in clinical transplantation protocols, a statement that the research is to occur altruistically; that is, the donor may not direct into whom the tissue or derived cells may be transplanted

g) In cases where the fetal tissue or derived cell lines may be used in clinical transplantation protocols, a statement as to whether the identity of the donor will be made known to the recipient
h) A statement that derived cells/and or cell lines may be kept for many years and may be shared with multiple researchers at multiple research institutions
i) The prospect of commercial interests in the cells or cell lines; that is, that there is a possibility that the results of this research may have commercial potential

Statement of Policy: Research Use of Human Fetal Tissue to Derive Human Embryonic Germ (EG) Cells

JDRF recognizes that existing federal (U.S.) policy permits research involving the derivation and use of embryonic germ (EG) cells from human cadaveric fetal tissue, and such research is eligible for federal funding. JDRF also recognizes, however, that existing statutes and regulations may not clearly specify that the ethical safeguards that exist for fetal tissue transplantation also apply to the derivation and use of EG cells from cadaveric fetal tissue.

JDRF considers EG cells to be a form of human fetal tissue. As such, JDRF may fund research proposals that derive and/or use EG cells following elective termination of pregnancy provided that the research meets the requirements for human fetal tissue research generally (see above).

In addition to review by the JDRF Medical Science Review Committee and Lay Review Committee, all applications that propose the derivation and/or use of human pluripotent stem cells will be subject to review by a JDRF oversight panel to ensure that the ethical issues addressed in the guidelines are fully met.

Applicants who propose research to derive human EG cells from cadaveric human fetal tissue should address within the research application:

- The source of fetal tissue
- The basic procedures of the protocol for the derivation of human EG cells
- A plan for obtaining donor informed consent for the research use of human fetal tissue; submission of draft patient information and consent documents is required
- A statement as to why this source of tissue is necessary to conduct the research

Prior to the initiation of funding of approved applications, JDRF will require

- Documentation of approval by an institutional review board (IRB) or the international local ethics review committee equivalent to ensure that appropriate protections are in place and will be followed
- Sample patient information and informed consent forms
- Assurance of the sponsoring institution that the research is in accord with local laws and regulations
- Guarantee that any research tools (for example cell lines, genetic arrays) derived from the research will be available to other academic groups without restrictive material transfer agreements

Required Elements of Informed Consent for Research Use of Human Fetal Tissue

Informed consent for the use of fetal tissue for research should include, as applicable for the proposed research, all elements listed (a-i) on pp.1-2. In addition, informed consent should include a statement that fetal tissue obtained from an elective termination of pregnancy may be used for research involving embryonic germ cells to derive human pluripotent stem cell lines.

Contacts

Questions regarding JDRF's policy on research use of human fetal tissue should be directed to:

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6.0 APPENDICES

APPENDIX A: PARTICIPATION OF CHILDREN IN RESEARCH

U.S. Department of Health and Human Services Regulations Title 45 Part 46 Subpart D requirements for the participation of children in research

Subpart D of the human subjects regulations establishes requirements for research participation of children based on defined categories of potential risk and benefit of the research. The categories of research based on assessment on potential risks and benefits:

1) No greater than minimal risk, where minimal risk means "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"
2) Greater than minimal risk and presenting the prospect of a direct benefit to the child, in which the anticipated benefit justifies the risk and is at least as favorable as that of alternative approaches
3) A minor increase over minimal risk with no prospect of a direct benefit to the subject, but likely to yield generalizable knowledge about the child's disorder or condition that is of vital importance for the understanding or amelioration of the disorder or condition AND the intervention or procedure presents experiences to the child that are reasonably commensurate with those in the child's actual or expected medical, dental, psychological, social, or educational situations.
4) Any other research, including research that poses more than a minor increase over minimal risk (for research in the United States and subject to the regulations, requiring the approval of the Secretary of Health and Human Services following consultation with a panel of experts and following publication and public comment).

APPENDIX B: INFORMATION TO BE INCLUDED IN THE CONSENT DOCUMENT

Informed consent forms provide written documentation of an ongoing and interpersonal process. Information to be included in consent forms is listed below.*

1) A statement that the study involves research; identification of the research sponsor(s), principal investigator(s), and institution(s) performing the research;
2) An explanation of the purpose of the research, an invitation to participate and explanation of why the subject was selected, and the expected duration of the subject's participation;
3) A description of procedures to be followed and identification of which procedures are investigational and which might be provided as standard care to the subject in another setting. Use of research methods such as randomization and placebo controls should be explained;
4) A description of any foreseeable risks or discomforts to the subject, an estimate of their probability and magnitude, and a description of what steps will be taken to minimize or prevent them; as well as acknowledgement of potentially foreseeable risks;
5) A description of any benefits to the subjects or to others that may reasonably be expected from the research, and an estimate of their likelihood;
6) A disclosure of any appropriate alternative procedures or courses of treatment that might be advantageous to the subject;
7) A statement, when applicable, that participation in the research may limit the subject's eligibility for participation in future research studies.

8) A statement describing to what extent records will be kept confidential, including examples of who may have access to research records such as hospital personnel, the FDA, the drug sponsors;
9) For research involving more than minimal risk, an explanation and description of any compensation and any medical treatments that are available if subjects are injured through participation; where further information can be obtained, and whom to contact in the event of a research-related injury;
10) An explanation of whom to contact for answers to questions about the research and the research subject's rights;
11) A statement disclosing the research sponsor(s).
12) A statement that research is voluntary and that refusal to participate or a decision to withdraw at any time will involve no penalty or loss of benefits to which the subject is otherwise entitled;
13) A concluding statement indicating that the subject is making a decision whether or not to participate, and that his/her signature indicates that he/she has decided to participate having read and discussed the information presented.

* From the National Institutes of Health Intramural Clinical Research Program, with minor modification.