JDRF Scientific Guidelines for applicants	
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Contents

Introduction

The following guidelines applies to all applications regardless of award mechanism related to
(1) Involving human subjects research or
(2) Use of human 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 funds projects that demonstrate the highest probability of completing on time and within budget, and of meeting all milestones and deliverables in conformance to these guidelines. Therefore, applicants should submit realistic budgets and research plans without the expectation of extending the project period beyond the originally approved period of performance.

JDRF clinical terms of award

Nonexempt human subject's research

JDRF follows the U.S. National Institutes of Health (NIH) Guidelines for the use of human subjects in research. To assure that JDRF is supporting high quality clinical research, the grantee's institution should provide appropriate oversight and monitoring of the conduct of its clinical research portfolio, which includes observational studies that vary in size and complexity and interventional clinical trials. This guideline helps to ensure that all clinical research and clinical trials conducted under grants supported by JDRF are well designed, conducted with rigor, and monitored adequately, and that JDRF is kept informed of study progress through reporting. Applicants shall comply with all applicable federal, state, and local laws, regulations, and requirements.

Full application stage

All Clinical research studies are expected to adhere to the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines and applicable country specific regulatory requirements. These awards undergo a review by JDRF Grant Review Committee with an expert clinician on the panel. Funding for these grants will not be awarded until the review process is completed. Additional ethics and/or statistical review may be done if deemed appropriate by the committee. It is strongly recommended that the principal investigator [PI] speaks with the JDRF scientific manager *prior to* submitting the study documents. The following documents will be required at the full application stage.

Clinical Project Research Plan

If your proposal includes a clinical trial [as defined by NIH clinical trial definition-please see reference section on later pages of this document], then complete all required sections of clinical project research plan template. Provide as much information as available/possible at full application. JDRF expects the content and format of the final IRB study protocols to be in compliance with ICH GCP-E6/ country specific regulatory requirement. Applicants are allowed to use their institute/IRB specific template, in such cases they should ensure compliance with ICH GCP-E6. For more clinical research toolkit, please visit NIH's website at http://www.nidcr.nih.gov/research/toolkit/. Also provide a protocol synopsis, template is referenced in the online grants management system.

Human Subject Research Plan

Please refer the Applicant's Guidelines for Clinical Classification at the link below
https://grantcenter.jdrf.org/wp-content/uploads/2012/12/Clinical-classification-27Jun2013.pdf
Below listed are the scenarios where human subjects research plan is required.

Types	Needed

No Human Subjects Research Proposed	Justification why the proposed studies do not constitute research involving human subjects
Non-Exempt Human Subjects Research	HSRP and CRRP
Human Subjects Research Claiming Exemption 1, 2, 3, 4, 5, or 6	Identify which exemption(s) (1, 2, 3, 4, 5, or 6) you are claiming and justify why the research meets the criteria for the exemption(s) that you have claimed.
Delayed-Onset Human Subjects Research	Either provide as much of the information that is requested as possible in HSRP & CRRP, OR describe why it is not possible to provide the information due to delayed-onset of human subjects research

Draft informed consent document

JDRF expects the content and format of the informed consent to be in compliance with ICH GCP-E6/ country specific regulatory requirement. The guidance document is available at http://www.fda.gov/RegulatoryInformation/Guidances/ucm404975.htm. A brief checklist is also provided as an appendix to human subjects research plan template.

Post award stage

Clinical milestones

The applicant should work with the JDRF's scientific contact to establish appropriate project milestones to track the progress throughout the lifecycle of an award. These milestones are finalized at the time of activation.

Process Prior to Subject Enrollment for Any Clinical Research

The Grantee Institution must comply with all Federal, state and local government regulations regarding the participation of human subjects and the use of animals in research. No part of the Award may be used to support any research involving human subjects that does not have the approval of the appropriate Ethics Committee (EC).

All projects with human subjects must have up-to-date ethical approval documentation at all times. For projects involving non-exempt human research, the Grantee Institution bears ultimate responsibility for protecting human subjects under the Award, including human subjects at all participating and consortium sites, and for ensuring that an Assurance approved by the Office for Human Research Protections ("OHRP") and certification of IRB approval have been obtained before human subjects research can be conducted at each collaborating site.

Where possible, JDRF strongly encourages the use of a Central IRB to improve the efficiency of conducting multi-site clinical studies. The Grantee Institution must ensure that JDRF receives required, up-to-date documentation for all sites in accordance with the Award milestone schedule and is current at the time of submission of award annual renewal materials. Failure to maintain and provide evidence of the necessary IRB certification or the equivalent would constitute a material breach of the award Terms and Conditions. The JDRF administrative resources available at www.jdrf.org describe in detail the documentation required to satisfy the ethical approval requirement.

Any changes to ethical documentation must be submitted to JDRF as approved. In the event that the IRB/EC has determined that the study is exempt, the documentation demonstrating the exempt status must be submitted to JDRF.

The Grantee Institution must notify JDRF within 24 hours if there are any regulatory issues, protocol violations or policy changes that impact the ability of the research investigative team to conduct the research as part of this Award.

Foreign Institutions: Ethical approval documentation submitted in a language other than English require a cover letter signed by the Grantee Institution's department head (in English) verifying the content of the form and countersigned by the Grantee Institution's Research Office of record.

Regulatory approval –e.g. Investigational New Drug or Investigational Device Exemption Requirements

The applicant is required to follow the laws pertaining to the need of applicable regulatory authority where the research is going to be conducted which for an international trial may vary from one country to another. The awardee must provide JDRF with any such regulatory approval documentations.

For US, consistent with Federal regulations, clinical research involving the use in humans of investigational therapeutics, vaccines, or other medical interventions (including licensed products and devices for a purpose other than that for which they were licensed) under a research protocol must be performed under a Food and Drug Administration (FDA) Investigational New Drug application (IND) or Investigational Device Exemption (IDE). Exceptions must be granted in writing by the FDA.

If a clinical trial funded by JDRF will be performed under an IND or IDE or equivalent, the awardee must provide the name and institution of the IND or IDE sponsor, the date the IND or IDE was filed with FDA, the FDA IND or IDE number, copies of transmittal memos to the IND or IDE, all comments from the FDA, and the written responses to those comments.

The FDA requires that the investigator wait at least 30 days from the FDA receipt of an initial IND or IDE application for the IND/IDE to be in effect before initiating a clinical trial.

The awardee must notify JDRF if the FDA ever places the study on clinical hold and provide JDRF any written comments from the FDA, written responses to the comments, and documentation in

writing that the hold has been lifted. The awardee may not use award funds to enroll new subjects in a clinical study during a clinical hold.

Clinical trial registration

JDRF requires all applicable clinical trials [including all non-exempt human subjects research] be registered in a clinical trial registry [country specific or international] e.g. Clinicaltrials.gov database to ensure information is freely available on JDRF funded trials within the T1D community. The registration should be **no later than 21 days** after the first subject is enrolled.

Study Status/Progress Reports and Documentation

In order to stay apprised of JDRF supported clinical study activities and progress, JDRF scientific Program Manager will work with the PI requesting specific information in the quarterly and/or annual progress report in addition to the information requested in JDRF's online grants management system or the progress report template [e.g. recruitment, milestone, renewal, etc.]. Standard templates for such will available in JDRF's online grants management system.

Required Time-Sensitive Notifications for Clinical Trials

Clinical trials funded by JDRF must follow ICH GCP/applicable regulatory requirement related to guidelines for safety reporting and reporting of unanticipated problems. JDRF scientific program manager should be informed within 24 hrs of notifying the Serious Adverse Event (SAE) to IRB and/or regulatory as applicable.

Clinical trial-Final progress reporting, If applicable

For all clinical trials, at final progress reporting, JDRF requires applicant to fill out a clinical trial results synopsis. Reference template is available in the online grants management system. This document will be completed by the applicant and uploaded as a separate attachment at final progress reporting in the online system.

References

- JDRF scientific guidelines-version 2011
- Templates referenced in online grants management system
    - Pre-award
        - Clinical Research Plan
        - Protocol Synopsis
        - Human Subject Research Plan
    - Post-award
        - Final progress report-clinical trial section

NIH Definition of Clinical Trial

A research study[1] in which one or more human subjects[2] are prospectively assigned[3] to one or more interventions[4] (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.[5]

[1] See Common Rule definition of "research" at 45 CFR 46.102(d).

[2] See Common Rule definition of "human subject" at 45 CFR 46.102(f).

[3] The term "prospectively assigned" refers to a pre-defined process (e.g., randomization) specified in an approved protocol that stipulates the assignment of research subjects (individually or in clusters) to one or more arms (e.g., intervention, placebo, or other control) of a clinical trial.

[4] An "intervention" is defined as a manipulation of the subject or subject's environment for the purpose of modifying one or more health-related biomedical or behavioral processes and/or endpoints. Examples include: drugs/small molecules/compounds; biologics; devices; procedures (e.g., surgical techniques); delivery systems (e.g., telemedicine, face-to-face interviews); strategies to change health-related behavior (e.g., diet, cognitive therapy, exercise, development of new habits); treatment strategies; prevention strategies; and, diagnostic strategies.

[5] A "health-related biomedical or behavioral outcome" is defined as the pre-specified goal(s) or condition(s) that reflect the effect of one or more interventions on human subjects' biomedical or behavioral status or quality of life. Examples include: positive or negative changes to physiological or biological parameters (e.g., improvement of lung capacity, gene expression); positive or negative changes to psychological or neurodevelopmental parameters (e.g., mood management intervention for smokers; reading comprehension and /or information retention); positive or negative changes to disease processes; positive or negative changes to health-related behaviors; and, positive or negative changes to quality of life.

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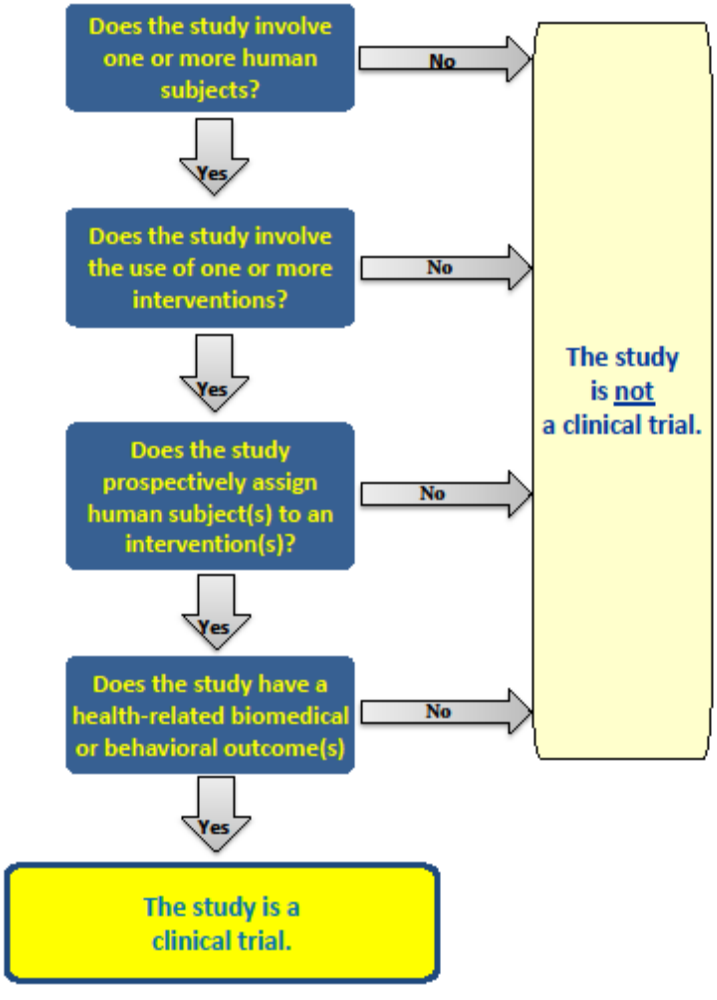
NIH Definition of Clinical Trial DecisionTree



Definitions

- Clinical Research: is research with human subjects that is: (1) Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes: (a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical trials, or (d) development of new technologies. (2) Epidemiologic and behavioral studies. (3) Outcomes research and health services research. Note: Studies falling under Exemption 4 for human subjects' research are not considered clinical research by this definition.
- ***Human Subjects*** The DHHS regulations "Protection of Human Subjects" (45 CFR 46, administered by OHRP) define a ***human subject*** as a living individual about whom an *investigator* conducting *research obtains*:
- o data through intervention or interaction with the individual or
- o identifiable private information.
- ***Investigator*** The OHRP considers the term investigator to include anyone involved in conducting the research. OHRP does not consider the act of solely providing coded private information or specimens (for example, by a tissue repository) to constitute involvement in the conduct of the research. However, if the individuals who provide *coded* information or specimens also collaborate on other activities related to the conduct of the research with the investigators who receive such information or specimens, they will be considered to be involved in the conduct of the research. (See OHRP's Guidance on Research Involving Coded Private Information or Biological Specimens: http://www.hhs.gov/ohrp/policy/cdebiol.html.)
- ***Research*** DHHS regulations define *research* at 45 CFR 46.102(d) as follows: *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.
- ***Obtains*** In general, obtaining identifiable private information or identifiable specimens includes, but is not limited to:
- (a) observing or recording private behavior;
- (b) using, studying, or analyzing for research purposes identifiable private information or identifiable specimens provided to investigators from any source; and
- (c) using, studying, or analyzing for research purposes identifiable private information or identifiable specimens already in the possession of the investigators.
- ***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. (45 CFR 46.102(f))

- ***Interaction*** includes communication or interpersonal contact between investigator and subject. (45 CFR 46.102(f))
- ***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 that has been provided for specific purposes by an individual and that 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. (45 CFR 46.102(f))
- ***Individually Identifiable Private Information*** According to its guidance for use of coded specimens, OHRP generally considers private information or specimens to be *individually identifiable* as defined at 45 CFR 46.102(f) when they can be linked to specific individuals by the investigator(s) either directly or indirectly through *coding* systems. Conversely, OHRP considers private information or specimens not to be individually identifiable when they cannot be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems.

HUMAN FETAL TISSUE IN RESEARCH

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:
   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. Assurance of the sponsoring institution that the research is in accord with local laws and regulations
   d. 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