Human Gene Transfer/Recombinant DNA Research

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Regulatory Requirements

Human gene transfer research is defined by federal regulations as ?any deliberate transfer of recombinant DNA, or DNA or RNA derived from recombinant DNA (technology), into human research participants.? Special provisions are necessary for conducting human gene transfer research at UCSF. PIs must complete a process of multiple reviews and approvals at both federal and local/institutional levels.

Applications to the following groups are required:

- FDA ? Food and Drug Administration
- IBC ? Biological Safety Committee at UCSF
- IRB at UCSF

PIs should consult before undertaking any gene transfer study.

These NIH guidelines apply to any research to be conducted at or sponsored by an institution receiving support for recombinant DNA research from NIH. Thus, they apply to all UCSF PIs involved in such research.

Applications at the Federal Level

FDA Review: The study sponsor or investigator-sponsor will need to submit an Investigational New Drug (IND) application to the FDA (see UCSF guidance on Investigational New Drugs and Biologics [1]). The IND number will be required for final IRB approval.

RAC Review: The NIH Guidelines, Appendix M [2], The Recombinant DNA Advisory Committee (RAC) within the NIH Office of Biotechnology Activities (OBA) has amended its reporting and review requirements and no long requires RAC approval. RAC [3] is a federal advisory committee that provides recommendations to the NIH Director related to basic and clinical research involving recombinant or synthetic nucleic acid molecules.

RAC is not required. Any recommendations resulting from the RAC review does not need to be included in the applicatiosn to the UCSF IBC and IRB.

FDA and local review is still needed.

Prepare protocols and consent forms in accord with NIH Guidelines, Appendix M, sections II-V [2]. See the NIH Guidance on Informed Consent for Gene Transfer Research [4] and RAC Frequently Asked Questions [5] for more information.

Applications at UCSF

After the study sponsor or investigator-sponsor has sought initial IND approval from the FDA, the UCSF PI must apply for institutional review of the gene transfer research.

IBC Review: The PI will need to obtain a Biological Use Authorization (BUA) [6].

IRB Review: The PI must also obtain approval from the IRB. In the "Other Approvals and Registrations" section of the IRB Application, indicate that the study involves human gene transfer. Attach the following as Other Study Documents:

- NIH Appendix M-II: Description of Proposal
- RAC correspondence, recommendations and review letter

Applications may be submitted simultaneously to the IBC and IRB for parallel review.

Coordination of Approvals

IRB and IBC: The IRB and IBC will coordinate resolution of any concerns raised by either committee before issuing final authorization and approval. A link will be maintained between the approved IRB Application and the BUA for the life of the study.

IRB and FDA: The IRB must receive the IND approval number (obtained from the FDA) before final IRB approval is issued.

Reporting Adverse Events

Should an adverse event occur within a gene transfer study, submissions may be required to the following groups:

IRB and IBC

The UCSF PI must consult and follow policies and procedures for reporting adverse events to the IRB [7] and the IBC [6].

OBA

PIs at all sites must report qualifying serious adverse events to the OBA according to the guidance provided in Appendix M-I-C-3 and M-I-C-4 of the NIH Guidelines [2]. PIs may delegate this task to another party (e.g., the sponsor), provided a letter of delegation signed by the PI is on file with the OBA. In either case, any OBA reports concerning UCSF-enrolled participants should also be submitted to the IRB and IBC.

FDA

If the study IND is held by a UCSF investigator (investigator-sponsor), the PI must also report qualifying SAEs directly to the FDA (see 21 CFR 312.32 [8]). If the study IND is held by an outside sponsor (sponsor-initiated), this responsibility falls to the sponsor.

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Links
[1] https://irb.ucsf.edu/investigational-new-drugs-and-biologics
[2] http://osp.od.nih.gov/sites/default/files/NIH_Guidelines_0.pdf
[3] http://osp.od.nih.gov/office-biotechnology-activities/biomedical-technology-assessment/hgt/rac
[4] http://osp.od.nih.gov/office-biotechnology-activities/biomedical-technology-assessment/hgt/guidance/web-based-informed-consent-guidance
[5] http://osp.od.nih.gov/office-biotechnology-activities/biomedical-technology-assessment/faq
[6] http://www.ehs.ucsf.edu/ucsf-institutional-biosafety-committee-0
[7] https://irb.ucsf.edu/adverse-event
[8] http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=312.32