

Section 36:

Gene Transfer Research (recombinant DNA)

Human gene transfer is an experimental procedure of recombinant DNA technology. The objective of human gene transfer trials is to replace absent or faulty genes that cause disease with working genes that ensure the production of healthy enzymes and proteins. The healthy DNA is transferred by way of “vectors,” such as viral vectors (e.g. Adenovirus, Herpes viruses), modified to make them less virulent and incorporating the DNA of interest.

Human gene transfer involves significant risks. To ensure the management and minimization of associated risks, IRBs, institutional biosafety committees (IBCs), and federal agencies, such as the FDA and the National Institutes of Health’s (NIH) Office for Biotechnology Activities (OBA) are responsible for overseeing such trials.

Gene transfer trials that are funded by the NIH or that take place at an institute that receives NIH support must also adhere to the guidelines issued by the OBA. Investigators are encouraged to review OBA Appendix M “Points to Consider in the Design and Submission of Protocols for the Transfer of Recombinant DNA Molecules Into One or More Human Research Participants” which can be found at http://oba.od.nih.gov/oba/rac/guidelines_02/NIH_Guidelines_Apr_02.htm. Submission of human gene transfer protocols to NIH must be in the format outlined in OBA Appendix M-1-A. This submission allows each trial to be registered with the NIH and provides the public with a current list of ongoing trials that involve gene transfer.

After receiving the proposed research, the NIH/OBA will determine whether the trial warrants full review by the Recombinant DNA Advisory Committee (RAC). The initial RAC review takes place within 15 days of receipt and one of the following two outcomes are possible:

1. The experiment does not present characteristics that warrant further review or discussion and is therefore exempt from public RAC review and discussion; or
2. The experiment presents characteristics that warrant public RAC review and discussion.

The overall PI will receive a letter from the NIH/OBA indicating the outcome of the review.

As stated in OBA Appendix M-1-B-1, research participants may not be enrolled until all of the following requirements are met:

- RAC review process is completed;
- IBC approval (from the clinical site) has been obtained;
- IRB approval has been obtained; and
- All applicable regulatory authorization(s) have been obtained (i.e., IND applications also must be filed with the FDA [[21 CFR 312.23](#), *IND Content and Format*]).

The state of Massachusetts does not allow discrimination against an individual based on genetic information. The state mandates:

1. Participant’s be given consent prior to genetics information being shared; and

2. The results cannot be disclosed to any person without the participant's prior written consent.

In the following cases, a waiver of consent will be considered by the IRB where the results will be used only as confidential research information for the purpose of:

1. Generating scientific knowledge about genes; or
2. Learning about the genetic bases of disease; or
3. Developing pharmaceutical or other treatments of disease

Serious and unexpected adverse events experienced by participants enrolled in gene therapy trials must be reported to the IRB, IBC, OBA, and other federal agencies, if applicable. For further instructions, see the chapter entitled "Serious Adverse Event (SAE) Reporting Policy."