

Section 11: Expanded Access to Investigational Treatment

The following are *not* considered clinical trials but instead offer expanded access to investigational treatment to those participants who have not benefited from conventional therapy.

11.1 Emergency Use

The DFCI IRB allows the emergency use of an investigational drug or biologic if the FDA requirements for emergency use are met.

The emergency use provision in the FDA regulations is an exemption from prior review and approval by the Institutional Review Board but does require obtaining informed consent from the participant, and may not be used unless each of the following conditions exist:

1. The patient is in a life-threatening or severely debilitating situation;
2. There is no standard acceptable treatment available; and
3. There is not sufficient time to obtain approval from the Institutional Review Board.

Life-threatening means diseases or conditions where the likelihood of death is high. The criteria for life-threatening do not require the condition to be immediately life threatening or to immediately result in death. Rather, the participants must be in a life-threatening situation requiring intervention before review at a convened meeting of the Institutional Review Board is feasible.

Even in an emergency situation, the investigator is required to obtain informed consent from the participant or the participant's legally authorized representative.

When these instances arise, the investigator must contact the Senior Director or Deputy Director of OHRS.

1. OHRS will review the applicable regulatory requirements and institutional requirements with the investigator.
2. The OHRS information sheet outlining regulatory and institutional policies and procedures will be provided to the investigator.
3. If the use of the test article does not meet the regulatory requirements, the investigator will be informed that he or she may not proceed with the use of the test article.
4. If the use does meet the regulatory requirements, the investigator will be informed regarding appropriate documentation for subsequent submission to the IRB.
5. The investigator will receive documentation that the request has been cleared and obtain a protocol number so that pharmacy can dispense and nursing can administer the investigational agent.
6. The investigator will be required to submit protocol and consent documents for review by fully convened IRB. These documents will be placed on the next available agenda.

7. The investigator must obtain permission from the sponsor.
8. The emergency use of an unapproved investigational drug or biologic requires an IND. However, the FDA may authorize shipment of the drug or biologic in advance of the IND submission when there is insufficient time. FDA contacts for obtaining an Emergency IND are available at <http://www.fda.gov/RegulatoryInformation/Guidances/ucm126491.htm>.

11.2 Treatment IND (Single Patient IND)

Some drugs that have not yet been approved by the FDA for marketing may be appropriate to use in the treatment of patients who are not in clinical trials. The FDA has developed a system to facilitate the availability of promising new drugs to desperately ill patients as early as possible in the drug development process, before general marketing begins, and to obtain additional data on the drug's safety and effectiveness.

For the purposes of the DFCI IRB, "treatment use" of a drug includes the use of the drug for diagnostic purposes. When an investigational drug meets the criteria listed below it will be submitted to the FDA as a "treatment protocol" or "treatment IND".

Criteria:

1. The drug is intended to treat a serious or immediately life-threatening disease;
2. There is no comparable or satisfactory alternative drug or other therapy available to treat that stage of the disease in the intended patient population;
3. The drug is under investigation in a controlled clinical trial under an IND in effect for the trial, or all clinical trials have been completed; and
4. The sponsor of the controlled clinical trial is actively pursuing marketing approval of the investigational drug with due diligence.

When the investigator determines that he or she is in this situation the following must occur:

1. Notify the Senior Director or Deputy Director of OHRS that a treatment IND will be submitted to the FDA; provide copies of the documentation to be submitted.
2. The study documents, including the protocol and informed consent form, will be placed on the next available convened meeting of the IRB for review and approval.
3. The investigator must obtain permission from the sponsor.
4. The investigator will be required to submit FDA documentation to the OHRS for inclusion in the study's file immediately after it becomes available. This is required for activation.
5. The treatment IND will be subject to all the requirements of human subjects research including reporting of unanticipated problems to the IRB, safety reports to the FDA, informed consent, and continuing review to highlight a few of these requirements.

11.3 Human Gene Transfer Research

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 Submissions of Protocols for the Transfer of rDNA Molecules Into One or More Human Research Participants” which can be found at www4.od.nih.gov/oba/rac/guidelines_02/APPENDIX_M.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 subjects may not be enrolled until all of the following requirements are met:

- RAC review process is completed;
- IBC approval 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](#), Subpart B, Section 23, *IND Content and Format*]).

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

1. Subject’s be given consent prior to genetics information being shared; and
2. The results cannot be disclosed to any person without the subject’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 subjects enrolled in gene therapy trials must be reported to the IRB, IBC, OBA, and other federal agencies, if applicable. For further instructions, see Serious Adverse Event (SAE) Reporting Policy.