

Title: Recombinant DNA Research	*Applicable to: Beaumont Health	Effective Date: 01/12/2018
		Last Periodic Review Date: 01/12/2018
Policy Owner: Administrative Director	Document Type: Policy	Functional Area: IRB and Clinical Research, Research Institute

***For This Document, Beaumont Health Includes:**
 Beaumont Corporate Shared Services
 Beaumont Hospital, Dearborn
 Beaumont Hospital, Farmington Hills
 Beaumont Hospital, Grosse Pointe
 Beaumont Hospital, Royal Oak
 Beaumont Hospital, Taylor
 Beaumont Hospital, Trenton
 Beaumont Hospital, Troy
 Beaumont Hospital, Wayne
 Beaumont Medical Group
 Beaumont Pharmacy Solutions
 Post Acute Care

I. PURPOSE:

The purpose of this policy is to provide guidelines for research involving gene transfer conducted at Beaumont Health. These guidelines include transfer of human or non-human genetic material, to human subjects (in clinical trials), non-human subjects (in experimental animal studies), or cell culture (*in vitro* experiments).

II. GENERAL:

This policy applies to investigators, key personnel, Institutional Biosafety Committee (IBC) members, Institutional Review Board (IRB) members, Animal Care Committee (ACC) members, and other Beaumont staff.

III. DEFINITIONS:

A. Cells Subject to Gene Transfer:

1. **Allogenic:** Cells which differ genetically, although they are obtained from the same species. In transplantation biology, this refers to cells that differ with regard to their cell surface (transplantation) antigens.
2. **Autologous:** Cells obtained from an individual, which are to be administered back to the same individual (often after their numbers are expanded in vitro).

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3. ***Xenogeneic***: Cells obtained from a different species.
- B. ***Genetic Engineering***: The process of manipulating the genetic material of organisms.
 - C. ***Gene Transfer***: The introduction of DNA from a different source into cells, usually by vectors such as plasmids or modified viruses. Cells may be modified in vitro in this manner for subsequent administration to humans, or may be altered in vivo by transfer of human or animal genes to the subject. The genetic manipulation of cells may be intended to have a therapeutic or prophylactic effect, or, in experimental animals, it may provide a way for marking cells for later identification. Genetically modified cells may be administered to patients in various ways (e.g., local or systemic injection, or surgical implantation).
 - D. ***Excipients, Additional Active Components, or Medical Devices***: Materials such as beads, fibers, matrices, or polymers which are used in addition to cells in the delivery of genetically modified cells into the body.
 - E. ***Ex Vivo***: Literally “out of or from life,” i.e., refers to tissues or cells removed from an organism.
 - F. ***In Vitro***: Literally “in glass,” i.e., in a test tube or Petri dish or other culture flask; the opposite of in vivo; describes biological reactions or manipulations that take place in laboratory containers.
 - G. ***In Vivo***: Literally “in life,” i.e., in the body. In a living organism; a reaction, process, or experiment in a living organism.
 - H. ***Recombinant DNA***: DNA which has been altered from its original form. This usually involves inserting a gene or gene segment from one organism into the genome of a different organism, creating DNA sequences that would not otherwise be found in biological organisms. The alteration and recombination of genetic material in the laboratory often involves cutting DNA molecules at specific sites and splicing together specific DNA fragments. The DNA may be natural or synthetic. The altered DNA fragment may be inserted into another DNA molecule by chemical, enzymatic, or biologic means.
 - I. ***Somatic Cell Gene Therapy***: The repair or replacement of a defective gene within somatic (body) tissue by administration to humans or animals of autologous, allogeneic, or xenogeneic living cells which have been genetically manipulated or processed *ex vivo*.

IV. **OVERVIEW:**

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Human gene transfer, also known as human gene cell therapy, is the process of transferring modified genetic material (DNA or RNA) into humans. Cells may have their nucleic acid modified *in vitro*, and the cells may then be transferred into human subjects, or genetic material may be transferred directly to the subject. When the genetic manipulation is performed *in vitro* on cells which are then administered to the patient/participant, this is a form of somatic cell therapy. The genetic manipulation may be intended to achieve a therapeutic or prophylactic effect, or to mark cells for later identification. Transfer of genetic material into human subjects requires further regulatory oversight, including review by the IBC and possibly other committees, in addition to IRB approval. Studies involving gene transfer are also subject to IBC review even if they do not involve human or experimental animal subjects.

The goal of gene therapy performed in human participants is to improve the quality of life for persons with genetic disorders, and to treat complex diseases (e.g., cancer, heart disease) or certain infectious diseases (e.g., AIDS). This document summarizes important aspects of the National Institutes of Health (NIH) and Food and Drug Administration (FDA) guidelines on human gene transfer research, including clinical protocols. A full copy of the NIH guidelines may be found at: http://osp.od.nih.gov/sites/default/files/NIH_Guidelines.html.

V. PROCEDURES:

A. IRB

IRB initial applications for studies involving gene transfer research must include completion of the questions in the application relating to gene therapy. IRB initial approval or exemption for gene therapy studies will not be granted until authorizations are received from the IBC, the FDA and other federal regulatory organizations as required. Participants may not be enrolled into a gene transfer study until all regulatory requirements have been met. IRB initial applications, full board amendments, progress reports and expedited amendments also require IBC review and approval prior to IRB approval being granted. Amendments which only request addition or removal of key personnel (other than the Principal Investigator) do not require IBC review prior to IRB review and approval.

B. Institutional Biosafety Committee

Approval from the IBC must be obtained for each new study involving the use of recombinant gene therapy in human participants before IRB approval will be granted, and in animals before ACC approval will be granted. IBC approval must also be obtained for new

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protocols, amendments, progress reports, etc. employing recombinant DNA technology even if the protocols do not involve human or animal subjects.

The IBC application is available on the Research Institute website, and may be obtained by contacting the IBC Secretary (Mary Farwell), or the IBC Chair (Dr. Stewart Graham). Investigators should submit IBC applications using the IRB application form (via iMedRIS) if the application is also being submitted to the IRB. The IRB will then route the application to the IBC Chair for review. If the application involves experimental animals, it should be submitted by the PI directly to both the ACC and the IBC. The committee will notify the IRB or ACC of its decision once the study has been reviewed. If the study also requires IRB approval, the IBC decision will also be posted in iMedRIS.

If neither IRB nor ACC approval is required, but IBC approval is required (because the protocol, although being conducted *in vitro*, involves gene transfer or the use of potentially pathogenic organisms), the PI must submit an application directly to the IBC.

C. Federal Oversight Bodies National Institutes of Health (NIH)

Investigators conducting gene transfer research sponsored by an institution that receives NIH support for recombinant DNA research must comply with Appendix M of the NIH Guidelines, found at: http://osp.od.nih.gov/sites/default/files/NIH_Guidelines.html. Appendix M outlines the main points for investigators to consider when submitting a protocol to the Federal Office of Biotechnology Activities (OBA). If a protocol is subject to the NIH Guidelines, the investigator must register the protocol with the OBA and, typically, with the NIH Recombinant DNA Advisory Committee (RAC). The OBA serves in an advisory capacity, but has no power to approve protocols. Once a protocol is initiated, it must be reported to the OBA. If registered with the RAC, a filing must be made again twenty (20) days after the first subject is enrolled into a clinical trial. In addition, the OBA and the RAC require principal investigators to submit annual reports in accordance with Appendix M. Unanticipated Problems/Adverse Events must be reported to the IRB (according to IRB Policy [Reporting an Unanticipated Problem Involving Risk to Participants or Others](#)), the IBC and the OBA in accordance with Appendix M. The investigator is responsible for submitting the Unanticipated Problem form and OBA form to the OBA.

D. Food and Drug Administration

The FDA is responsible for the review and approval of gene therapy products as Investigational New Drugs (INDs). Full copies of the FDA guidelines are available at <https://www.fda.gov/BiologicsBloodVaccines/guidanceComplianceRegulatoryInformation/Guidances/CellularandGeneTherapy/default.htm>.

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The FDA's primary objective in the review of INDs is to assure the safety and rights of participants in all phases of the investigation. In Phase 2 and Phase 3 trials, the FDA assures the quality of the scientific evaluation of the investigational product is adequate to permit the determination of its safety and effectiveness. The FDA also requires related serious adverse event (SAE) reporting and annual reports.

E. **Informed Consent**

Gene transfer concepts are often difficult for potential study participants to understand. Thus, the OBA has developed guidelines on the issue of informed consent in gene transfer studies (<https://auth.osp.od.nih.gov/office-biotechnology-activities/biosafety/biosafety-guidance>). The guidelines focus on the issues of conflict of interest, comprehension, timing of consent, and assent. The guidelines may be used as a resource for investigators in developing an informed consent document for a gene transfer protocol by discussing each topic that should be covered. The Beaumont Informed Consent and Authorization template should be used to ensure all required elements of informed consent have been addressed.

For more information on this topic, investigators should visit:

<https://auth.osp.od.nih.gov/office-biotechnology-activities/biosafety/biosafety-guidance>.

VI. **APPLICABLE REGULATIONS AND GUIDELINES:**

NIH Guidance on Informed Consent for Gene Transfer Research
 NIH Guidelines, Appendix M
 FDA Center for Biologics Evaluation and Research Cell and Gene Therapy
 45 CFR 46.116- Informed Consent
 21 CFR 50- Subpart B- Informed Consent

VII. **REFERENCES TO OTHER APPLICABLE POLICIES:**

RI Administration Policy [Biosafety Committee Operations](#)
 IRB Policy [Reporting an Unanticipated Problem Involving Risk to Participants or Others](#)
 IRB Policy [IRB Initial Review of Research Protocols](#)
 IRB Policy [Informed Consent and Authorization in Research](#)

CORPORATE AUTHORITY:

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Beaumont Health (“BH”) as the corporate parent to William Beaumont Hospital, Botsford General Hospital, and Oakwood Healthcare Inc., (“Subsidiary Hospitals”) establishes the standards for all policies related to the clinical, administrative and financial operations of the Subsidiary Hospitals. The Subsidiary Hospitals, which hold all health facility and agency licenses according to Michigan law, are the covered entities and the providers of health care services under the corporate direction of BH. The Subsidiary Hospitals’ workforces are collectively designated as BH workforce throughout BH policies.