TITLE: Institutional Review Board Special Considerations
SC 514 Review of Genetic Research

ORIGINATOR: Institutional Official

APPROVAL: Institutional Official

POLICY STATEMENT: Mercy Health IRB requires that special consideration be given during the review of studies involving genetic research and genetic information. The risks of participating in genetic studies are many such as risks to individual dignity, invasion of privacy, violation of confidentiality, stigmatization of a subject or group, potential for discrimination in insurance or employment, psychological harm, generation of conflict within a family, harm to relatives, inappropriate commercialization of findings, or use of samples in projects objectionable to the subject. Investigators must take great care in protecting the genetic information when conducting research.

Additionally, the consent process should include explicit descriptions of the type and scope of genetic information that will be collected and used in the research project. In addition to federal regulations, all research conducted at Mercy Health regional sites complies with the CHE Trinity Health Mission, Core Values, and Catholic moral/ethical principles, as delineated in the "Ethical and Religious Directives for Catholic Health Care Services." In this regard, IRB review and decision making gives special consideration for research participants' cultural, racial, social, religious, and economic circumstances.

Investigators must also take into consideration the effects of the knowledge that the participant may be the carrier of a disease gene that might affect their life course, employability or insurability if results were to be shared. If subjects want to be told of results, precautions must be taken to minimize the potential harm of receiving bad news and to preserve the confidentiality of the results. The precautions needed in conveying genetic screening results depend upon the age of onset of the disorder, the burden of illness, and the availability of treatment or prevention. The communication of genetic information carries with it the responsibility to interpret the results and provide care for the individual; and thus, it is ideally done in the setting of a clinical rather than research relationship with the subject.

The IRB requires investigators provide a written plan to ensure the privacy and confidentiality of participant's genetic information, minimize the risks associated with genetic research, and provide a plan for adequate disclosure of genetic results that may be clinically relevant to the participant. The IRB will consider whether the written plan for disclosure of results and the protections against disclosures of genetic data to anyone other than the participant are adequate.

GENERAL PROVISIONS:
The IRB realizes that information developed in the course of genetic studies may vary considerably with respect to its impact and/or value to subjects. With that in mind the IRB has developed the following guidelines for investigators, and acknowledge that there are many ways of responding to each item. The acceptability of the responses will be determined in the context of each study.

With respect to disclosure, however, the IRB prefers written information in conjunction with other methods of disclosure (such as a verbal discussion) be used. The IRB also prefers that appropriate personnel (such as genetic counselor, physician, and the principal investigator) be included in the team that discloses the genetic results to the participant. In these guidelines, the use of the word "participant" or "patient" refers to competent individuals. In the case of decisionally impaired or incompetent adults, the guidelines would apply to their proxy.
Genetic counseling provided to individuals in our organization will never support the abortion of a non-viable fetus if genetic screening were to identify an issue that may affect a fetus's life course.

**Confidentiality:** Investigators must establish a method to secure information related to genetic testing in a highly secure and confidential manner, and communicate this method in a manner satisfactory to the IRB. Many genetic studies involve the long-term storage of specimens or data in biorepositories. In some of these studies, it is not clear what results the future testing on banked specimen will yield, so it is essential that participants be fully informed about their subsequent knowledge of research results and future research results. If identifiers are removed from the test results (data) or the banked specimens, it should be clear to participants that they will not be informed of future results because their data/specimens cannot be linked back to them. Likewise, there is the consideration of future participant withdrawal. If data/specimens cannot be linked back to participants, the consent document must indicate that future withdrawal will be impossible to accomplish.

**Privacy:** With respect to studies which are investigations of hypotheses related to the genetic determination of a disease, identity of the participants in the study will not be disclosed, except as described in their informed consent document.

**Non-Paternity:** Because the discovery of non-paternity is also a special problem in genetic studies, the informed consent process should clarify this risk to participants when appropriate.

**Insurability and Employability:** If there is a potential risk to the participants insurability or employability as a result of participation in the study, the consent document should disclose this. In the United States, the Genetic Information Nondiscrimination Act of 2008 (GINA) prohibits discrimination in health coverage and employment based on genetic information. All entities that are subject to GINA must, at a minimum, comply with all applicable GINA requirements, and may also need to comply with more applicable State laws. GINA, together with the Health Insurance Portability and Accountability Act (HIPAA), generally prohibits health insurers or health plan administrators from requesting or requiring genetic information of an individual or the individual’s family members, or using it for decisions regarding coverage, rates, or preexisting conditions. The law also prohibits most employers from using genetic information for hiring, firing, or promotion decisions, and for any decisions regarding terms of employment.

**Disclosure of Information:** Identifiable results will not be disclosed to the participant or anyone else except in compliance with an approved protocol for contacting participants and/or family members. Information about results may be released to participants when IRB criteria for clinical application of results are met, (i.e., the claimed association between marker or gene and disease is generally accepted by the medical genetics community). Information about results may be released to the participant's family members or others if, and only if, the participant gives written permission.

**Process for Disclosure of Results:** Because of the potentially sensitive and private nature of the results of genetic testing, the IRB must have a clear understanding of who will have access to study information, and under what circumstances access will be granted. Keep in mind that when participants are informed about the results of their genetic testing, complete anonymity is virtually impossible to accomplish.

In addition, there are specific requirements in place regarding the certification of the lab(s) conducting the testing, and the qualifications of individual(s) disclosing the results to participants.

**CLIA Certification:** Laboratories performing testing on human specimens and reporting patient-specific results must be certified under the provisions of the Clinical Laboratory Improvement Amendments of 1988 (CLIA) (57 CFR 7139, Sec. 493.1). If researchers wish to provide diagnostic results to participants or use test results to alter care, they should have laboratory tests performed under the auspices of a clinical laboratory that has been certified in accord with CLIA.

**Individual Participant(s) and Age Considerations:** Investigators and their IRB must weigh the risks and benefits that may result from giving a participant access to their own test results. The investigator should indicate what individual (including their title and qualifications) will disclose results. Additionally, the investigator should indicate which participants will receive results. If age is a consideration in determining who will receive results, the investigator should indicate that and indicate at what age participants will receive their results directly. Because of the vulnerability of minor subjects, special attention should be paid to whether it is appropriate to disclose genetic information to participants less than 18 years of age. Justification for disclosure before the age of 18 might include age of onset of the condition and whether therapeutic interventions currently are available.
Methods: The investigator should indicate what method of disclosure (i.e., written, telephone, in person, etc.) will be used.

Genetic Counseling: The investigator should indicate what provisions have been made to answer questions that may arise as a result of disclosure. Regardless of whether or not genetic counselors are utilized, there should be an indication of who will respond to such questions and how long the services will be available to participants. In addition, it should be indicated how the services will be paid for.

Post-Disclosure or Follow-Up: The investigator should indicate what plans there are for regular post-disclosure contact or follow-up with participants.

Costs: The investigator should indicate what specific costs the participant may be responsible for in conjunction with disclosure.

Coercion: Genetic research may involve the study of a certain family pedigree or specific social or ethnic group. Recruitment from such a narrow pool of participants may place undue pressure on individuals to participate. Because coercion by family members is conceivable and a different or more serious problem in genetic studies than in studies of other types, study protocols should be designed to minimize this risk so that family members who are not interested in participating are not burdened to do so. Investigators are encouraged to deal with this issue directly in the informed consent process and also in their description of how they will enroll patients in their studies. Federal regulations direct that the “selection of subjects is equitable” [45 CFR 46.111(a)(3)], and that “an investigator shall seek such consent only under circumstances that provide the prospective subject...sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence” (46.116).

Additional Considerations
1. Investigators may want to consider acquiring a Certificate of Confidentiality.
2. If the results of the genetic testing yield abnormal test results, investigators should consider whether or not they plan to disclose those findings to the participant's primary care physician for clinical use.
3. Additional considerations must be included when the study includes genetic testing and vulnerable populations (e.g. children, persons with impaired decision-making capacity or impaired mental function, etc.). The investigator should consider what circumstances would warrant the use of a Legally-Authorized Representative (LAR) in a study involving genetic testing.
4. Protections should be considered when the time comes for the investigator to publish the results of the study. Investigators and the IRB must consider if the publication plans threaten the privacy or confidentially of participants.
5. If the research involves ancillary participants (i.e. family members):
   - The IRB should consider if recruitment methods have been designed so that the privacy of family members is not violated. The IRB should also consider if recruitment information will be obtained through the clinical medical records of family members. If yes, the IRB should determine if the resultant participants should be consented separately, or if the permission of the primary participant is sufficient.
   - The IRB should consider if family members will be protected against disclosure of medical or personal information about themselves to other family members.
6. The IRB should consider if primary and resultant participants be given the option to not receive information about themselves.
7. The IRB should consider if there will be limits on such protections when family members, etc. need to be informed about health risks. They must also consider in what situations it would be appropriate to overrule the participants’ decision to not receive results. The IRB should also determine if these situations are clearly delineated in the consent document.

IRB members may defer questions related to the Ethical Directives to the Mercy Health Ethics Committee for review and consultation.

Gene Therapy
Human gene transfer is the process of transferring genetic material (DNA or RNA) into a person. At present, human gene transfer is experimental and is being studied to see whether it could treat certain health problems by compensating for defective genes, producing a potentially therapeutic substance, or triggering the immune system to fight disease. Human gene transfer may help improve genetic disorders, particularly those conditions that result from inborn errors in a single gene (for example, sickle cell anemia, hemophilia, and cystic fibrosis). It may also hold promise for diseases with more complex origins, like cancer and heart disease. Gene transfer is also being studied as a possible treatment for certain infectious diseases, such as AIDS. This type of experimentation is sometimes called “gene therapy” research.
Review of Gene Transfer Research

Investigators must submit all information and documents for gene transfer research to the IRB. This information must include the following:

- delivery methods
- target population
- required follow-up

The assigned IRB reviewer(s) may work with the IRB Chairperson to identify and contact an external consultant, as necessary, to provide independent guidance to the IRB.

Research involving gene transfer to human subjects must be reviewed and approved by the National Institutes of Health Recombinant DNA Advisory Committee and the Mercy Health Ethics Committee prior to IRB approval. The Ethical and Religious Directives for Catholic Health Care Services will be closely considered in the review of gene transfer research. Monitoring must be adequate and a DSMB is required for Gene Transfer Research projects.

From a Catholic moral perspective the use of gene therapies in research raises a range of questions that will need in-depth ethical review dependent upon the scientific nature of proposed research. In general, however, the following moral principles should guide Mercy Health research protocols:

- The dignity of the human person demands unconditional respect from conception to natural death
- Procedures used on somatic cells (cells other than reproductive and which make up the tissue and organs of the body) for strictly therapeutic purposes are in principle morally licit. However, it is necessary to establish beforehand that the person being treated will not be exposed to excessive or disproportionate risks to his/her health or physical integrity. Informed consent is required of the patient or his/her legitimate representative.
- At the present time, germ cell therapy in all of its forms is NOT morally licit. In the present state of research, the risks associated with this therapy are considerable and may cause harm to the resulting progeny.

DEFINITION:

Human Genetic Research: Genetic studies include but are not limited to: (a) pedigree studies (to discover the pattern of inheritance of a disease and to catalogue the range of symptoms involved); (b) positional cloning studies (to localize and identify specific genes); (c) DNA diagnostic studies (to develop techniques for determining the presence of specific DNA mutations); (d) gene transfer research (to develop treatments for genetic disease at the DNA level), (e) longitudinal studies to associate genetic conditions with health, health care, or social outcomes, and (f) gene frequency studies. Unlike the risks presented by many biomedical research protocols considered by IRBs, the primary risks involved in the first three types of genetic research are risks of social and psychological harm, rather than risks of physical injury. Genetic studies that generate information about subjects' personal health risks can provoke anxiety and confusion, damage familial relationships, and compromise the subjects' insurability and employment opportunities. For many genetic research protocols, these psychosocial risks can be significant enough to warrant careful IRB review and discussion. Those genetic studies limited to the collection of family history information and blood drawing should not automatically be classified as "minimal risk" studies qualifying for expedited IRB review. Because this is a developing field, there are some issues for which no clear guidance can be given at this point, either because not enough is known about the risks presented by the research, or because no consensus on the appropriate resolution of the problem yet exists. OHRP representatives have advised that “third parties,” about whom identifiable and private information is collected in the course of research, are human subjects. Confidentiality is a major concern in determining if minimal risk is involved.

REFERENCES:

National Society of Genetic Counselors  http://www.nsgc.org/
DHHS Statement of Genetic Testing  http://www.hhs.gov/asi/testify/t990421c
45 CFR 46
21 CFR 50, 56
Office for Protection from Research Risks- Issues to Consider in the Research Use of Stored Data or Tissues, November 7, 1997.
ATTACHMENTS:
SC 514-A Worksheet for Review of Genetic Research
SC 514-B Informed Consent Language for Genetic Research

PROCEDURE:

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<th>Responsibility</th>
<th>Action</th>
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<td>IRB Specialist/IRB Coordinator</td>
<td>1. Review incoming submission and determine if they involve the collection and utilization of genetic materials or information.</td>
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<td>2. Inform IRB Chairperson that the submission involves genetic research and provide the chair with a prepared review packet which includes the Worksheet for Review of Genetic Research.</td>
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<td>3. Assist the Chairperson in gathering the information needed to allow for an adequate review.</td>
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<td>4. Place item on next IRB meeting agenda if it is to be reviewed by the full IRB committee</td>
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<td>5. Place item on next IRB meeting agenda under expedited reviews (if applicable)</td>
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<td>4. Prepare correspondence as advised by the IRB Chairperson.</td>
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IRB Chairperson

1. Review submission and determine if there is enough information included in the submission to allow for an adequate review.
2. Assign a reviewer to complete the review of the genetic research and request referencing the Worksheet for Review of Genetic Research.
3. Provide a summary of the review to the committee at the time of full board committee meeting (if applicable) or request the item be placed on the next IRB meeting agenda under expedited review section (if applicable)

IRB Committee

1. Review submission and determine the following:
   - Is the plan is adequate to ensure the privacy and confidentiality of the participants genetic information?
   - Are the risks minimized?
   - Is there a clear plan for disclosure of genetic results?

IRB Assigned Reviewer

1. Review submission and reference the Worksheet for Review of Genetic Research.
Investigator

1. Provide the IRB with a written plan for protecting genetic information and disclosure of testing results to participants.
2. Utilize the Mercy Health informed consent template language for genetic research when appropriate.

CONCURRENT CONSENTS:

Institutional Official

[Signature]