TEXAS A&M UNIVERSITY
SAN ANTONIO

Institutional Review Board

GUIDELINE # 9: GENETIC RESEARCH

I. PURPOSE

This guideline is to ensure that human subjects' research conducted complies with federal, state and local laws, regulations, directives and instructions.

II. STATEMENT

All human subjects research, irrespective of the source of funding, conducted by A&M- SA faculty, staff and students must be submitted and reviewed in accordance with the Federal research regulations, Texas A&M System Guidelines, A&M-SA IRB policies and local consideration.

For this guideline, genetic research pertains to relevant human genetic information including heritable genotypes, mutations, chromosomal changes, gene expression, and epigenetics, and nucleic acids (DNA & RNA) based specimens. Microbiome studies are not considered to be genetic research.

III. SCOPE

This guideline applies to all research conducted where the A&M- SA IRB serves as the Reviewing IRB.

The scope of the guideline includes all-

i. genetic analysis that can be either the main goal of the study, or an optional sub-study, or otherwise a part of the study.
ii. genetic analysis in small scale study (e.g. one SNP location) or a large scale study (e.g. whole genome).

IV. Risk Considerations for Genetic Research

Information developed during genetic studies may vary considerably with respect to its impact and value to subjects. When using the following guidance, it is acknowledged that there are many ways of responding to each item. The acceptability of the responses will be determined in the context of each study.

Privacy and Confidentiality Considerations:

Privacy in this context refers to a participant's feeling of control over the extent, timing, and circumstances of sharing one's genetic information and resultant health status with others. Confidentiality refers to the protection of the data associated with genetic research, such that the participant has control over the extent, timing, and circumstances of sharing this information.

Investigators must use appropriate methods to secure and disclose information related to genetic testing to protect privacy and confidentiality. For additional privacy and confidentiality protection, investigators may want to consider acquiring a Certificate of Confidentiality (see IRB guidance on Certificates of Confidentiality).

Information about Family Members:

Because genetic information can have implications for a participant's relatives, it is important to consider the privacy and confidentiality of family members as well. Recruitment of a participant's family members must be designed so that the privacy of family members is not violated. Personal, private information about an individual should be protected against disclosure to other family members in the study. Investigators must consider appropriate methods when disclosure of individual results to a participant will infer genetic and health status of others in the family. This could include the discovery of non-paternity, therefore, consideration on how such information is handled should be considered.

Undue Influence:

Genetic research may involve the study of family pedigrees or specific social and ethnic groups. Recruitment from such a narrow pool of participants may place undue influence on individuals to participate. Because undue influence 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 compelled 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 participants 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 subjects sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence" (46.116).

Insurability and Employability:

If there is a potential risk to the participant's 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. The

Affordable Care Act (ACA) prohibits discrimination in health insurance based on pre-existing conditions. This law provides substantial protection for individuals with genetic conditions or who are at risk of future health conditions based on genetic test results.

Disclosure of Incidental Findings

Investigators must be prepared for the possibility of identifying incidental findings during genetic analysis. Investigators must have a plan for determining which incidental findings should be returned to the participants; including a description of the information and expert consultation that will be used to make this determination. Non-paternity is considered an incidental finding.

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. Investigators are not expected or required to complete exhaustive genetic testing to identify all possible, known genetic variants as part of the research. Additionally, it may be appropriate to exclude analysis of variants that are irrelevant to the research objectives.

If investigators may disclose incidental genetic findings to participants, the A&M- SA IRB has required language that should be used in the consent form.

Genetic Research using stored tissue samples

Genetic research using stored tissue samples poses an array of benefits and risks to individuals, researchers, and society. A&M-SA IRB only allows the use of any tissue in genetic research that is obtained with written informed consent. Researchers are not allowed to transfer genetic materials from another institution without written informed consent.

In line with the recommendations of the National Center for Human Genome Research and the Centers for Disease Control and Prevention regarding informed consent, A&M-SA IRB follows the conditions noted below-

(1) informed consent is required for all genetic research using linkable tissue samples unless conditions for limitation or waiver are met;

(2) informed consent is not required for genetic research using anonymous samples but may be considered if identifiers are to be removed from currently linkable samples;

(3) IRB will review all protocols that propose to use samples for genetic research and determine the course of action. Self-determination by the PI is not permitted.

Standard Institutional Process for Disclosure of Incidental Findings to Participants

1. Ensure that the approved protocol and consent document(s) allow for disclosure of results and incidental findings to participants and/or affected family members.
    a. In cases where the informed consent allows individuals to be excluded from genetic testing, the informed consent document must provide these options explicitly.
    b. The informed consent must also clarify if the results will be or will not be disclosed to the individual participants. PIs should weigh the risk and benefits of their choice of disclosure and provide justification for either choice. However, if the consent form doesn't include disclosure as an option, but the researchers have a medically important finding, an amendment must be filed by the PI with the proposed mechanism of dissemination of the information.
    c. Information about results may be released to the participants' family members or others only if the participant gives written permission. It is possible that individuals may be excluded from genetic testing while remaining a part of the larger study. The informed consent document must provide these options explicitly.
2. Determine the appropriateness of disclosing genetic information to participants and/or affected family members. This includes the following considerations:
    a. Whether the information to be disclosed has evidence of clinical application, i.e., the claimed association between marker/gene and disease is generally accepted by the medical genetics' community.
    b. If age is a consideration in determining who will receive results, the investigator should indicate the age of minor subjects, special attention should be paid to whether it is appropriate to disclose genetic information to subjects 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 are currently available. Participants over 18 must be reconsented as adults and can choose the options as outlined in a, b, c.
    c. Legal analysis and consultation with University General Counsel may be necessary to evaluate how state and federal laws influence whether genetic/health information can be disclosed.
3. Begin the process of discussion and disclosure with the participant. This process must be conducted by a genetic counselor or other trained professional who can discuss the implications of genetic findings. All parts of the discussion and disclosure process should be documented and included in the research record and/or medical record as appropriate. The following process should be followed and documented:
    a. Initial contact: Initial contact may be made by phone or in person. The genetic counselor states that there is a finding from the research that may be relevant to the participant's health and asks the participant if he/she would be interested in learning more about the result. The participant must be told that if the receipt of results is not required and he/she may choose to decline

receiving further notification. If the participant expresses interest, the genetic counselor or the PI or a physician involved in the study may provide general information about the result or the category of the result, such as, "This result could have implications for your risk of cancer/heart disease/etc." If the participant has continued interest in receiving the result, a pre-test counseling appointment is scheduled.

b. Pre-test counseling appointment: The genetic counselor or the PI or a physician involved in the study discusses the research finding with the participant and the need for clinical testing in a Clinical Laboratory Improvement Amendments (CLIA) approved lab. The consent form should clarify that only genetic findings that are available on the CLIA approved list of tests that can be performed in a CLIA lab will be shared with the participant. Information about the costs of additional testing should also be discussed, including whether the participant or the participant's insurance will be billed for the costs. The participant must be told that if the research result is not confirmed, gene variants could still exist for which testing was not performed. After the participant provides standard clinical consent to receive additional testing for receipt of the results, the participant must be scheduled for CLIA-certified testing. The research results may be used by the CLIA-certified laboratories to target research-related findings, which may reduce the cost to participants.

c. Post-test counseling appointment: The genetic counselor or the PI or a physician involved in the study discusses the clinical results with the participant. Additional referrals for medical care and follow-up may be made as part of standard clinical care.

4. Important details to be considered for completing review of the IRB application.
    a. All sampling procedures that are necessary to perform the genetic research/analysis are adequately described.
    b. The application clearly indicates the study involves genetic testing and/or analysis of genetic data.
    c. The informed consent provides specific information about the risks, privacy protections, confidentiality protections, and return of incidental findings related to the genetic research/analysis being performed.
    d. Consent document:
        - Describe the reason(s) for performing the genetic research/analysis required for the study, including any sampling procedures that are necessary.
        - Describe the relevant risks of the genetic research/analysis being performed by the study.
        - Describe the confidentiality protections for the participants' data related to the genetic research/analysis being performed by the study.

- State whether incidental findings will be returned to the participants. If yes, include the language for return of incidental findings.
- For research involving biospecimens, the informed consent should describe whether research will (if known) or might include whole genome sequencing.
- Supplemental consent for collection, storage, and use of biological samples for future research, including genetic research, authorization for use and disclosure of protected health information.

REFERENCES

Counselors	http://www.nsgc.org/
Guidance on the Genetic Information Nondiscrimination Act: Implications for Investigators and Institutional Review Boards	http://www.hhs.gov/ohrp/policy/gina.html
Utah Genetic Testing Privacy Act	https://le.utah.gov/xcode/Title26/Chapter45/C26-45_1800010118000101.pdf
National Human Genome Research Institute	https://www.genome.gov/20019523

https://pubmed.ncbi.nlm.nih.gov/7500511/

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