Definitions

**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 FR 7139, Sec. 493.1). If researchers wish to provide diagnostic results to subjects 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.

**Constitutional (host) genes** are genes common to all normal tissues in the body. Research on constitutional genes will likely involve sensitive information about research participants that IRB’s should be concerned about.

**Genome Wide Association Study (GWAS)** is “an approach that involves rapidly scanning markers across the complete sets of DNA, or genomes, of many people to find genetic variations associated with a particular disease” (National Human Genome Research Institute).

**Incidental Findings** are previously unknown genetic results that are discovered unintentionally and are unrelated to the research analysis being performed.

Research involving **pathologic human tissue** (e.g. malignancies) rarely poses a risk (and no direct benefit) to participants because genetic abnormalities in this setting are usually focused on non-constitutional mutations, and are not representative of the participant’s individual genetic makeup.

**Whole Exome Sequencing (WES)** is the identification of exome DNA sequence; an exome contains sequence data for all of the known genes that are used by the body to make proteins.

**Whole Genome Sequencing (WGS)** is the identification of both coding (exome) and non-coding DNA sequence data for an individual.

Introduction

Information developed in the course of 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.

Risk Considerations for Genetic Research

**Privacy and Confidentiality Considerations:** Privacy in this context refers to a participant’s feeling of control over the extent, timing, and circumstances of sharing ones 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 in order 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.

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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 the 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).

Insurability and Employability: If there is a potential risk to the patient’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.

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. Information about results may be released to the participants’ family members or others only if the participant gives written permission.

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 at what age subjects 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 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.

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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 receipt of results is not required and he/she may choose to decline. If the participant expresses interest, the genetic counselor provides 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 discusses the research finding with the participant and the need for clinical testing in a CLIA-approved lab. 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 discusses the clinical results with the participant. Additional referrals for medical care and follow-up may be made as part of standard clinical care.

Points to Address

Application:
1. Study Information page, question 6: Describe any sampling procedures that are necessary in order to perform the genetic research/analysis.
2. HIPAA and the Covered Entity page, question 72i: Indicate “Yes”, the study involves genetic testing and/or analysis of genetic data.
3. Genetic Research page: Complete all questions, providing specific information about the risks, privacy protections, confidentiality protections, and return of incidental findings related to the genetic research/analysis being performed.

Consent Document:
1. Background or Study Procedures section: Describe the reason(s) for performing the genetic research/analysis required for the study, including any sampling procedures that are necessary.
2. Risks section: Describe the relevant risks of the genetic research/analysis being performed by the study.
3. Confidentiality or Authorization section: Describe the confidentiality protections for the participants’ data related to the genetic research/analysis being performed by the study.
4. New Information section: State whether incidental findings will be returned to the participants. If yes, include the verbatim language for return of incidental findings found in the Consent and Authorization Template.

4.5. Whole Genome Sequencing: For research involving biospecimens, the informed consent should describe whether research will (if known) or might include whole genome sequencing.

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