**Department: UAMS Institutional Review Board**

**Policy Number: 19.1**

**Section: Human Genetics Guidance**

**Effective Date: July 31, 2002**

**Revision Date: January 30, 2004; February 15, 2016**

**SUBJECT: Human Genetics Guidance**

**I. Purpose**

Human genetic research involves the study of inherited human traits. This research can involve identifying DNA mutations or predispositions that can contribute to the onset or severity of disease, developing methods to identify those mutations in patients, and improving interventions to help patients avoid, delay the onset or minimize the severity of, or treat those problems. The identification of genetic mutations enables clinicians to predict the likelihood that patients will develop a given health problem in the future. Genetic findings also may indicate whether patients’ blood relatives may also be at increased risk or should be referred for screening. Genetic research can either be central to a particular study’s overall purpose or be an ancillary part of a research study that does not have genetic research as its main focus. Regardless of whether it is a main or ancillary focus of a project, genetic research creates additional ethical and human subject protection concerns for the IRB to consider. These include the potential for significant time delay between the identification of the mutation or genetic predisposition and the development of the disease, the current inability to treat or predict the severity of some of these diseases, the possibility of incidental findings unrelated to the research question, and the psychological implications of informing subjects about a risk they may not be able to alter. Due to the inheritability of some genetic mutations, genetic research also has implications for people who are not research subjects but who are family members of research subjects. The identifiability of genetic samples has also been debated. Samples deidentified in accordance with 45 CFR 46 and that do not contain any of the 18 HIPAA identifiers may not readily be identifiable at this time. However, the potential for future developments to more readily allow identification of these samples, and/or the possibility that some samples may contain information related to rare conditions, cannot be discounted when considering the identifiabilty of genetic information and samples.

IRB considerations when reviewing genetic research include the researchers’ plan for the management of personal genetic information, including whether any information will be returned to participants or their family members, and plans for the storage and possible future use of information that may be either currently or potentially identifiable. The IRB must also consider whether the informed consent process will adequately inform subjects of risks and benefits, the potential for future use of genetic material in new studies, or, in studies using previously collected material, whether those subjects were appropriately informed of any subsequent use of the material, or if appropriate informed consent waivers are applicable.

**II. DEFINITIONS**

Genome: The entire set of genetic instructions found in a cell.

Genotype: The genetic constitution of an individual.

Large-scale human genomic data: includes genome-wide association studies (GWAS), [[34]](https://www.federalregister.gov/articles/2014/08/28/2014-20385/final-nih-genomic-data-sharing-policy#footnote-34) single nucleotide polymorphism (SNP) arrays, and genome sequence,1transcriptomic, metagenomic, epigenomic, and gene expression data

Phenotype: The physical manifestation of a gene function.

Proband: The person whose case serves as the stimulus for the study of other members of the family to identify the possible genetic factors involved in a given disease, condition, or characteristic.

**III. Policy**

**Subject Recruitment and Retention:** In reviewing research, the IRB will consider whether the proposed recruitment plan is appropriate, including but not limited to whether family members of the research subject (proband) will be, or should be, approached for participation or offered any genetic testing or counseling outside of the study as well. If family members are to be included, the IRB should consider whether the proposed recruitment strategy unacceptably influences the decision to participate or infringes upon the proband’s privacy. Recruiting individuals in the presence of other family members may unduly influence an individual’s decision to join a study. The IRB must also consider whether the proposed recruitment process may induce a subject to participate due to a misguided belief that the research study will provide some sort of treatment or clear answer as to whether the subject is at risk for a condition of interest.

**Informed Consent**: The IRB routinely requires research that anticipates the retention of samples or data for possible future use to inform subjects of that possibility and describe the possible future use during the informed consent process. This requirement also pertains to possible future research involving previously collected genomic samples or the derivation of genetic information from previously collected samples.

For new research involving the use of previously collected genetic data, specimens, or specimens from which genetic information is to be derived, the IRB will review the consent form under which the data/specimens were originally collected to confirm that the new use is not inconsistent with the information provided in the original consent process, if that consent process was part of a research study overseen by the UAMS IRB. The UAMS IRB also may ask to review the consent form under which the data/specimens were originally collected if the data/specimens originated at a different institution, or otherwise seek assurance that the proposed use is not inconsistent with information previously given to participants.

Research that falls under the scope of the NIH’s Genomic Data Sharing Policy has specific data submission and informed consent requirements. The policy requires investigators to submit large-scale human genomic data and relevant associated data (e.g. phenotype and exposure data) to an NIH-designated repository. For studies initiated after the effective date of the GDS policy, the NIH expects investigators to obtain participants’ consent for their genomic and phenotypic data to be used for future research purposes and to be shared broadly. The consent should include an explanation about whether participants’ individual-level data will be shared through unrestricted- or controlled-access repositories. NIH will expect this consent to be obtained even if the cell lines or clinical specimens are de-identified, and the IRB will review and approve this consent process.

For studies using data from specimens collected *before* the effective date of the Genomic Data Sharing Policy, there may be considerable variation in the extent to which future genomic research and broad sharing were addressed in the informed consent materials for the primary research. In these cases, an assessment by an IRB, privacy board, or equivalent body is needed to ensure that data submission is not inconsistent with the informed consent provided by the research participant. The UAMS IRB will complete that assessment.

Research that falls under the scope of the [NIH’s Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies (GWAS)](http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-088.html#policy) also has specific data submission requirements. The IRB will ensure that any informed consent process on a study subject to GWAS requirements is consistent with this data submission.

**Consideration of Risk and Benefits**

In addition to typical physical risks possible in research, genetic research involves additional psychological and social risks, generally referred to as “psychosocial” risks, specific to this type of research. Subjects may learn they are affected by a genetic disorder that has not yet manifested itself, and/or that their family members are also at risk for this disorder. In many cases, the information yielded by this genetic research pertains only to probabilities, not certainties, and cannot be considered an indicator of the timing of onset or the severity of the condition in question. There may also not be an effective treatment for the condition. Incidental findings not related to the main research question are also possible. Potential benefits of returning information include allowing subjects to consider whether other blood relatives may be at risk and/or allowing subjects to better plan for the future.

In its review, the IRB shall consider whether it is appropriate to return any individual or aggregate research results to participants. If results are to be returned, the IRB shall also consider whether counseling should be made available to participants and whether any proposed counseling is adequate.

Risks of disclosure of genetic information are also potentially significant, as they may affect an individual’s employability or insurability. The IRB shall ensure that protections described in the [Genetic Information Nondiscrimination Act of 2008 (GINA)](http://www.hhs.gov/ohrp/policy/gina.html) shall be addressed as appropriate in genetic research. GINA is a federal law that prohibits discrimination in health coverage and employment based on genetic information.

GINA defines a genetic test as an analysis of human DNA, RNA, chromosomes, proteins, or metabolites that detect genotypes, mutations, or chromosomal changes. Routine tests that do not detect genotypes, mutations, or chromosomal changes, such as complete blood counts, cholesterol tests, and liver enzyme tests, are not considered genetic tests under GINA. Also, under GINA, genetic tests do not include analyses of proteins or metabolites that are directly related to a manifested disease, disorder, or pathological condition that could reasonably be detected by a health care professional with appropriate training and expertise in the field of medicine involved.

The following is suggested language for inclusion in informed consent forms regarding GINA protections. The language may be revised as appropriate to individual studies:

A new Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

* Health insurance companies and group health plans may not request your genetic information that we get from this research.
* Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
* Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

All health insurance companies and group health plans must follow this law by May 21, 2010. All employers with 15 or more employees must follow this law as of November 21, 2009.

Be aware that this new Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

The IRB may also require the PI to seek a Certificate of Confidentiality for genetic research.

**Identifiability of Genetic Data**

Genetic information that does not include direct identifiers, such as the 18 items listed as identifiers under HIPAA, is not currently considered to be identifiable. The Genomic Data Sharing and GWAS studies also refer to data submitted to central repositories without any direct identifiers as “de-identified,” though these data may include a code, the key to which is kept at the originating site. However, the possibility of new techniques allowing the identification of this deidentified data in the future cannot be eliminated. In addition, differing types of genetic analysis may have different levels of identifiability, even in the absence of direct identifiers. The IRB shall therefore individually consider each study anticipating the use of genetic information and make a determination as to whether the genetic data are identifiable.

**Risk Determinations for Studies Involving Genetic Research**

The IRB shall consider any risks created by any study-related genetic research along with other study risks when making risk determinations for studies that involve genetic research. Many variables can influence the risks associated with genetic research, including, but not limited to, the nature of what the genetic research may reveal, the age and overall health of participants, the possibility of discovering incidental findings not related to the study’s main aim, and the inheritability of the genetic characteristic(s) in question.

References: [Final NIH Genomic Data Sharing Policy](https://www.federalregister.gov/articles/2014/08/28/2014-20385/final-nih-genomic-data-sharing-policy) 08/28/2014

[Genetic Information Nondiscrimination Act (GINA): OHRP Guidance (2009)](http://www.hhs.gov/ohrp/policy/gina.html)

[Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies (GWAS)](http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-088.html#policy)