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IRB Connection

HUMAN SUBJECTS OFFICE

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Genetic Research Edition

Federal Regulations and Guidance

Human biological materials are increasingly valuable in biomedical research. Human specimens and associated data provide critical resources for basic scientific discoveries and translating those discoveries into improved medical care. Although these developments offer great promise, they also heighten concerns about privacy and confidentiality of human subjects from whom specimens are obtained. Federal regulations governing research on human subjects were drafted well before the dramatic increase in the use of specimens for research. Federal regulatory agencies have developed guidance to address many aspects of collection, storage, distribution and use of specimens for research. However, there is no single comprehensive guidance that covers the full spectrum of these activities. As a result, neither the regulations nor the regulatory guidance documents directly address many issues related to the use of specimens in research. In 2008, the Office for Human Research Protections (OHRP) provided updated guidance about what constitutes human subjects research in the context of research with human specimens. OHRP's Guidance on Research Involving Coded Private Information or Biological Specimens states that research involving only coded private information or specimens does not involve human subjects when the private, identifiable information or specimens were not collected specifically for the current proposed research project and the investigator is either unable to or agrees not to connect the private information or specimens to the individuals from whom they were collected.

GINA and the Criteria for IRB Approval of Research

The Genetic Information Nondiscrimination Act of 2008 (GINA) is a federal law that together with provisions of the Health Insurance Portability and Accountability Act (HIPAA) prohibits discrimination based on genetic information in connection with health coverage and employment, no matter for what purposes the information was collected. GINA defines genetic information as:

- An individual's genetic tests
- Genetic tests of an individual's family members (dependents and up to and including 4th degree relatives)
- Genetic tests of any fetus of an individual or family member who is a pregnant woman and genetic tests of any embryo legally held by an individual or family member utilizing assisted reproductive technology
- The manifestation of a disease or disorder in an individual's family members (family history)
- Any request for, or receipt of, genetic services or participation in clinical research that includes genetic services (genetic testing, counseling, or education) by an individual or an individual's family members

When reviewing genetic research, IRBs consider the protections provided by GINA when determining whether the research satisfies the criteria for IRB approval of research, including (45 CFR 46.111):

- Risks to subjects are minimized
- Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects
- There are adequate provisions to protect the privacy of subjects and maintain the confidentiality of data

GINA protects individuals from potential adverse effects on insurability or employability if genetic information about the subject obtained as part of the research is disclosed to, sought by, or can be easily accessed by insurers or employers. The standard Informed Consent Document (ICD) template provided by the UI IRB contains suggested language for genetic research, in addition to GINA template language to address these protections. This template language is inserted into the ICD for all new project applications when investigators indicate genetic testing or research will be conducted in Section VII.C.1 of the HawkIRB application.

Read more about GINA here.

Is it Genetic Research?

Research activities that meet the UI IRB's definition of genetic research must be indicated as such in Section VII.C of the HawkIRB application. This section collects information for the IRB to approve the collection, storage, testing and/or sharing of DNA samples for research purposes. The UI IRB defines genetic research as those activities involving the analysis of human DNA to study heritable (passed to offspring) conditions. Analysis of human DNA for non-heritable conditions typically does not meet the criteria for genetic research. Everyone has a unique DNA sequence, even twins who began life from the same cell will have changes in their DNA sequences during their lifetimes. Changes or "mutations" happen when the DNA is altered from its natural state. Mutations become heritable when they occur in the germ cells; the sperm and the egg. Some germline mutations serve as genetic markers, predicting an individual's likelihood of developing a specific disease. For example, certain germline mutations on the BRCA1 gene are associated with an increased risk of breast cancer. Other types of mutations may be acquired during a person's lifetime; they are not passed down from parent to child. These types of mutations are called somatic mutations and can cause disease. Investigators often analyze the DNA found in tumor tissue, an organ, or specific types of cells to learn more about somatic mutations. Analyzing biologic samples for somatic mutations does not meet the UI IRB's definition of genetic research. The way we look and our health-related characteristics, such as blood type or whether or not we have a certain disease, is determined by our DNA. Enzymes in our cells make copies of our DNA called messenger RNA (mRNA). mRNA tells our bodies which proteins we are supposed to make. Investigators often want to analyze RNA in order to determine why certain proteins are made. Sometimes proteins cause disease or are markedly present or absent in people with specific diseases. Studies of proteins and RNA that are related to a specific manifest disease are not considered genetic research by the UI IRB. An exception would include an investigator who is already aware that the protein or RNA change they are studying is directly linked to a germline mutation in an individual's DNA. This example does meet the UI IRB's definition of genetic research and must be indicated as such in the HawkIRB application.

Incidental Findings

Any time genetic testing will be performed, investigators and IRBs must consider the possibility of incidental findings and their associated risks, as well as benefits, to research participants. Incidental findings, or unexpected results unrelated to the reason for testing, may include evidence that a subject has a genetic predisposition for a particular condition, which may or may not be treatable. Findings may also include evidence that an individual is not biologically related to a parent, news that a person has a racial ancestry s/he is not aware of, or the identification of diseases or traits that may be stigmatizing or culturally sensitive to a group. When conducting genetic research involving human subjects, investigators should describe plans in the HawkIRB application to address how the discovery of incidental findings will be handled, as well as whether and how subjects will be notified. Incidental findings are not limited to genetic research and necessitate consideration in other fields of research. Planning for these potentially harmful findings is important to address complicated issues that may arise during the course of a research study. Psychological distress or social and economic risks associated with such discoveries could dramatically affect subjects and their families if divulged to the wrong source or if results are not appropriately communicated to subjects.

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