Informed Consent for Genomics Research (from the NHGRI)

https://www.genome.gov/27026588

Introduction

Advances in genomic technology, the development of sophisticated analytical and software tools, and the willingness of investigators to collaborate to obtain sufficiently large sample sizes are facilitating the discovery of human genetic variation related to health and disease. These discoveries are essential to improving the understanding of how genes interact with the environment to influence disease risk. It is also essential that the interests of research participants (i.e. human research subjects) who contribute samples and health-related information to these projects are respected throughout the research process.

Informed consent involves two fundamental components: a document and a process. The informed consent document provides a summary of the research project (including the study's purpose, research procedures, potential risks and benefits, etc.) and explains the individual's rights as a research participant. This document is part of an informed consent process, which consists of conversations between the research team and the participant and may include other supporting material such as study brochures. The informed consent process provides research participants with ongoing explanations that will help them make informed decisions about whether to begin or continue participating in the research project. Thus, informed consent is an ongoing, interactive process, rather than a one-time information session.

The eight basic required elements of informed consent can be found in the HHS regulations (45 CFR 46.116)

These elements include:

- A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.
- A description of any reasonably foreseeable risks or discomforts to the subject.
- A description of any benefits to the subject or to others which may reasonably be expected from the research.
- A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.
- A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained.
- For research involving more than minimal risk, an explanation as to whether any compensation or any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.
- An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.
- A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

The regulations (45 CFR 46.116) also suggest inclusion of the following elements where appropriate:

- A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable.
- Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.
- Any additional costs to the subject that may result from participation in the research.
- The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.
- A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject.
- The approximate number of subjects involved in the study.

Studies Involving Children

Including children in genomic studies to better understand how genetic variation influences child health and development is important. However, concerns arise when study protocols include testing asymptomatic children for particular conditions, disease susceptibilities, or carrier status. The American Society of Human Genetics (ASHG)[3] and the American Academy of Pediatrics (AAP)[4] have published policy statements on this issue. Borry et al. published a review of presymptomatic and predictive genetic testing in minors that might be a helpful resource.[5]

For children or others who are not legally able to provide consent to participate in a study, a parent or legal guardian provides permission for the person to participate. Even though a child may not be legally able to provide consent, they are still informed about the clinical research to the degree that they are able to understand. They may also have the opportunity to provide their agreement to participate via the process of **assent**.[6]

The Office of Human Research Protection (OHRP) developed a comprehensive Frequently Asked Questions About Human Research resource. Within this resource is a section dedicated specifically to Informed Consent FAQs [hhs.gov]. For a summary of the requirements for assent and parental permission in research involving children, please refer to the Informed Consent FAQ response to What are the requirements for assent and parental permission in research with children? [answers.hhs.gov].

Researchers should also consider whether any of the minors enrolled in their study will reach the legal age of consent during the study period.

Studies Involving Research Participants with Diminished Decision-Making Capacity

The OHRP Informed Consent Frequently Asked Questions (FAQ) resource outlines what should be considered in seeking informed consent from individuals with diminished decision-making capacity (for example, as a result of trauma, mental retardation, some forms of mental illness, or dementia). Regulations require that the IRB ensure that "additional safeguards have been included in the study to protect the rights and welfare" of all subjects that are "likely to be vulnerable to coercion or undue

influence." The regulations include "mentally disabled persons" in this category (45 CFR 46.111(b) [hhs.gov]).

In research involving adult subjects with mental illnesses or cognitive impairments, the IRB and investigator(s) must be knowledgeable about the condition and any level of impairment that is likely to be present in the subject population. The regulations do speak to the fact that the IRB must possess "the professional competence necessary to review specific research activities" (45 CFR 46.107(a) [hhs.gov]). This is achieved either by having members with the appropriate experience and expertise or inviting consultants with competence in the special area to assist in the review of issues that require expertise beyond or in addition to that available on the IRB (45 CFR 46.107(a) and (f) [hhs.gov]). Ensuring such expertise on the IRB improves its ability to make determinations about subject recruitment, enrollment, and informed consent requirements that best match the needs of the subjects.

OHRP notes that for research projects with a longitudinal component that involves studying progressive disorders or aging populations, enrolled research participants may be competent to consent on their own behalf at the outset, yet may experience effects of progressive or intermittent disorders that lead to decisional impairment during the course of the study. In these situations, IRBs and investigators should consider the need to discuss with the prospective participants whether they should designate someone to serve as a legally authorized representative (LAR) at the outset of the study, consistent with all applicable laws.(Please refer to the OHRP Informed Consent FAQ response to: Who can be a legally authorized representative (LAR) for the purpose of providing consent on behalf of a prospective subject? [answers.hhs.gov]) Even if a participant has consented on his or her own accord, a designated representative would be ready to step in as the legally authorized representative if the participant's ability to assess his or her own needs and interests becomes compromised during the study.[7]