

# Informed Consent for Genomics Research

## 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 subject) who contribute

samples and health-related information to these projects are respected throughout the research process.

These online materials provide the research community with information to assist the development of informed consent materials for genomics-related research projects such as genome-wide association (GWA) and genome sequencing studies.

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.

Given the complexity of the scientific and ethical issues that arise when conducting genomics research in the collaborative research setting that includes activities such as deposition of individual-level data into controlled-access databases for broad sharing, evolving IT technology, and the prospect of changing attitudes about privacy, **this material is by nature dynamic and not meant to provide definitive answers. Instead, it is meant to be a first iteration of an evolving discussion that serves as a useful resource for scientific investigators as they work with their collaborators, IRBs, research participants, and communities to develop appropriate informed consent materials for genomic studies.**

## Explore Informed Consent Materials

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# Elements of Informed Consent Described in Federal Regulations

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

## 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\(b\)](#)) 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.

Study investigators are not limited to including the 14 elements listed above. Any information that might be useful for the individual as he or she decides whether or not to take part in the study should be included. Furthermore, an Institution's IRB may require additional elements that are not specifically listed in the regulations to ensure that adequate information is presented in accordance with institutional policy and law.

# Informed Consent Elements Tailored to Genomics Research

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The main elements required by federal regulations to be included in a consent form for a research project involving human subjects (i.e. research participants) are listed below. Beneath each element is a discussion of relevant issues to consider in the context of genomics research and example language adapted from existing consent documents developed for various National Institutes of Health (NIH) sponsored research projects.

Genomics studies may involve prospectively collecting new samples and information or using previously collected samples and information. For genomics studies involving the use of previously collected samples and information, re-consent of research participants is usually necessary. Therefore, some of the example language below reflects language that could be used in re-consent forms (see section “Three Consent Form Examples” to view an example of a re-consent form for a genome-wide association study).

The following considerations are intended to be complementary to requirements, regulations and guidance documents, including: [45 CFR 46](#) [access.gpo.gov], [21 CFR 50](#) [access.gpo.gov], [21 CFR 56](#) [access.gpo.gov], and other guidance from [The Office for Human Research Protections](#) [hhs.gov] and the [Food and Drug Administration](#) [fda.gov]

**Note:** When developing a consent form it is important to use simplified language that is not overly technical and takes into consideration the literacy level of potential research participants. Furthermore, potential participants should be given ample time to consider participating in a project so that they can develop informed questions as their understanding of the research project matures.

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## Purpose of Research Project

Potential research participants should be given a succinct explanation of why they have been approached for the proposed study and who is sponsoring the project. This section should include topics such as a brief description of the underlying genomic science, the study design, the diseases(s) or condition(s) being studied, and the immediate and long-term goals of the study. Use of simplified language that is not overly technical may help potential research participants understand the rationale for the study.

## Example Language

### ***Why is this research study being done?***

*We are requesting your participation in a study involving blood and tissue samples as well as medical information that were previously collected from you as part of [Insert Name of Project]. Your blood and tissue samples contain genes, which are made up of DNA and which serve as the “instruction book” for the cells that make up our bodies. Your samples and medical information will help us study how genes interact with other factors to influence the development of diseases such as cancer, cardiovascular disease, diabetes and glaucoma.*

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## Description of the Research Procedures

It is important for potential research participants to understand what they will experience as research participants. Dividing the research procedures into stages may make the information easier to understand. The description should cover topics such as:

- The process for the collection of samples (blood or other tissue) and health information.
- How samples and health information will be coded and stored.
- Whether there will be access to a research participant’s medical records and, if so, the process for accessing them (*e.g.*, one-time vs. ongoing collection of information from medical records).
- The duration of storage.
- Whether and how samples and health information will be shared with qualified investigators for appropriate research use both during the study period and after the study ends.
- A general description of the types of researchers who will have access to samples and data (*e.g.*, academic, industry, government)
- Whether and how future contact (*i.e.* re-contact) is planned.

**Sharing of data:** One of the main factors that distinguishes genomic-related research studies from other studies involving human research participants is that they generate large datasets of genomic and health information that are increasingly being deposited in databases or larger data repositories for sharing with the broad biomedical research community. These databases and data repositories may be fully open or accessible only with the permission of a Data Access Committee (*e.g.* [dbGaP](#)), depending on the nature of the data, local policies, and other factors.

Many of these datasets are useful beyond the particular aims of the study for which they were originally collected, especially as various diseases turn out to have mechanisms in common. Thus, the value of these data can increase when they are allowed to be shared with the broader research community and are not restricted in use to particular diseases or for a limited period of time.

This section should describe the mechanism(s) that will be used to store and share the data including an indication of whether and for how long samples and genomic data will be

shared with the broader research community both inside and outside the sponsoring institution.

Investigators should note that the NIH GWAS Policy ([Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies \(GWAS\)](#) [grants.nih.gov]) states that "for prospective studies, in which GWAS are conceived within the study designs at the time research participants provide their consent, the NIH expects specific discussion within the informed consent process and documentation that research participants' genotype and phenotype data will be shared for research purposes through the NIH GWAS data repository" (currently the [database of Genotypes and Phenotypes \(dbGaP\)](#)).

**Future Contact:** This section should clearly outline the investigator's intentions for future contact with the research participant, if any, and how the investigator or other study staff will contact the research participant at a later date.

## Example Language

### **Description of the Research Procedure**

#### **Collection of Samples and Medical Information**

- *If a blood sample (or other tissue sample) was collected from you, we seek permission to receive some of this blood (or other tissue) and genetic material that already may have been extracted from this blood (or other tissue).*
- *If an adequate blood sample is not available for this project, we will collect a sample from you by drawing about 4 tablespoons of blood from a vein in your arm. If you object to having blood drawn, we will collect tissue from you by swabbing cells from the inside of your cheeks.*
- *We also will collect information from your medical records, including your age, ethnic background, diagnosis, disease history, medical treatments, and response to treatments.*

#### **Coding of Tissue Samples and Medical Information**

- *Your blood (or other tissue) sample and medical information will be labeled with a code.*
- *Only Dr. \_\_\_\_\_ at (Institution) will have the information that matches the code to traditionally-used identifying information, such as your name, address, phone number, or social security number. Dr. \_\_\_\_ will keep the information that matches the code to this traditionally-used identifying information in a safeguarded database. Only very few, authorized people, who have specifically agreed to protect your identity, will have access to this database. All other researchers and personnel, including those who will be working with your samples and medical information, will not have access to any of your traditionally-used identifying information.*

#### **Storage and Release of Samples and Medical Information**

- *Your coded blood (or other tissue) samples will be sent to an NHGRI-sponsored sequencing laboratory for detailed analysis. Remaining portions of your samples will be stored for an unlimited period of time for future use in research related to diseases or, perhaps, in other research projects.*
- *Information from analyses of your coded samples and your coded medical information will be put into databases along with information from the other research participants. These databases will be accessible by the Internet.*

- *Anonymous information from the analyses will be put in a completely public database, available to anyone on the Internet.*
- *Your coded medical information and information from more detailed analyses of your coded samples will be put in a controlled-access database. The information in this database will be available only to researchers who have received approval from an NIH Data Access Committee, which was established to help make sure that your data are used appropriately*
- *Please note that traditionally-used identifying information about you, such as your name, address, telephone number, or social security number, will NOT be put into either the public or controlled-access databases for this project.*

**Re-contact:** *In the future, we may want to obtain additional samples or follow-up information about your health or medical care. Should this be needed, a person from [Insert Institution Name] will contact you to ask whether you would be interested in participating in this additional research.*

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## Financial Compensation, Costs and Commercialization

It is important to communicate to the potential research participant whether there will be any 1) financial compensation for taking part in the research project, 2) costs for taking part in the research project, and 3) compensation for a research-related injury.

Any proposed compensation should not be included in the "Benefits" section of the consent form.

It is possible that some of the genomics research conducted either by the primary investigator or secondary users could eventually lead to the development of new diagnostic tests, new drugs or other commercial products. The section should indicate that if this should occur, there is no plan for research participants to receive any part of the profits generated from such products.

### Example Language

#### ***What are the costs and payments?***

*You will not be paid to participate in this project.*

*Your blood (or other tissue) samples and your medical information will be used only for research purposes and will not be sold. It is possible that some of the research conducted using your samples or information eventually will lead to the development of new diagnostic tests, new drugs or other commercial products. Should this occur, there is no plan to provide you with any part of the profits generated from such products.*

*We do not charge you for participation in the study.*

*The chance that you will be physically injured as a result of participating in this project is very small. However, if you are physically injured as a result of participating in this project, emergency medical treatment for your research-related injury will be provided to you at no cost.*

## Potential Benefits of Participating in the Project

Potential benefits to the research participant and to others should be described in the consent form. It is important to include potential benefits for society, but investigators should be careful to distinguish between potential benefits to the individual research participant versus society.

### Example Language

***Are there any benefits to participating in the project?***

*You will not benefit personally from giving a sample for this project because this kind of research usually takes a long time to produce medically useful results. However, your participation will help researchers around the world understand more about human genetic variation and how it relates to health and disease.*

## Potential Risks of Participating in the Project

Research participants need to be informed of the risks in any research project, including genomics research projects where large amounts of genomic- and health-related data will be generated, stored, and broadly shared with other qualified investigators for appropriate use. The risks attached to genomics research and the extent to which we understand them need to be clearly articulated to research participants through the informed consent process. Discussing the likelihood of the risk as well as the severity of the risk may help research participants better understand the context of these kinds of risks. Possible risks may vary depending upon the study protocol, but as with most genomics research, the potential risks are centered on psychological and social risks for the research participant and, possibly, their family.

### Examples include risks such as:

- Risks related to broad sharing of phenotype and genomic data (e.g. genotype, DNA sequence, expression profiles, etc.).
- Risks of the data sharing model for the study (e.g. the possibility that the coded<sup>1</sup> data may be released to members of the public, insurers, employers, and law enforcement agencies).
- Risks of receiving information that is unwanted by the research participant.
- Risks of computer security breaches or other unanticipated distributions arising from maintaining data in an electronic format
- Risks to relatives or identifiable populations or groups.

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<sup>1</sup> Coded means that any identifying information (such as name or social security number) that would enable the investigator to readily ascertain the identity of the individual to whom the private information or specimens pertain has been replaced with a number, letter, symbol or combination thereof (i.e., the code); and a key to the code exists, enabling linkage of the identifying information to the private information or specimens. From [Guidance on Research Involving Coded Private Information or Biological Specimens](#) [hhs.gov]

- The uncertainty of findings related to genetic risk for a given disease or trait.
- Privacy risks, both those known and those unforeseen at this time.
- Any physical risks, such as those associated with collecting blood or other tissue samples.

Recently, federal legislation ([The Genetic Information Nondiscrimination Act, or GINA](#)) was passed that will provide baseline protection against discrimination in employment and health insurances decisions across the nation. President Bush signed the act into federal law on May 21, 2008. The parts of the law relating to health insurers will take effect by May 2009, and those relating to employers will take effect by November 2009. Please note that this federal protection may be eclipsed by more extended state privacy or discrimination laws, so it is important to clearly present the issues to consider in the context of where the research is being done.

For more details regarding GINA, please refer to the National Human Genome Research Institute's information on GINA at <http://www.genome.gov/24519851> and at <http://www.genome.gov/10002328>.

An individual's participation in a research study could have implications for his/her family members. When appropriate, researchers should try to include willing family members in the consent process through discussion and, if possible, educational materials.

## Example Language

### **Physical Risks**

- *If a blood sample is not taken from you, there are no physical risks associated with this project.*
- *If a blood sample is taken from you, there are very few physical risks. Possible side effects from drawing the blood sample include mild pain, bleeding, bruising, and infection at the site of the needle insertion. Fainting or light-headedness can sometimes occur, but usually last only a few minutes.*

### **Psychological or Social Risks Associated with Loss of Privacy**

- *Your privacy is very important to us and we will use many safety measures to protect your privacy. However, in spite of all of the safety measure that we will use, we cannot guarantee that your identity will never become known. Although your genetic information is unique to you, you do share some genetic information with your children, parents, brothers, sisters, and other blood relatives. Consequently, it may be possible that genetic information from them could be used to help identify you. Similarly, it may be possible that genetic information from you could be used to help identify them.*
- *While neither the public nor the controlled-access databases developed for this project will contain information that is traditionally used to identify you, such as your name, address, telephone number, or social security number, people may develop ways in the future that would allow someone to link your genetic or medical information in our databases back to you. For example, someone could compare information in our databases with information from you (or a blood relative) in another database and be able to identify you (or your blood relative). It also is possible that there could be violations to the security of the computer systems used to store the codes linking your genetic and medical information to you.*
- *Since some genetic variations can help to predict the future health problems of you and your blood relatives, this information might be of interest to employers, health providers, insurance companies, and others. Patterns of genetic variation also can be*



*used by law enforcement agencies to identify a person or his/her blood relatives. Therefore, your genetic information potentially could be used in ways that could cause you or your family distress, such as by revealing that you (or a blood relative) carry a genetic disease or by leading to the denial of employment or insurance for you (or a blood relative).*

- *There also may be other privacy risks that we have not foreseen.*

*While we believe that the risks to you and your family are very low, we are unable to tell you exactly what all of the risks are. There are some state laws that protect against genetic discrimination by employers or insurance companies, but there is no federal law in effect to prohibit such discrimination. We believe that the benefits of learning more about diseases outweigh these potential risks.*

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## Confidentiality

Genome-wide association studies, genome sequencing projects, and related genomics research studies typically generate rich phenotypic and genomic datasets that are often deposited in controlled-access databases for storage and wide-spread sharing with the research community. This presents special challenges to privacy and confidentiality protections. For a more detailed discussion of these challenges, see the Lowrance and Collins paper on identifiability in genomics research.<sup>2</sup>

It is important to address research participants' concerns about protection of their identities against undesired intrusions (privacy) and about limiting the access to study information that might identify them (confidentiality). This section of the consent document should describe the level of confidentiality of the research data and the measures planned to ensure that confidentiality is maintained. Research participants should know whether their samples will be anonymous/non-identifiable (i.e. personal identifiers will not be kept with their sample and the sample will not have a code number that can be used to identify the participant) or coded and considered de-identified (i.e. any identifying information such as name or SS# will be replaced with a code and only a few authorized people will have access to this code to link samples and data back to personal identifiers).

In special circumstances, such as for reportable conditions like HIV status and child abuse, absolute confidentiality may not be possible. If this or a similar possibility exists, then state the conditions under which information must be disclosed and to whom.

**Certificates of Confidentiality** are an important tool to protect the privacy of research participants. The NIH encourages their appropriate use and has made information on their applicability and use available to investigators at the [Certificates of Confidentiality Kiosk](#).

Certificates of Confidentiality are issued by the NIH to protect identifiable research information from forced disclosure. They allow the investigator and others who have access to research records to refuse to disclose identifying information on research participants in any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level. Certificates of Confidentiality may be granted for studies collecting information that, if disclosed, could have adverse consequences for research participants or damage their financial standing, employability, insurability, or reputation. By protecting researchers and institutions from being compelled to disclose information that would identify

<sup>2</sup> Lowrance, W.W. & Collins, F.S. Ethics. Identifiability in genomic research. *Science*, 317, 600-2. 2007. [[PubMed](#)]

research participants, Certificates of Confidentiality help achieve the research objectives and promote participation in studies by assuring confidentiality and privacy to research participants.

If a Certificate of Confidentiality is in effect, it should be reflected in the consent form. Research participants should be given a fair and clear explanation of the protection that it affords, including the limitations and exceptions noted in the "Extent and Limitations of Coverage" section of [Certificates of Confidentiality: Background Information](#).

## Example Language

### **Confidentiality**

*We will make every attempt to protect your confidentiality and to make sure that your personal identity does not become known. This signed consent form will be stored in a locked file that will be accessible only to a very small number of authorized people involved in this project. We will carefully follow the coding, storage, and release plan explained in the **Description of the Research** section of this document.*

*We have obtained a **Certificate of Confidentiality** from the Department of Health and Human Services. The Certificate is designed to prevent us from being forced to disclose identifying information for use in any federal, state, or local civil, criminal, administrative, legislative, or other court proceeding, even if faced with a court subpoena. You should understand, however, that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. We may not withhold information if you give your insurer or employer or a law enforcement agency permission to receive information about your participation in this project. This means that you and your family must also actively protect your own privacy.*

*The Certificate does not prevent us from taking steps, including reporting to authorities, to prevent serious harm to yourself or others. Such disclosures will be made as described below.*

#### **The research team may share your information with:**

- *The Department of Health and Human Services (HHS), to complete federal responsibilities for audit or evaluation of this project;*
- *Public health agencies, to complete public health reporting requirements;*
- *Hospital or university representatives, to complete hospital or university responsibilities for oversight of this study;*
- *Your primary care physician if a medical condition that needs urgent attention is discovered;*
- *Appropriate authorities to the extent necessary to prevent serious harm to yourself or others.*
- *[Insert any additional necessary language related to any applicable state mandatory reporting requirements (e.g., findings of STDs, TB, etc.)]*

*[Insert here, or below, the institutionally-required language for the Notice of Privacy Practices under the Health Insurance Protection and Accountability Act (HIPAA).]*

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## Returning Results to Research Participants

The return of individual research results to research participants must be carefully considered because the information can have implications for the participant's health and well-being. This information might also increase participants' stress and anxiety. While clinically valid and meaningful results may have a positive impact on an individual's health, harms such as incorrect medical treatment or unnecessary anxiety might occur if research results without documented clinical relevance are provided back to participants or used for medical decision-making.<sup>3</sup>

Genomics research such as GWA and sequencing studies will find many associations between particular genetic loci and diseases. However, these initial findings will need much additional research before their clinical significance is understood and appropriate actions are determined.

The decision on whether to return research results to participants (either individual research results or general research findings through newsletters, study website, etc) should be made by the study investigator in consultation with his/her IRB. This decision, including the format and process for returning results, should be clearly communicated.

In some cases, applicable state or local laws may require the return of specific test results to participants (*e.g.*, the diagnosis of particular communicable diseases). In such cases, a statement to this effect should be included in the consent form.

## Example Language

### **Research Results**

*In general, we will not give you any individual results from the study of the samples you give us. This is because it will probably take a long time for this project to produce health-related information that we will know how to interpret accurately. However, we will tell you if we find that you have a communicable disease that we are required by law to report. We will also periodically summarize interesting general findings from this project and how they are contributing to our understanding of health and disease on our project website and through a periodic newsletter.*

The National Heart Lung and Blood Institute (NHLBI) convened a Working Group on Reporting Genetic Results in Research studies to discuss if, when, and how genetic information should be reported to study participants. The conference report and recommendations for reporting genetic research results is a useful resource.<sup>4</sup>

In March 2008, a consensus statement based on an interdisciplinary workshop convened to develop research ethics recommendations for whole-genome research was published.<sup>5</sup> Two recommendations address the return of results: (1) "Personal genome projects should have an established process approved by a research ethics committee for evaluating whether findings (incidental or otherwise) meet criteria for offering results to individual participants. This process should be highlighted in the initial consent and should acknowledge the participants' rights not to know certain results." (2) "The process of identifying and disclosing research results should involve professionals with the appropriate expertise

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<sup>3</sup> Excerpted from the [NIH Genome-Wide Association Studies Points to Consider for IRBs and Institutions](#)

[grants.nih.gov] 

<sup>4</sup> Bookman, E.B. et al. Reporting genetic results in research studies: summary and recommendations of an NHLBI working group. *Am J Med Genet A*, 140, 1033-40. 2006. [[PubMed](#)]

<sup>5</sup> Caulfield, T. et al. Research ethics recommendations for whole-genome research: consensus statement. *PLoS Biol*, 6, e73. 2008. [[PubMed](#)]

required to provide the participant with sufficient interpretive information. In general, the results offered should be scientifically valid, confirmed, and should have significant implications for the subject's health and well-being. Plans to return other forms of data—such as significant non-health-related data—should be built into the study design and governance structure. "

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## Withdrawal

Participants have the right to withdraw from the study at any time and the implications and consequences of withdrawal should be discussed in this section of the form and as part of the overall consent process.

For certain genomic studies, complete withdrawal of samples and information may not be possible once samples have been distributed to laboratories and information has been posted for broad data sharing. In such circumstances, a full explanation of the inability to withdraw all samples/information should be provided.

If participant samples are being shared with other investigators and labs or there is the potential for sharing of these samples in the future, the consent form should clearly explain whether or not these samples can be destroyed and what the process will be.

For studies where individual-level genomic, demographic, and health data will be deposited in a public or controlled-access data repository for broad sharing with the research community, the consent form should reflect the data repository policy. For example, a data repository may allow submitting investigators and their institutions to request removal of data on individual participants from the data repository if a research participant withdraws consent. These participants' data can then be excluded from future distributions, but data that have already been distributed for approved research use will not be able to be retrieved.

## Example Language

### ***Withdrawal from the Project***

*If you would like to withdraw from this project you can contact [Insert Name & Contact Information of Principal Investigator] at [Insert Name of Institution] and he/she will destroy any remaining tissue samples of yours that have been obtained for the study. In addition, it may be possible for him/her to destroy the link between you and your genetic and medical information. However, the samples and data generated from your samples that have already been distributed to other research centers or placed in the research databases cannot be able to be withdrawn.*

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## Alternatives to Participating in the Project

As outlined in 45 CFR 46.116(a), the consent form needs to include a disclosure of appropriate alternative procedures or courses of treatment, if any, that might be available to the research participant. For genomics studies, this generally means that the individual may choose not to participate in the project.

## Example Language

### Alternatives to Participating in the Project

*The alternative option is not to participate.*

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## Voluntary Participation

As outlined in 45 CFR 46.116 (a), this section should convey that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the research participant is otherwise entitled, and the participant may discontinue participation at any time without penalty or loss of benefits to which the participant is otherwise entitled.

## Example Language

### Voluntary Participation

*The choice to participate in this research by donating your tissues and medical information is completely up to you. No matter what you decide to do, your decision will not affect the medical care or benefits to which you are otherwise entitled.*

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## Contact Information

This section should list whom the research participant should contact for 1) answers to pertinent questions about the research and research participants' rights and 2) in the event of a research-related injury.

Depending on the study population, the contact persons may need to be prepared to respond to research participants in other languages

## Example Language

### Contact Information

*If you have any questions about the project or about your rights as a research participant, please contact [Insert Specific Institutional Language Here]. If you believe you have a research-related injury, please contact [Insert Specific Institutional Language Here]*

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# Special Informed Consent Considerations

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[📄 Obtaining Consent in Diverse Populations](#)

[📄 Community Consultation/Community Engagement](#)

[📄 Studies Involving Children](#)

Studies Involving Research Participants with Diminished Decision-Making Capacity

[📄 Educational Materials](#)

## Approaches for Obtaining Consent in a Research Project

A common approach to obtaining consent for genetics/genomics research is to ask the research participant to agree to participate in all aspects or parts of a study. In this model, if an individual does not agree to participate in all aspects or parts of the study, they are asked not to participate. The [three example consent forms](#) use this approach.

Alternatively, a "tiered" consent approach refers to giving the research participants a set of choices and allowing them to choose some choices over others to give them greater control over the use of their biological samples and medical information.<sup>6</sup>

Considerations for the tiered consent approach:

- (1) The consent form should be designed in a way that does not allow research participants to make conflicting choices within the same consent form.
- (2) If a study investigator provides research participants with a set of choices or levels of participation in the research project, then it is important that the investigator and, as appropriate, the data repository have the appropriate mechanisms in place to track the individual choices and to ensure that the data are used in a manner consistent with those choices.

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## Obtaining Consent in Diverse Populations

(Adapted from [Simplification of Informed Consent Documents](#) [cancer.gov])

It is essential to include diverse populations in research. Developing the informed consent document and communicating with the potential research participant, family members and, in some cases, the community through the informed consent process requires cultural sensitivity. The standards for valid consent should not be compromised in the face of language, cultural, or physical challenges, but the process may need to be adapted to accommodate cultural preferences.

The information that is given to the subject or the representative must be in language understandable to the subject or the representative (see [45 CFR 46.116](#)). Oral and written translations are part of the process of presenting informed consent information to non-English-speaking persons.

The contact individuals listed in the consent form may need plans to communicate with potential participants in other languages. Culturally-appropriate consent documents and supplemental materials such as videos, audiotapes, and interactive computer programs may be especially helpful in communicating information to individuals from diverse populations, whether or not English is their primary language.

Consent documents should be adapted to the needs of individuals with limited literacy skills and those who are vision impaired. A single research project may require several versions of the informed consent document to tailor the information to a variety of populations.

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## Community Consultation/Community Engagement

Research on human genetic variation has implications not only for the individuals who give samples, but also for the broader communities and populations of which they are a part. This is because the research involves the potential for comparing allele frequencies and disease prevalence among groups with different ancestries, sometimes in a context where societal or ethnic discrimination already exists.

Thus, in some situations, in addition to obtaining informed consent from individual sample donors, it may be appropriate to conduct a process of community engagement or community consultation. The goal of community engagement/consultation is to give a broad range of members of the communities approached for the donation of samples an opportunity to:

- Obtain information about the project so that the decisions of community members regarding donation of samples will be better informed.
- Share their views about the ethical, social, and cultural issues the project raises for them, their immediate communities, and the broader communities and populations of which they are a part.
- Provide input into such matters as how the samples from their locality will be collected and described.
- Remain informed about how the data and the samples are being used and about findings from future studies based on the data and the samples.

In some cases it may also be appropriate to establish a Community Advisory Group to provide ongoing feedback about the project and about how the community's samples are being used.

The National Institute of General Medical Sciences (NIGMS) has developed a bioethics resource: [Bioethics Resources on the Web](http://bioethics.od.nih.gov) [bioethics.od.nih.gov]. This resource includes the [Points to Consider When Planning a Genetics Study That Involves Members of Named Populations](http://bioethics.od.nih.gov) [bioethics.od.nih.gov] that was developed by the National Institute of General Medical Sciences (NIGMS).<sup>7</sup> This resource contains an introduction to community consultation, working with tribal communities to conduct genetics research and frequently asked questions.

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## 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)<sup>8</sup> and the American Academy of Pediatrics (AAP)<sup>9</sup> 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.<sup>10</sup>

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 person 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**.<sup>11</sup>

The Office for Human Research Protection (OHRP) developed a comprehensive [Human Research Frequently Asked Questions \(FAQ\)](#) resource. Within this resource is section dedicated specifically to [Informed Consent FAQs](#). For a summary of the requirements for assent and parental permission in research involving children, please refer to the Informed Consent FAQ response to **(Q.22) [What are the requirements for assent and parental permission in research with children?](#)** [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. Please refer to the OHRP Informed Consent FAQ response to **(Q. 25) [What happens if a child reaches the legal age of consent while enrolled in a study?](#)**

## 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\(b\)](#)).

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\(a\)](#)). 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 \(f\)](#)). 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?](#) [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.<sup>12</sup>

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## Educational Materials

As mentioned in the above section on "Obtaining Consent in Diverse Populations," supplemental materials such as videos, audiotapes, and interactive computer programs may be helpful tools to incorporate into the informed consent process to communicate information to research participants.

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[6] McGuire, A.L., Hamilton, J.A., Lunstroth, R., McCullough, L.B. & Goldman, A. DNA data sharing: research participants' perspectives. *Genet Med* 10, 46-53. 2008.

[7] Available at [Points to Consider When Planning a Genetic Study That Involves Members of Named Populations](#) [bioethics.od.nih.gov]

[8] Points to consider: ethical, legal, and psychosocial implications of genetic testing in children and adolescents. American Society of Human Genetics Board of Directors, American College of Medical Genetics Board of Directors. *Am J Hum Genet*, 57, 1233-41. 1995.

[9] Nelson, R.M. et al. Ethical issues with genetic testing in pediatrics. *Pediatrics*, 107, 1451-5. 2001.

[10] Borry, P., Stultiens, L., Nys, H., Cassiman, J.J. & Dierickx, K. Presymptomatic and predictive genetic testing in minors: a systematic review of guidelines and position papers. *Clin Genet*, 70, 374-81. 2006.

[11] From [Eunice Kennedy Shriver National Institute of Child Health and Human Development \(NICHD\) "About Clinical Research."](#)

[12] This response was excerpted from [OHRP Informed Consent Frequently Asked Question #21](#).

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## Three Consent Form Examples

These consent documents were developed for various National Institutes of Health (NIH) sponsored research projects, including a genome-wide association study from the GENEVA consortium (part of the [Genes, Environment and Health Initiative](#) [gei.nih.gov]), the [NHGRI Medical Sequencing Program](#), and the [1000 Genomes Project](#) [1000genomes.org].

Although these consent forms were developed for specific research initiatives, they serve as examples of how the issues relevant to genomics research may be usefully discussed and presented in the consent form.

- [Reconsent for a Genome-wide Association Study with Broad Data-Sharing](#)  (*Genes, Environment, and Health Initiative*)
- [DNA Sequencing Consent](#)  (*NHGRI Medical Sequencing Program*)
- [Consent for Non-Identifiable Samples Collected to Study Human Genetic Variation](#)  (*1000 Genomes Project*)

Additional references and links to example consent forms can be found under the **Additional References** section of this resource.

To view the PDFs on this page you will need Adobe Reader.



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# Additional Resources

## Requirements for Human Subjects Research

- **[Office for Human Research Protections \(OHRP\)](https://www.hhs.gov/ohrp)** [hhs.gov/ohrp]: The Office for Human Research Protections (OHRP) protects the rights, welfare, and well-being of subjects involved in research conducted or supported by the Department of Health and Human Services (HHS) and helps ensure that such research is carried out in accordance with the regulations described [in the Code of Federal Regulations: Title 45, Part 46](#); also referred to as [45 CFR 46](#). **Such research must abide by the Protection of Human Subjects requirements in 45 CFR 46.**

OHRP has tips for informed consent at [Tips on Informed Consent](#) [hhs.gov/ohrp] and at [Informed Consent Frequently Asked Questions](#) [hhs.gov]. OHRP also has tips for other elements of the research process at [Human Research Questions & Answers](#).

- **Food and Drug Administration (FDA):** The U.S. Food and Drug Administration (FDA), through its Office of Health Affairs, has developed its own set of regulations on the protection of human subjects (Code of Federal Regulations: [Title 21, Part 50](#) and [Title 21, Part 56](#); also referred to as 21 CFR 50, 56).

The regulations apply to any clinical trial that involves an investigational drug, biological product, or other device that is regulated by the FDA under the Food, Drug, and Cosmetics Act — regardless of whether or not the trial receives Federal funding. If a trial is supported by the Department of Health and Human Services and involves an FDA-regulated drug or device, then it is subject to both organizations' regulations. (For more information, see [Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors](#)).

## Guidance Documents

- **NIH Policy for Genome-Wide Association Studies (GWAS):** The NIH released the final "Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies (GWAS)" in the NIH Guide and the Federal Register on August 28, 2007. Under this policy, investigators who are performing whole genome association studies conducted or supported by the NIH are expected to submit their data to the NIH GWAS data repository (currently dbGaP) for broad sharing with the research community.

**See:** [Genome-Wide Association Studies \(GWAS\)](#) [grants.nih.gov]

- **Institutional Review Boards (IRBs):** The IRB is an administrative body established to protect the rights and welfare of human research subjects recruited to participate in research activities conducted under the auspices of the institution with which it is affiliated. Guidance regarding IRBs can be found at:

- The National Institutes of Health (NIH): As a complement to the NIH GWAS Policy, the NIH has developed a [Points to Consider](#) document for IRBs and institutions in their review of data submission plans for institutional certifications under NIH's GWAS Policy.
- The Office for Human Research Protections (OHRP): OHRP has developed an [IRB Guidebook](#) to help researchers and IRB members to understand the policies, principles, and issues that pertain to designing and reviewing research proposals. OHRP also has IRB information at the [Human Research Questions & Answers](#) resource.
- The Food and Drug Administration (FDA): [Title 21, Part 56](#) of the Code of Federal Regulations addresses IRBs. They also maintain a website of [Good Clinical Practice in FDA-Regulated Clinical Trials](#).
- The Department of Energy: The Department of Energy has a [Human Subjects Protection Resource Book](#) that provides information for IRBs and their investigators. A chapter in this resource is dedicated to issues pertaining to genetics and genomics research.

## Additional Consent Form References and Examples:

- [Beskow LM, Dean E. Informed consent for biorepositories: assessing prospective participants' understanding and opinions. Cancer Epidemiol Biomarkers Prev. 2008 Jun; 17\(6\):1440-51. See Appendix A.](#)
- [Beskow LM, Burke, W, et al. Informed Consent for Population-Based Research Involving Genetics. JAMA. 2001; 286:2315–2321.](#)
- [The Graduate School at the University of Wisconsin-Madison: Consent Form Templates](#)

## Other Organizations and Resources

- **Group Health Center for Health Studies:**  
The Project to Review and Improve Study Materials (PRISM) is a Group Health Center for Health Studies initiative to improve the quality of print materials used in communication with research participants. The primary goal is to create written study materials that are readable and participant-centered through the [PRISM Readability Toolkit](#).
- [Public Responsibility in Medicine and Research \(PRIM&R\)](#) helps to educate medical personnel and the public about the ethical, legal, and policy issues involved in clinical research.
  - [PRIM&R Human Tissue/Specimen Banking White Paper](#)
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