Cary Institute of Ecosystem Studies

Cary Institute IRB Informed Consent Policy

POLICY STATEMENT

The 2018 revisions to the Common Rule (Revised Common Rule) implemented changes to the informed consent procedures for research involving human subjects. This is in part due to changes in the definition of human subjects, which removed the term "data" and now references "information and biospecimens."

The main purpose of informed consent is to ensure that the subject is fully aware of and understands the reasons for why one might or might not want to participate in the research. Consent documents must be written to facilitate such an understanding by presenting key information at the beginning of the document. The conditions of informed consent are summarized below to ensure that all projects from Cary Institute Principal Investigators (PIs) are compliant with the requirements and that all human subjects are fully informed and aware of their participation in the research.

Additional information is provided about the new elements concerning broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens that are collected for either research studies other than the proposed research, or for non-research purposes.

This policy also describes the appropriate documentation required for informed consent for participation in research, including the participation of children in research.

In the context of obtaining informed consent from a prospective participant in human subjects research, consent may be obtained from the individual participant or from that individual's legally authorized representative. According to the regulations at 45 CFR Part 46, *legally authorized representative* means "an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research. If there is no applicable law addressing this issue, *legally authorized representative* means an individual recognized by institutional policy as acceptable for providing consent in the nonresearch context on behalf of the prospective subject to the subject's participation in the procedure(s) involved in the research." In the sections below, whenever the term research participant, prospective participant, or research subject in the context of informed consent, this is meant to mean the participant or that participant's legally authorized representative.

OBTAINING INFORMED CONSENT

General Requirements for Informed Consent

There are general requirements that must be provided to prospective research participants (or their legally authorized representative) to ensure that they are fully informed about the research they will be participating in. Below is a list of items that must be considered when seeking consent from prospective participants:

1. Before beginning research involving human subjects, the investigator must receive written or oral consent.
2. The prospective participant must be allowed sufficient opportunity to discuss and consider whether to participate in the research. The participant should be able to ask questions of the investigator.

3. The information provided to the prospective participant must be in a language that is understandable.
4. The prospective participant must be provided with information that a reasonable person would want to have to allow them to make an informed decision about participating, and give an opportunity to discuss that information.
5. Except for broad consent (described later), informed consent must:
    a. Begin with concise and focused presentation of key information that will be most helpful to the prospective participant in understanding the reasons why one might or might not want to participate in the research. Facilitate comprehension.
    b. Provide sufficient detail in an organized way.
6. Do not include language where the participant waives or appears to waive any of their legal rights, or releases or appears to release the investigator, sponsor, institution, or its agents from liability for negligence.

Basic Elements of Informed Consent

The following list contains the basic informational elements of informed consent that shall be provided to each participant being sought for research:

1. Include a statement that the study involves research, an explanation of the purpose of the research and the expected duration of participation, description of the procedures to be followed, and identification of any procedures that are considered experimental;
2. Describe any reasonably foreseeable risks or discomforts to the research participant;
3. Describe any benefits that the participants or others may reasonably expect from the research;
4. Disclose appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the participant;
5. Describe the extent, if any, to which confidentiality of records that could identify the participant will be maintained;
6. For research involving more than minimal risk, explain if there will be compensation and if any medical treatments will be available if injury occurs, and if so, what they are or where the participant can get more information;
7. Explain who to contact for answers to questions about the research and the participants' rights, and contact information for who the participant should contact if a research-related injury occurs;
8. Include a statement that participation is voluntary, and that refusing to participate will not involve any penalties or losses of benefits to which the participant is otherwise entitled, and indicate that the participant may discontinue participation at any time without penalty or loss of benefits to which they are otherwise entitled;
9. Include one of the following statements about research that involves the collection of identifiable private information or identifiable biospecimens:
    a. A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the participant, if this is a possibility; or
    b. A statement that the participant's collected information or biospecimens will not be used or distributed for future research studies, even if identifiers are removed.

Additional Elements of Informed Consent

There may be other elements of information that also should be provided to research participants, if they are applicable:

1. 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) that are currently unforeseeable;
2. Anticipated circumstances under which the subject's participation may be terminated by the investigator regardless of the subject's consent;
3. Explain any additional costs to the subject that could result due to their participation in the research;
4. Explain the consequences if the subject decides to withdraw from the research and what the procedures will be for an orderly termination of participation;
5. A statement that significant new findings developed during the course of the research that may relate to the subject's willingness to continue participation will be provided to them;
6. Provide the approximate number of subjects that are involved in the study;
7. A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether or not the subject will share in this profit;
8. A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions; and
9. For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

Elements of Broad Consent

Broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens is a new provision with the 2018 requirements. This type of consent is an alternative to the informed consent requirements provided above (basic and additional elements of informed consent).

If the participant or subject is asked to provide broad consent, the following shall be provided:

1. Specific items from the above section on Basic Elements of Informed Consent:
    a. Statement of risks (item 2);
    b. Statement of benefits (item 3);
    c. How confidentiality will be maintained (item 5); and
    d. Participation is voluntary and the participant can withdraw at any time without penalty (item 8);
2. General description of the types of research that may be conducted with the identifiable private information or identifiable biospecimens;
3. Description of the identifiable private information or identifiable biospecimens that might be used in the research, if sharing of this information or biospecimens might occur, and the types of institutions or researchers that might conduct research with the information or biospecimens;
4. Indication of the time period for which the identifiable private information or identifiable biospecimens may be stored and maintained (the period could be indefinite), as well as the period of time that the information or biospecimens may be used for research purposes (this period could also be indefinite);
5. Statement that the participant will not be informed of the details of any specific research studies that might be conducted using their identifiable private information or identifiable biospecimens (unless they will be provided details about the specific research studies), including the purposes of the research, and let them know that they might have chosen not to consent to some of those specific research studies;

6. Statement that clinically relevant research results may not be disclosed to the participant (unless it is known that the results will be disclosed to the participant in all circumstances); and
7. Contact information for those seeking answers about the participant's rights and about the storage and use of their identifiable private information and identifiable biospecimens, as well as who to contact in cases of research-related harm.

Waiver or Alteration of Consent

In two cases, the IRB has the ability to approve a consent procedure that waives or alters some or all of the elements of informed consent, provided certain requirements are met. The first is research involving public benefit and service programs conducted by or subject to the approval of state or local officials (Section 46.116(e)). The second is a general waiver or alteration of consent (Section 46.116(f)). For both, neither may omit or alter any of the General Requirements for Informed Consent. In addition, the IRB cannot waive consent for the storage, maintenance, or secondary research use of identifiable private information or identifiable biospecimens if an individual was asked to provide broad consent and refused to consent.

Sections 46.116(e) and (f) provide the requirements that must be met for an IRB to allow a waiver and/or alteration of informed consent. For example, granting a general waiver or alteration of informed consent requires that the research involves no more than minimal risk, and the research could not practicably be carried out without the requested waiver or alteration.

Screening, Recruiting, or Determining Eligibility

An IRB may approve research where an investigator will obtain information or biospecimens in order to screen, recruit, or determine the eligibility of prospective subjects without obtaining their informed consent if either of the below two conditions are met:

1. the investigator will receive the information through oral or through written communication with the prospective subject or legally authorized representative; or
2. the investigator will obtain the information by accessing records or stored identifiable biospecimens.

Posting of Clinical Trial Consent Forms

There are new requirements related to posting an IRB-approved consent form used to enroll subjects in clinical trials. This form must be posted on a publicly available federal website established for such purposes after the clinical trial is closed to recruitment and no later than 60 days after the last study visit by any subject, as required by the protocol. If it is determined that some information should not be posted publicly, there is the ability to redact some of the posted information.

DOCUMENTATION OF INFORMED CONSENT

Informed consent shall be documented by the use of a written informed consent form approved by the IRB and signed (in ink or electronically) by the subject or legally authorized representative, and a copy provided to the subject.

The informed consent form may be either of the following:

1. A written consent form that meets the general requirements for informed consent and the subject has been given adequate opportunity to read the form before signing it. The form may also be read to the subject or the subject's legally authorized representative.
2. A shortened written informed consent form that states that the elements of informed consent have been orally presented to the subject and the key information (required by 46.116(a)(5)(i)) was presented first to the subject, before other information, if any, was provided. The IRB must approve a written summary of what is to be said to the subject. To use this method, a witness must observe the oral presentation. Only the short form itself if signed by the subject. The witness must sign both the short form and a copy of the summary, and the person obtaining consent must sign a copy of the summary. A copy of both signed documents is provided to the subject (or legally authorized representative).

An IRB may waive the requirements for an investigator to obtain a signed consent form for some or all of the subjects if it finds any of the below:

1. That the only record linking the subject and the research is the informed consent form and the principal risk would be potential harm resulting from a breach of confidentiality. The subjects will be asked if they want documentation linking them to the research, and their wishes will prevail;
2. The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context; or
3. If the subjects are members of a distinct cultural group or community in which signing forms is not the norm, the research presents no more than minimal risk of harms, and there is an appropriate alternative mechanism for documenting that informed consent was obtained.

In cases where the informed consent documentation requirement is waived, the IRB may require the investigator to provide the subjects with a written statement regarding the research.

Policy of Assenting of Children in Human Subjects Research

Some pertinent definitions related to the involvement of children in human subjects research are below.

1. "Children" are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.
2. "Assent" means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent. (45 CFR 46.402(b)).
3. "Permission" means the agreement of parent(s) or guardian to the participation of their child or ward in research.
4. "Parent" means a child's biological or adoptive parent.
5. "Guardian" means an individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care.

"Assent" means the child must actively show his or her willingness to participate in the research, rather than just complying with directions to participate and not resisting in any way. When judging whether children are capable of assent, the IRB is charged with taking into account the ages, maturity, and psychological state of the children involved. The IRB has the discretion to judge children's capacity to assent for all of the children to be

involved in a proposed research activity, or on an individual basis. In some cases, the assent of the children is not a necessary condition for proceeding with the research (described in more detail below).

In addition, the IRB shall determine that adequate provisions are made to solicit and obtain the permission of each child's parent(s) or guardian. In accordance with Subpart D, the IRB may find that the permission of one parent if sufficient for research that does not involve greater than minimal risk (45 CFR Part 46.404) or research that involves greater than minimal risk but presents the prospect of direct benefit to the individual subject (45 CFR Part 46.405). That is, the risk is justified by the anticipated benefit to the subjects, and the relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches.

The IRB may wish to seek permission from both parents (unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child), in cases where the research involves greater than minimal risk and there is no prospect of direct benefit to individual subjects (but likely to yield generalizable knowledge about the subject's disorder or condition) per 45 CFR Part 46.406, or research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children (45 CFR Part 46.407).

For research activities involving adolescents whose capacity to understand resembles that of adults, the assent procedure should likewise include information similar to what would be provided for informed consent by adults or for parental permission. For children whose age and maturity level limits their ability to fully comprehend the nature of the research activity but who are still capable of being consulted about participation in research, it may be appropriate to focus on conveying an accurate picture of what the actual experience of participation in research is likely to be (for example, what the experience will be, how long it will take, whether it might involve any pain or discomfort). The assent procedure should reflect a reasonable effort to enable the child to understand, to the degree they are capable, what their participation in research would involve.

The Cary Institute's IRB policy requires, in most cases, the assent of children as outlined in the following examples, which will depend on the age and mental capacity of the children involved. The following breaks down the examples of the types of consent that could be required when working with children of different age groups.

<u>6 years old and younger</u>
The child should be told what the research is about and what their involvement will be in the presence of their parent(s), but a signature from the child is not required. A required part of the parental consent form should be a section that states that the child 6 years old and younger has been told (in age-appropriate language) what he/she will be taking part in.

<u>7-12 years old</u>
For children in this age range, an acceptable way to show assent is by having them print and sign their names on the parental consent document. In such a case, there should be some statement that the parent(s) and child and/or parent(s) and child in the presence of the researcher have discussed the research in a manner that the child understands and that the child agrees with participating and that they can end their participation in the research at any time and for any reason.

13-18 years old

In this age range, children are typically capable of understanding the research that they would be participating in. The child should sign an age appropriate assent form. This may be a separate form, or may be combined with a parental consent form.

Is child assent always required when human subjects research involves children?

No, the IRB is responsible for deciding whether child assent is required in proposed research activities. Child assent is required except in the following three circumstances described at 45 CFR 46.408(a):

1. The capability of some or all of the children is so limited that they cannot reasonably be consulted;
2. The intervention or procedure involved in the research holds out the prospect of direct benefit to the health or well-being of the children and is available only in the context of the research;
3. The research meets the same conditions as those for waiver or alteration of informed consent in research involving adults. These are specified in the regulations at 45 CFR 46.116(e) and (f), which are waivers or alteration of consent in research involving public benefit and service programs conducted by or subject to the approval of state or local officials, and general waiver or alteration of consent, respectively.

For research at the Cary Institute, the conditions of 45 CFR 46.116(f), General Waiver or Alteration of Consent, would be most relevant.

An IRB may approve a consent [assent] procedure that does not include, or alters, some or all of the elements of informed consent set forth in this section, or waives the requirements to obtain informed consent, provided the IRB finds and documents that:

1. The research involves no more than minimal risk to the subjects;
2. The research could not practicably be carried out without the waiver or alteration;
3. If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format;
4. The waiver or alteration will not adversely affect the rights and welfare of the subjects; and
5. Whenever appropriate, the subjects (or legally authorized rep) will be provided with additional pertinent information after participation.

However, even if the above conditions are met, the Cary Institute IRB may still require assent.

Is parental consent always required when human subjects research involves children?

No, in addition to the provisions for waiver contained in 45 CFR Part 46.116 (General requirements for informed consent), if the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements, provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with federal, state, or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.