

INFORMED CONSENT

Adapted from the Code of Federal Regulations - [45 CFR 46.116](#)

4.1 A process - not a form

Since subjects retain the right to withdraw from a study, consent is an ongoing process. It starts well before any forms are signed and continues until the subject's participation is complete.

The informed consent process is different from the consent form. It involves meeting with a potential subject, finding out whether he or she is capable of giving consent, and discussing the purpose, risks, and benefits of participation. The consent form formalizes the agreement to participate and should be designed to document the process. Obtaining informed consent is not just giving a prospective subject a consent form and getting it signed.

If consent is to be informed, the subjects must genuinely understand the study. Hence, researchers should strive to convey information to subjects, not merely disclose it to them. Subjects should be able to demonstrate their understanding of the study procedures, risks, and benefits in which they are agreeing to participate.

4.2 When to discuss participation

To achieve understanding, potential subjects should not be presented information all at once or only at the last minute. People need time to think about whether or not they want to participate. They may wish to discuss the decision with family, close friends, or religious advisors. They should not feel rushed or coerced. They need time, especially if the information is disturbing or particularly complex, to digest the information and come to terms with it.

Information must be comprehensible. Even highly educated people need to have technical information presented in simple terms. How information is best expressed will vary with the population of course. In studies involving nurses as subjects, for example, researchers can explain a project using some medical terminology, but lay persons need to have information presented as simply and straightforwardly as possible. Some of the suggestions offered here for writing readable consent forms are also useful for presenting information in discussions.

4.3 What must be said about the research

Consent for research involving clinical procedures should be discussed during prior visits to the clinic, not on the day of the procedure. Whenever possible, subjects should be approached when they are rested, lucid, and able to use eyeglasses or hearing devices if they need them.

Federal regulations for human research identify some information as "essential" for understanding any research project [45 CFR 46.116(a)&(b)]. At a minimum, investigators should:

- Explain the purposes of the research;
- Report the expected duration of the subject's participation;
- Describe the procedures to be followed;
- Identify any procedures or products that are experimental;
- Explain why the subject is eligible to participate;
- Describe any foreseeable risks or discomforts that the subject will bear;
- Describe any benefits to the subject or to others that can reasonably be expected;
- Disclose appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
- Explain the confidentiality of any records that identify the subject;
- Explain, for research that involves physical contact or physical activity, whether compensation or medical treatment will be available if the subject is injured and where to get further information about this;
- Identify people who can answer questions about the research, including the principal investigator and a neutral third party who can explain the rights of research subjects and who should be contacted if the subject suffers injury related to the research (the "out-of-study" contact for patients in the Fairview-University Hospitals and Clinics is the Patient Relations Department); and
- Explain that participation is voluntary, that refusal to participate will involve no penalty or decrease in benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits.

In addition to this essential information, circumstances may require researchers to:

- Explain that a treatment or procedure might involve currently unforeseeable risks (including risks to an embryo or fetus, if a participant is or becomes pregnant).
- Explain conditions under which the investigator can remove people from the study without their concurrence.
- Explain any additional costs that participating in the study might involve.
- Discuss the consequences of and the procedures for withdrawing from the study.
- Declare that research findings that could affect participants' willingness to remain in the study will be disclosed to them.
- State the approximate number of people involved in the study.

- Identify pilot or feasibility studies. Some subjects are willing to participate in a study that has a track record but are not willing to participate in a pilot phase. Participants need to be told if they are among the first people to receive the treatment or intervention.
- Inform women of child-bearing age whenever a pregnancy test is part of the research protocol. They must also be told whether such tests will be repeated during the course of a research project and whether they must use contraceptives to participate in a clinical trial. Men, too, need to be told if contraception is recommended for them.
- Make clear whether the procedures or drugs used in a study are standard, standard but used in a non-standard manner, or experimental.

If the study involves experimental drugs or devices, inform the subject that the research and medical records may be reviewed by the Food and Drug Administration (FDA) and by the company sponsoring the research.

Avoid stating that drugs or devices have been approved for human use by the FDA if any part of the study is outside the licensed and approved indications of those items. Patients interpret such a claim to mean that the FDA has licensed and approved this use of the item, not that the FDA has merely granted permission to investigate the use of the item.

Distinguish between consent to a study and consent to a treatment. In "treatment studies" (in which a patient who is undergoing a treatment is given a choice between undergoing it as part of a study or undergoing it in a standard health care context), the study and the treatment involve different benefits, risks, and alternatives.

If consent to the research and consent to the treatment can be confused, they should be presented in separate consent forms.

In discussing risks, the subject should be informed that there might not be any benefit to being treated "on study" instead of "off study."

In discussing risks, the subject should be informed whether the risks of being treated "on study" are different from the risks of being treated "off study."

In discussing alternatives, the subject should be told whether the study treatment (drug or device) is or is not available outside of the study context.

4.4 What must be said about the conduct of the research

Confidentiality

The researcher should describe the level of confidentiality of the research data and the measures that will be taken to ensure that confidentiality is maintained.

The phrase "only aggregate data will be presented" is appropriate only when it is true. Strictly understood, it means that the researcher will not describe a patient individually, even if the patient has a unique event. What is more common, however, and what the subject should be told, is that the subject's identity will not be disclosed.

Finder's fees

Companies sometimes offer researchers incentives for recruiting subjects or conducting research on an investigational drug or device manufactured by the company. The incentive may be either a monetary fee or a donation of equipment or materials. Researchers should report these incentives to the IRB, which may require that this information be disclosed to prospective subjects.

Payments to research subjects

If researchers plan to compensate subjects for participating in a study, the consent form must describe the terms of payment and the conditions under which subjects would receive partial payment or no payment (for example, if they withdraw from the study before their participation is completed).

4.5 Assessing the subject's understanding

The responsibility of ensuring that someone who might participate genuinely understands the research and the risks and benefits involved falls upon the researcher, not upon the prospective subject. Hence it is critical to the consent process that the researcher not only field questions but also ask questions. Asking questions can further the discussion, elicit questions from the prospective subject, prompt the prospective subject to think more carefully about the project, and help the researcher decide whether the person has adequately understood the project. These questions must be prepared in advance.

Useful questions will be open-ended and non-directive. Rather than asking for yes or no answers, they ask for explanation because these questions often can be answered in a variety of ways, and do not already contain the correct answer. Open-ended questions are often introduced with "what," "where," "how often," "when," and "please describe." Examples of open-ended questions are:

"Just so that I'm sure you understand what is expected of you here, would you please explain to me what you think we're going to ask you to do?"

"Describe in your own words the purpose of the study."

"What more would you like to know?"

"What is the possible benefit to you of taking the new experimental drug? What are the possible risks?"

In contrast, examples of closed-ended and far less useful questions are:

"Do you understand?"

"Do you have any questions?"

"Do you see that there are some risks to taking this drug?"

Instead of furthering the discussion, closed-ended questions tend to bring it to a stop and so should be avoided.

4.6 Documenting the subject's consent with a consent form

Once a subject understands a study and has expressed a willingness to participate, researchers must document the subject's consent with a consent form. Although a dated signature certifies the subject's willingness to participate, it is not equivalent to assuring that the subject has understood the research. Including a date with the signature avoids confusion about whether the subject began to participate before giving informed consent.

A researcher may need to prepare several consent forms, depending on who the subjects are likely to be. For example, a single project may require a consent form for the guardian or parent of a child, a consent form for the competent adult subject, and a simplified assent form for the 8- to 18-year-old or for the adult who is not competent to give consent alone. [See following sections for discussion of assent forms.] Foreign-language versions of consent forms will be needed if people who do not speak English are to be enrolled. [See section 4.11 for discussion of translated consent forms. This section also discusses unexpected enrollment of non-English-speaking subjects.]

The person who prepares the documents should:

- Print all documents in type no smaller than 12 points to make sure they are readable. If the subjects will have difficulty with 12 point font, a larger font is necessary.
- Place the title of the study on the first page, exactly as it appears in the IRB files unless there is a compelling reason to shorten or change the title. "Informed Consent" is not an acceptable title because it obscures the fact that informed consent is a process, not the document itself, and implies a completeness that the form may not have.
- Number each page after the title page so that pages appear in a logical order and missing pages are readily noted (example: "page 2 of 4").

- Print the IRB code number assigned to the study on the consent form.
- Include a consent form version date. This date should be updated each time a new version of the consent form is approved by the IRB.

Format and Specific Requirements

The consent form should:

- Identify the researchers by name along with their University and Departmental Affiliation on the first page of the consent form.
- The form should not say that the study is "sponsored" or "endorsed" by the University.
- If the project is conducted by faculty or staff, the first page of the consent form should be printed on departmental letterhead. For student projects, the words "University of Minnesota" should appear in the header on the first page, and advisers' names and phone numbers should be given with the student's name and contact information.

Invite Participation

Consent forms should "invite" participation. They should not say that a patient's physician or friend recommends participation, nor should they "offer the opportunity" to participate. It may be appropriate to point out that withdrawing from a study could have adverse consequences to subject treatment.

Summarize Cautiously

Information described earlier in the consent form should be summarized only in order to clarify. Summaries that suggest a warning or limitation of liability or opportunity for redress are not acceptable. Examples that are unacceptable are:

"You understand that..."

"The possible risks associated with this study have been presented."

"The method and purpose of administration of this study have been explained to you."

"You have been made aware of certain risks and consequences."

Readability and Technical Language

In writing consent forms, researchers should:

- Use declarative sentences suited for an eighth-grade reading level.

- Write in the second person ("you") rather than the first person ("I"), and avoid shifting from one to other.
- Avoid strike-out formats (such as "You/Your spouse/Your child"), since they depersonalize the form and often make it difficult to read.
- Keep the description of the study as brief as possible, even if the study is complex. The details can be placed in an appendix.
- List only the major risks associated with an experimental drug or procedure. Some effective consent forms simply state, "The risk of being on this study is that the treatment may not turn out to be as successful as we hope, and may even be less effective than our previous standard treatment. In addition to this risk of being on the study, the drugs used in the treatment have their own risks and side effects. The most important ones are: ..." Again, the details go in an appendix.
- Use paragraph headings and illustrations. Use flow charts or calendar-like tables to explain studies that involve multiple visits, that ask subjects to go from one place to another, or that involve different protocols depending on research benchmarks.
- Describe quantities in lay terms (teaspoons, for example). Communicate size with an illustration or a reference to a common household object of the same size.
- Ask a neighbor, friend, or someone else who is unfamiliar with the field to read the final draft of a consent form. Software packages that evaluate a text's "readability" may be helpful.

Replace technical language with lay terms. Some commonly used technical terms and possible replacements follow:

Term Definition

acute - new, recent, sudden

adverse effect - side effect

assay - lab test

benign - not malignant, usually without serious consequences

bolus - an amount given all at once

carcinogenic - capable of causing cancer

catheter - a tube for withdrawing or introducing fluids

chronic - continuing for a long time

clinical trial - an experiment with patients

controlled trial - a study in which the experimental procedures are compared to a standard (accepted) treatment or procedure

culture - test for infection, or organisms that could cause infection

double blind - study in which neither investigators nor subjects know which drug the subject is receiving

dysplasia a- abnormal cells
edema - increased fluid
efficacy - effectiveness
extravasate - to leak outside of a blood vessel
hematoma - a bruise, a black and blue mark
heparin - lock needle placed in the arm with blood thinner to keep the blood from clotting
monitor - check on, keep track of, watch carefully
morbidity - undesired result or complication
mortality - death or death rate
necrosis - death of tissue
oncology - the study of tumors or cancer
percutaneous - through the skin
placebo - a substance of no medical value, an inactive substance
PRN - as needed
protocol - plan of study
random - by chance, like the flip of a coin
relapse - the return of a disease
retrospective - looking back over past experience

4.7 When to submit the form to the IRB

Researchers must submit consent forms when they first apply for IRB review and approval, and when they apply for continuing review. Since the standards for consent forms change over time, in part due to changes in regulatory mandates and community styles and expectations, the IRB reviews the form at renewal to ensure that it is up to date.

In addition, the IRB may ask researchers to modify consent forms at other times, when circumstances warrant. Any revisions made to a previously approved consent form must be submitted to the IRB for approval before use.

4.8 When the consent requirement can be waived

On rare occasions, the federal regulations for human subjects research allow a waiver of the requirement for informed consent. For example, a waiver is possible if a study investigates certain aspects of public benefit or service programs. Also, either a waiver or a consent process that omits or modifies the essential elements of informed consent is possible if the IRB finds that:

- The research involves no greater than minimal risk to the subjects;
- The waiver or alteration will not adversely affect the rights and welfare of the subjects;

- The research would be impracticable without the waiver or alteration; and
- The subjects will be informed of the study when it is over (if at all possible).

Only the IRB can waive or modify the consent process. Researchers are not authorized to make this decision.

4.9 The Certificate of Confidentiality - an additional protection

A "Certificate of Confidentiality" protects subjects' anonymity by protecting research records from subpoena. The assistant secretary for health in the Department of Health and Human Services issues the certificate under two conditions: the research is on a sensitive topic, and the protection is necessary to achieve the research objectives. The certificates are granted sparingly. The study's funding source is not relevant to the decision.

The certificate goes beyond the consent form in ensuring confidentiality and anonymity. Without the certificate, researchers can be required by a court-ordered subpoena to disclose research results (usually as part of a criminal investigation of the subjects).

Research can be considered "sensitive" if it involves the collection of:

- Information about sexual attitudes, preferences, practices;
- Information about the use of alcohol, drugs, or other addictive products;
- Information about illegal conduct;
- Information that could damage an individual's financial standing, employability, or reputation within the community;
- Information in a subject's medical record that could lead to social stigmatization or discrimination; or
- Information about a subject's psychological well-being or mental health.

This list is not exhaustive. Researchers contemplating research on a topic that might qualify as sensitive should contact the IRB office for help in applying for a certificate. The IRB sometimes requires investigators to apply for a certificate.

4.10 Children and adolescents

Written parental permission is required for studies involving children under the age of 18. If the research involves greater than minimal risk, signatures from both parents are required unless the

second signature is not reasonably available. A single signature is sufficient if only one parent has legal responsibility for the care and custody of the child or if one parent is deceased, unknown, or incompetent. Parental permission is documented in a form similar to an adult subject consent form, tailored to invite "your child" to participate rather than "you".

On rare occasions, the IRB can grant a "waiver of parental consent," but only if the research will yield great benefit to the population being studied and if obtaining parental consent would pose a considerable risk to the potential subjects.

Once parental permission has been obtained, the agreement of the child is required. Parental permission overrules a child's decision not to participate in therapeutic settings.

The child's agreement is documented with an "assent form," a child-friendly document that outlines the essential information about the research. All children 8 years through 17 years old should be given an opportunity to assent, since most children 8 years old have the cognitive and emotional maturity to understand a research project and to decide whether they want to participate in it.

Some children under the age of 8 may also be capable of granting and withholding assent, and the IRB asks researchers to be sensitive to the needs of these children on an individual basis. Researchers should try to draft a form that is age-appropriate and study-specific, taking into account the typical child's experience and level of understanding, and composing a document that treats the child respectfully and conveys the essential information about the study. The form should:

- Tell why the study is being conducted;
- Describe what will happen and for how long or how often;
- Say it's up to the child to participate and that it's okay to say no or withdraw;
- Explain if it will hurt and for how long and how often;
- Say what the child's other choices are;
- Describe any good things that might happen;
- Say whether there is any compensation for participating; and
- Ask for questions.

The document should be limited to one page if possible. Illustrations might be helpful, and larger type makes a form easier for young children to read. Studies involving older children or adolescents should include more information and may use more complex language.

In instances where critical therapeutic research is involved, parental permission overrules a child's decision to participate. In such cases, a child's dissent would not be honored; therefore an "information sheet" rather than an assent form should be used. The information sheet should include the same info found in an assent form except:

- It should not indicate that the decision to participate is up to the child nor that it is okay to say no.
- It should not include signatures.

Subpart D of 45 CFR 46.401-409, "Additional Protections for Children Involved as Subjects in Research," outlines the conditions of participation for minor subjects.

4.11 Consent and language barriers

When planning research which will include non-English speaking subjects, researchers should prepare both English-language and translated consent forms for proposals involving non-English-speaking subjects. An explanation of the translations and the expertise of the translator should be provided for IRB review. The IRB may consult with language experts or require a "back-translation" into English.

As an alternative to translated consent forms, an oral presentation of informed consent information in conjunction with a short form written consent document (stating that the elements of consent have been presented orally) and a written summary of what is presented orally can be approved by the IRB. A witness to the oral presentation is required, and the subject must be given copies of the short form document and the summary.

When this procedure is used with subjects who do not speak English:

- The oral presentation and the short form written document (see sample attached) should be in a language understandable to the subject;
- The IRB-approved English language informed consent document may serve as the summary; and
- The witness should be fluent in both English and the language of the subject.

At the time of consent, the following signatures should be obtained:

- The short form document should be signed by the subject (or the subject's legally authorized representative);
- The summary (i.e., the English language informed consent document) should be signed by the person obtaining consent as authorized under the protocol; and

- The short form document and the summary should be signed by the witness. When the person obtaining consent is assisted by a translator, the translator may serve as the witness.

The IRB must receive all foreign language versions of the short form document as a condition of approval (see 46.117(b)(2)). Expedited review of these versions is acceptable if the protocol, the full English language informed consent document, and the English version of the short form document have already been approved by the convened IRB.

Download short forms in different language (languages available: Arabic, Cambodian, Croatian, French, Hmong, Lao, Oromo, Russian, Somali, Spanish, Vietnamese)

Sometimes a subject understands English but does not read or write English. An impartial witness should document that the subject understands the study and the consent process and consented to participate.

4.12 Cross Cultural Consent Issues

The requirements for documenting informed consent vary among cultures. The IRB does not exempt projects conducted in foreign countries or with other cultural groups here from the consent requirement, but it can waive the requirement for written documentation of consent. In some settings, the process of signing the form is very intimidating and is thought to be riskier than the research itself.

Researchers planning to conduct cross cultural research should justify their proposed method of documenting consent. The justification should include a description of customs if they constrain the typical informed consent process.

Subjects in foreign sites should be given local contacts for any questions they may have about the research or about their rights.

4.13 Research in acute care settings

Although the subject's consent must be obtained whenever possible, research on drugs or devices that are employed during emergencies is sometimes an exception.

Food and Drug Administration (FDA) regulations for human subjects research allow for an emergency exception to informed consent if the situation is life-threatening and if there is no alternative approved therapy with an equal or greater likelihood of saving the patient's life (21 CFR 50.23 [a]). The intent is to allow physicians, exercising their judgment about patients' conditions, to use innovative treatments on incompetent patients.