

Guide to Obtaining Legally Effective Informed Consent

The requirement to obtain informed consent of subjects before involving them in research is one of the key principles of ethical conduct. Investigators are required to obtain “legally effective informed consent” from subjects unless the study qualifies as “exempt research” or unless a waiver of the informed consent requirement has been granted. When consent is required, it must occur before any research-specific procedures take place. Legally effective informed consent is a process by which:

- consent is obtained from the subject (or the subject’s representative, when the research involves a pediatric population or adults with cognitive impairment);
- consent is documented as required by regulations;
- consent is obtained under circumstances that allow the subject sufficient opportunity to consider whether or not to participate;
- consent is obtained in an environment that is free from coercion (overt or implicit threat of harm) or undue influence (offer of excessive or inappropriate reward); and
- consent information is provided in language that is understandable to the subject.

NOTE: For the purposes of federal regulations, “investigators” are all individuals who are involved in the conduct of human subjects research projects. Investigators can include, among others, scientists, health care professionals, research assistants and students. When the term “investigator” is used in the following discussion, it refers to all approved members of the study team.

The Process of Informed Consent

When federal regulators state that informed consent is a process, they mean that informed consent is much more than having the subject sign a document at a single point in time; it is an ongoing exchange of information between the investigator and the subject. The process begins when the potential subject first learns about the research opportunity, and it continues during the entire course of the study. Throughout the research, the investigator discloses information needed for subjects to make an informed, voluntary decision about entering and remaining in the trial. The investigator is charged with facilitating the understanding of what has been disclosed and keeping subjects aware of any new information that may impact their safety or their willingness to participate.

The Setting

The potential subject should be presented with the informed consent document in a private setting, apart from noise and other distractions that may lead the subject to feel rushed or pressured to sign the consent. Ample time must be provided to allow the subject to consider the study. When time permits, investigators are encouraged to discuss the study and allow the potential subject to take home the consent form, returning to discuss and sign at a subsequent visit.

The Consent Document

Information about a research project must be presented in such a way that enables understanding, so that the potential subject may voluntarily decide whether or not to participate. The consent document should be written in lay language with simple, declarative sentences. Visual aspects of

the document also can promote understanding; investigators are encouraged to use short paragraphs, sufficient white space, and diagrams or charts. The HSC website has other tips for creating a consent form that promotes comprehension and readability.

Federal regulations prescribe certain elements that must be discussed in the consent document. Investigators are encouraged to use the consent form templates posted on the HSC website. Multiple versions of the consent form may be necessary if the study includes both adults and children or adults with and without cognitive impairment.

Investigators must ensure that subjects sign only the current, HSC-approved version of the consent form. The approved version will have the HSC stamp in the lower right corner, indicating the valid dates. If the consent form is amended during the approval period, investigators must ensure they use the correct amended version.

The Consent Conversation

In order for the consent process to be legally effective, investigators must explain the study to the potential subject in terms the subject can understand. Simply handing the consent form to the patient and returning later for the signature does not accomplish legally effective informed consent. The investigator and subject should engage in a conversation about the study, “talking through” the various sections of the informed consent document.

Federal regulations allow consent to be obtained either by the principal investigator or by other study personnel/investigators who are knowledgeable about the study. Even if the principal investigator is not the primary individual who obtains consent, he or she should be available to answer questions. The principal investigator remains ultimately responsible for the consent process, even when delegating the task of obtaining informed consent to another knowledgeable individual.

In discussing the research project, investigators should cover the following topics:

- a. voluntariness of study participation
- b. background information that led to the scientific question being investigated
- c. the purposes of the study
- d. details about the drugs, devices, supplements or therapies being tested (if applicable)
- e. the expected duration of the project
- f. the procedures to be followed
- g. use of placebo (if applicable)
- h. whether or not investigators will be unblinded (for randomized trials)
- i. procedures or data collection that are being done solely for research purposes
- j. whether or not subjects will be told about results of study assessments
- k. foreseeable risks and discomforts
- l. possible benefits of the study
- m. provisions for confidentiality of the data
- n. additional costs incurred by research participation and any payments to subjects
- o. provisions for care, in the event of a research-related injury
- p. alternatives to participating in the study
- q. assurance that questions can be asked at any time

- r. commitment to keep subjects informed of new information that could impact their willingness to continue participating
- s. subjects' right to decline participation or withdraw from the study without penalty
- t. conditions under which subjects might be removed from the study without their consent
- u. contact information, if subjects have questions or problems during the study

“The Therapeutic Misconception”

Research on the informed consent process has consistently shown that potential research subjects often do not understand the difference between standard medical care and research participation. Potential subjects may not comprehend the goals of research (creating generalizable knowledge) as distinct from the goals of clinical care (improving the health of the individual). Ethicists refer to this confusion as “the therapeutic misconception.” The distinction between research and medical care is further confused by the fact that some studies do hold out the prospect of therapeutic benefit.

When research subjects are interviewed by a third party after an informed consent process has taken place, many are not aware that the research may have risks beyond those of standard care. They demonstrate therapeutic misconception by making statements such as “I’m sure the doctor wouldn’t have told me about this study if it wasn’t the best treatment option for me” and “My doctor knows I need the real drug; he’ll make sure I’m not assigned to the placebo.”

Subjects who misunderstand the intent of research cannot make meaningful decisions about study participation. Both subjects and researchers must remain clear that the immediate goal of research is not individual patient benefit; the immediate goal is the advancement of science.

When a study involves a placebo, it is especially important to confirm the subject’s understanding of this fact. Additionally, the investigator should highlight any other study procedures that are being done solely for the purpose of the research.

Researchers are obligated to ensure that potential subjects understand that the research is being done to answer a scientific question; there may be additional risks from study participation; and there is no guarantee of personal benefit. This reality should be communicated to the subject several times during the initial consent conversation, and researchers should be prepared to address the issue again as the study progresses.

Assessing Comprehension

The burden of ensuring the potential subject comprehends the research lies with the investigator, not the potential subject. It is crucial that investigators assess the subject’s comprehension before he or she is asked to sign the consent document. The most effective approach is usually to ask the subject open-ended questions. Closed-ended questions such as “Do you understand?” or “Do you have any questions?” will rarely elicit a helpful response from the potential subject. Rather, investigators should use open-ended questions such as:

- “Tell me in your own words the purpose of the study.”
- “Just so I’m sure you understand, could you please explain to me what we’re asking you to do?”
- “What are the possible risks of this study?”
- “What are your choices if you decide not to participate?”
- “What more would you like to know?”

Documenting the Subject's Consent

Obtaining appropriate signatures is an important element of legally effective informed consent. The subject, parent or surrogate decision-maker must personally sign and date the consent. The consent is also signed by the study team member who obtained informed consent. For some pediatric studies, children will sign the “assent” section of the consent form. After consent is obtained, subjects must be provided with a signed copy of the consent form for their records.

Some consent forms have blanks that need to be filled in at the time of consenting. For instance, the contact names and phone numbers may vary by location, or subjects may be choosing among several options in the research. **When the consent process is complete, the person obtaining consent must ensure that every “blank” in the document is filled in, whether for study information in the body of the consent or for signatures, times and dates at the end.**

For studies involving an FDA-regulated product, a health care professional should place a note in the medical record that informed consent for research was obtained. In general, this documentation will be in the form of a progress note. Investigators should be aware of and follow the pharmaceutical sponsor's requirements for documenting consent for research in the medical record.

There are special circumstances where the signature requirement can be waived. Please see the discussion at the end of this document, on consents without signatures and verbal consent.

Obtaining Assent from Children and Adolescents

When the HSC reviews a study involving children or adolescents, the Committee is required to ensure that adequate provisions are made for soliciting the assent of the participants, if they are capable of providing assent.

“Assent” means a child's affirmative agreement to participate in research. In determining whether children are capable of assenting, the HSC takes into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in research under a particular protocol, or for each child, as the HSC deems appropriate. The child should be given an explanation of the proposed research procedures in a language that is appropriate to the child's age, experience, maturity, and condition.

For healthy children, assent is generally appropriate for ages 7 and older. 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, 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.

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. Depending on the nature of the study, investigators may want to consider having a private conversation with the adolescent subject. This separate conversation would confirm the willingness to participate apart from the parent's permission and also provide an opportunity to discuss any private questions the adolescent may have.

The format of the assent form will vary, depending on the age and health of the subjects. The assent should be brief with very simple sentences. A diagram or picture may be helpful in communicating the requirements of the study. A larger font size is suggested. The assent form and the assent conversation should:

- tell why the study is being conducted;
- describe what will happen and what the child will be asked to do;
- communicate the child's freedom to decide whether to participate and the freedom to withdraw before the study is over;
- explain if it will hurt and for how long and how often;
- describe any possibility that participation might provide a benefit to the child;
- outline the child's other choices in lieu of study participation;
- provide the child an opportunity to ask questions.

In studies involving critical therapeutic research, the HSC may determine that parental permission overrules the child's decision to participate and the child's dissent would not be honored. Under those circumstances, the assent process should not indicate that the decision to participate is up to the child. Instead, it should simply provide information about the study and an opportunity for the child to ask questions.

Consent with Non-English Speaking Subjects

Federal regulations require that informed consent information be presented "in language understandable to the subject." If an investigator *expects* to enroll non-English speaking subjects, the HSC requires the use of a foreign-language translation of the informed consent document. However, there may be times when a non-English speaking subject is unexpectedly found to be eligible for enrollment. In this case, investigators will not have an HSC-approved written translation of the consent form in the subject's native language.

In such cases, the investigator may use a written "short form" in the subject's native language as written documentation of the consent process, along with an oral translation of the complete English version of the informed consent document. The translator may be a qualified hospital/clinic staff member or a professional translator. Family members are not allowed to serve as translators for research consent. The family member may or may not understand medical terminology and may have a biased viewpoint about the potential subject's participation in the study.

When this method of obtaining consent is used, there must be a witness to the oral presentation. The witness should be fluent in both English and the subject's language. The translator may serve as the witness.

The written "short form" indicates that the elements of informed consent required by the regulations have been presented orally to the subject. The HSC must have approved the content of what is to be orally presented to the subject; therefore, the HSC-approved consent form becomes the basis of the oral translation. An independent witness

It is important to note that simply finding a translator to verbally translate a research consent form is not compliant with federal regulations. The verbal process must be accompanied by the written short form. The HSC website has specific instructions about how to

obtain legally effective informed consent in these circumstances. Researchers also may call the HSC office at (913) 588-1240 for assistance.

Use of Surrogate (Proxy) Decision-Makers

The state of Kansas has special rules about persons who can provide surrogate consent when adult research subjects are not capable of giving informed consent. Incapacity may arise from cognitive impairment, trauma or severe illness. If a legal guardian or durable power of attorney has not been named, then permission may be provided by (in order of preference):

1. The subject's spouse, unless they are legally separated;
2. An adult child;
3. A parent;
4. An adult relative by blood or marriage.

The law places a caveat on surrogate decision-making, in that no decision in favor of research participation may be made if the potential research subject has previously expressed contrary wishes, either orally or in writing.

When conducting the initial review of a study, the HSC must specifically approve involvement of persons who cannot consent for themselves. From an ethical perspective, a study may enroll these vulnerable subjects only if the research goals cannot otherwise be accomplished.

If the HSC approves enrollment of decisionally-impaired subjects, investigators should use a Surrogate Decision-makers version of the consent form that documents permission by an appropriate proxy and the relationship of that person to the research subject. Investigators must contact the HSC office if they wish to enroll a person with decisional impairment on a study that has not been approved for vulnerable subjects. Such a change would constitute a protocol amendment and would need prior approval from the HSC.

Record-keeping

Investigators are responsible for retaining originals of all signed consent documents along with other study documentation. The KUMC Records Retention Policy requires study records to be maintained for at least 15 years. If the research involves pediatric subjects, then the records must be retained for a minimum of 25 years after completion or termination of the study.

Re-consenting

During the course of the study, the HSC must give prior approval to any changes in the research, unless an overriding safety concern dictates that those changes be made immediately. When the consent form is changed during the study, the HSC evaluates whether or not former or current subjects need to be re-consented. Current subjects should be re-consented if the new information alters their study participation, if the new information relates to safety or risks, or if the new information could otherwise impact subjects' willingness to continue in the study. Former subjects must be notified if the new information could impact their safety or welfare.

Consent Documents without Signatures

Under specified circumstances, federal regulations allow the HSC to waive the requirement for a signature on the consent document. The signature requirement can be waived if the HSC determines:

1. That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research and the subject's wishes will govern;
- or*
2. That 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

When researchers are conducting research on sensitive topics such as risky behaviors, immigration status or substance abuse, it may be appropriate for the HSC to waive the requirement for a signed consent document. These examples fit category 1 above. Note that the consent document still contains all the elements required by federal regulation; only the signature lines on the last page will be omitted. Subjects should be given a copy of the (unsigned) consent document so they can continue to refer to the information and so they can contact the investigator if they have questions.

Consent by Telephone

Sometimes written informed consent is not feasible because the only interaction with the subject will be on the telephone. The most common example is a low-risk phone survey. This type of study fits category 2 above, and the requirement for a signed consent form can be waived. The investigator should create a consent "script" that incorporates the required elements of informed consent (purpose, procedures, risks, benefits, etc.). The HSC must review and approve the script. Study records should document the fact that consent script was reviewed verbally, along with the date and time of the conversation.

Consent by Fax or Mail

Under certain circumstances, the HSC may approve obtaining informed consent by fax or mail. These determinations are made on a case-by-case basis when in-person consent is not feasible and the study does not require study visits to the KUMC campus or another research site. If the HSC approves consent by fax or mail, a consent conversation must take place over the phone after the potential subject has received a copy of the informed consent document. While the potential subject has the informed consent document in hand, the principal investigator or other knowledgeable member of the research team reviews all aspects of the written document. After the study has been discussed and all questions have been answered, the subject signs and dates the consent form and returns by fax or mail. Research participation may not begin until the investigator has received the signed document. Once returned, the research team member completes the signature/date lines for the person obtaining consent. A fully signed copy of the consent document must be returned to the subject, to fulfill HIPAA requirements.

In addition to the above circumstances, there may be studies for which the HSC approves the use of a surrogate decision-maker for subjects who are critically ill. In those cases, the surrogate consent may be obtained by sending the family member a copy of the surrogate consent document and proceeding with a telephone conversation and signature process as described above. Research procedures may not be initiated until the investigator has received the faxed consent form.

Waiving the Consent Requirement

Unlike the examples above where subjects are given consent information but do not sign a consent document, there may be circumstances where the requirement for informed consent is waived altogether. Studies that have very low risk, such as retrospective chart reviews, do not need a consent form. At other times, the HSC is allowed to waive the requirement for informed consent if the study meets the following criteria:

- the research involves no more than minimal risk to the subjects;
- the waiver will not adversely affect the rights and welfare of the subjects;
- the research would be impracticable without the waiver; and
- when appropriate, the subjects will be informed of the study when it is over

Only the HSC can waive the consent process; investigators are not authorized to make this decision.

Contact the HSC Office

Investigators are encouraged to contact the HSC Office with questions on informed consent:

phone: (913) 588-1240

email: humansubjects@kumc.edu