

The Informed Consent Process

The informed consent process is central to the ethical conduct of research. It is an on-going conversation between the human research subject and the researchers which begins before consent is given and continues until the end of the subject's involvement in the research. There are various tools for the investigator to use to optimize this conversation, but the most important feature of informed consent is the investigator commitment to the process.

Goals of the informed consent process

- Give the subject **information** about the research
- Make sure the subject has **time** to consider all options
- Answer all of the subject's **questions** before the decision is made
- Make sure that all information is **understood** by the subject
- Obtain the subject's voluntary informed **consent** to participate
- **Continue to inform** the subject throughout the research study
- **Continue to re-affirm subject consent** to participate throughout the research study

Tools an investigator might use to assist the informed consent process

- Consent Form -- also called Informed Consent Form (ICF), Informed Consent Document (ICD) or Patient Consent Form (PCF)*
- Pamphlets or other reading materials*
- Internet information*
- Instruction sheets*
- Audio-visual presentations*
- Charts or diagrams*
- Discussions
- Consultation with others

**These items require IRB review before use.*

Investigator responsibilities in regard to informed consent

- Provide a **quiet, comfortable, and private setting** for the informed consent process whenever possible.
- **Explain** the consent process to the subject.
- Make sure the subject has **time to consider** all options; allow subject to take the form home before signing (whenever possible).
- Consider the **subject's reading abilities**. Check to make sure the IRB has not disallowed subjects unable to read. If enrollment of limited or non-readers is allowed, involve an impartial witness in the informed consent process.
- **Answer all questions.**
- To the extent possible, make sure the subject **understands enough information** about the research study to give informed consent.
- To the extent possible, make sure the subject can consent **free from coercion or other undue influence**.
- Since the informed consent process continues throughout the subject's participation in the study, **consent should be informally verified on a continuing basis**.
- **Significant new information** must be given to the subject, and continuing consent documented in some way; for example, new risk information is often presented to the subject in an addendum to be signed by subjects who agree to continue to participate.

Issues to consider during the consent process

- Was the subject alert and, in your opinion, able to read and understand the language in the consent form?
- If the subject was unable to read the consent form, and limited or non-readers were allowed to participate, did you have an impartial witness present for the entire process? (An impartial witness is someone with adequate reading ability who is independent of the trial, who cannot be unfairly influenced by people involved in the trial, who attends the informed consent process if the subject or the subject's legally acceptable representative cannot read, who reads the informed consent form and any other written information supplied to the subject, and who is willing to attest to this by signing the consent form.)
- If the subject is not fluent in English, was an approved translation of the consent form provided in the primary language of the subject? Was there also a bilingual translator present to assist with the informed consent process? Note: a translator alone is not considered adequate.
- Was the subject under any pressure (for example, family pressure, lack of medical insurance) to participate in the research? Was this discussed?
- Did the subject take time to carefully read the consent form, or read it along with you?
- Were the risks as set forth in the consent form carefully explained to the subject?
- Are there any other risks or concerns not stated in the consent form and were these explained to the subject?
- Was the subject asked if he or she had any questions about the study?
 - Did the subject have any questions or concerns? If so, what questions or concerns did the subject ask about?
 - Were the subject's questions answered?
 - Was the subject satisfied with the answer(s) they were provided?
- Did the person conducting the consent discussion check for subject understanding by asking some basic questions about the research? Did the responses reflect adequate understanding?
- Did the subject express a clear decision to proceed with the study?
- Was the consent form signed by the person who conducted the informed consent discussion?
- Was the consent form signed by a witness (if required)?
- Was the consent form signed by the Principal Investigator (if required)?
- If a Legally Authorized Representative is allowed to sign for the subject, were additional concerns about the subject's understanding and assent considered and addressed?

Assent

When a subject may not be able to legally consent to research participation, a Legally Authorized Representative provides the consent for the subject. However, the IRB may also require that subjects who are not able to consent for themselves assent to participation if possible.

Assent is usually required for research involving *underage subjects* and research involving *adults with diminished capacity*. Assessing an adult's capacity to consent may be difficult, depending on the subject's medical/mental condition and the requirements of the protocol. If the investigator anticipates that some subjects may be able to consent while others may not, the investigator should establish a process to assess capacity.

Whenever there is doubt about capacity, the subject is best protected by involving a Legally Authorized Representative who knows the subject and is willing and able to participate in the informed consent process with the potential subject.

Assent is not a legally binding action, but within research ethics it is used to signify the agreement of the potential subject to participate in the research. WIRB will usually indicate which subjects' assent must be obtained and the method by which assent is to be obtained. The usual direction is as follows:

- 6 years old and under, no assent required.
- 7 through 12 years old, assent is required using the separate Assent Form.

- 13 through 17 years old, assent is required using the assent section of the Consent Form.
- Adults, assent is required using the assent section of the Consent Form.

In order to assent, a subject must have at least a basic understanding of what might be asked of them in the research and what might happen. An Assent Form should present this in simple wording and format.

The additional challenges an investigator faces in the assent process depend on the level of understanding the subject may be able to achieve. This will vary with each individual potential subject. An investigator may be able to obtain information about the subject's ability to understand from the person providing consent.

Recognition of the potential for unintended "coercion or undue influence" or "intimidation" is essential for the assent process. The person obtaining assent must take extra care to minimize these aspects of the communication between subject and researcher. At times this may mean having a different individual conduct the assent process in order to optimize the communication.

The Consent Form

The primary informed consent tool that involves both the researcher and the IRB is the consent form. This document is used in all research for which there is no approved waiver of consent. Thus, most research will involve use of an IRB-approved consent form.

An approved consent form must comply with several regulatory requirements:

- The required elements (as defined by the regulations) must be appropriately included.
- The content of the consent form must be understandable to a non-scientist.
- No waiver of rights or other exculpatory wording may be present or appear to be present in the consent form.

Satisfying the above requirements presents a joint challenge to the IRB and the investigator. In order to obtain IRB approval of a consent form, the investigator may opt to do one, or a combination, of the following:

- Submit a *sponsor template* consent form for review (for multicenter studies, the sponsor template has often already been submitted to WIRB and reviewed)
- Submit an *investigator-written* consent form for review
- Request WIRB write the consent form

General guidelines for writing a consent form

Consent templates and/or outlines are usually available from the IRB, as well as from some NIH groups such as NCI, and other sources. Consent templates provide a framework and structure upon which to build a consent form.

- Consent forms should be written in simple, non-technical language for readers of a seventh-grade reading level who may not have taken science courses in school.
- Avoid statements that suggest any waiver of subject rights or release from liability of the investigator or sponsor.
- Avoid use of "I understand" or "you understand" language as this may imply a level of understanding that is not present, and may discourage questions, and write all of the consent form except the consent section in the second person ("you are asked to") rather than first person or third person.
- The consent section should be written in first person ("I consent to...").
- Avoid wording that is, or may seem to be, coercive or overly reassuring to a potential subject.
- Do not make claims of safety or efficacy for investigational articles or procedures.

Introductory Information and Purpose

- Explain the purpose of the research study and the expected duration of subject participation, and include the approximate number of subjects involved in the study.
- Reassure readers that it is appropriate to ask questions, and that they may take the form home for consideration (if appropriate for the given research).
- State clearly that the study is research.
- State the status of the test article based on the country where the research is being conducted; for example, in the U.S., drugs are *approved*, vaccines are *licensed*, and devices are *cleared* or *approved for marketing*, otherwise they should be designated as "investigational."
- State the purpose(s) of the research; for example, drug protocols usually test for safety and may also test for tolerability and effectiveness.
- State why the person is being asked to participate in the study; for example, "You are being asked to participate in this study because you have been diagnosed with..."

Description of Study/Procedures

- Describe the visits and procedures (to agree with the protocol), indicating which procedures are experimental.
- Briefly describe the study's design; for example, "This is a dose escalation study. As subjects participating in the study tolerate a specific dose level, the new subjects entering the study will be given a higher dose of the study drug."
- Explain the method used for determining if subjects will receive study drug or placebo, the method for assigning them to a group, and explain the chance of assignment to each group in the study.
- State the number of visits.
- Explain the length of study participation.
- Explain what happens at the visits.
- Outline any additional participation requirements such as contraception requirements or prohibited activities.

Risks and Discomforts

- Describe any reasonably foreseeable risks and discomforts to the subject. Risks and discomforts must be stated in non-technical, lay person's language.
- Provide the risks related to all drugs dispensed in the study, including rescue medications, over-the-counter analgesics, and approved control group drugs.
- Include the possibility of allergic reactions and that serious allergic reactions can be life-threatening.
- Describe the risks and discomforts of invasive or unusual procedures.
- Describe the risks and discomforts of blood draws, if subjects will have blood drawn.
- Include a statement explaining that there may be risks of participation and side effects which are still unknown.
- Whether known or unknown, explain the risks to women who are pregnant or who become pregnant during the study.
- Include a statement that unknown risks and discomforts are possible; if appropriate, include unknown risks to an embryo or fetus if a subject (or a subject's partner) is or becomes pregnant.
- Where applicable, include the risk that the subject's condition may worsen while they are in the study (whether assigned to active drug or placebo).
- If the study drug will be taken home and there is no child-proof packaging or warning labeling, include a warning to keep it out of reach of children, or others who may not be able to read or understand the label.

Expected Benefits

- Describe any possible benefits to the subject or others; indicate that benefits are not guaranteed.
- If statements regarding direct benefits of participation are included, they should be qualified as "possible" or that they "may" occur.
- Statements implying that participation leads to benefits for society or future patients may be included, but should be used cautiously.
- Receipt of procedures and study items may be listed as benefits to the subject, but not in conjunction with their being "free" or at reduced cost, as these statements imply a form of payment and thus should not be categorized as benefits. The FDA Information Sheet "Guidance for Institutional Review Boards and Clinical Investigators" (1998) states, "Payment to research subjects for participation in studies is not considered a benefit, it is a recruitment incentive." Forms of payment may be referenced elsewhere, but not listed as a benefit of participation.

Alternatives

- Describe appropriate alternative treatments or procedures, if available.
- List several alternatives to participation if they exist; alternatives may include alternative drugs or therapy, palliative care, hospice care, etc.
- The consent form may say, "your study doctor will discuss these with you."
- May include a brief summary of the risks and benefits of the alternatives.

Costs

- Describe any known or anticipated costs to the subject.
- State who is responsible for the costs of the study-related items such as medications, procedures, device, visits or hospitalization.
- Indicate which procedures and items will be provided at no charge
- If insurance will be billed for anything, include information about possible costs to the subject or their insurance. If anything is being billed to insurance, discuss what happens if the insurance does not pay.

Payment for Participation

- Describe proposed payment for participation, if any, including proration.
- Any money or other incentive of monetary value must be listed separately from the benefit section.
- If subjects are to be paid, state specifically for which visits subjects will receive payment and when such payment will be made; for example, "payment will be made at the end of each study visit," "payment will be made at the end of the last study visit" or "payment will be made within one month after the last study visit." Be as specific as possible to minimize confusion. Look at the total amount and the proration plan for aspects that may be coercive or unduly persuasive (WIRB does not allow more than half the total payment to be assigned to the last visit). The Board may require revision of the payment or payment schedule.

HIPAA Authorization or Confidentiality:

Describe the limits on confidentiality of research and/or personal medical information in this section.

Prior to HIPAA, the section on confidentiality was often titled "Confidentiality," but is now usually titled "Authorization To Use And Disclose Information For Research Purposes" and includes more information for the subject as outlined by the HIPAA regulations. Some sites (e.g., those outside the U.S.) are not bound by

the Privacy Rule and may opt to include only the confidentiality information required by the sponsor, 21 CFR 50 and 56 and/or 45 CFR 46. Some covered entities also opt to use a stand-alone authorization and exclude authorization language from their consent forms.

The authorization section presents the information required by the federal regulations regarding patient privacy rights. WIRB has developed standard template wording for the authorization section that identifies the parties who can use and disclose the PHI as well as the parties to whom the PHI may be disclosed. It also includes the following required information:

- A meaningful description of the PHI, which can be edited for each study.
- A description of each purpose for the use and disclosure.
- Information about the subject's rights related to the authorization.
- Information about the expiration of the authorization.
- Instructions on how to revoke the authorization.
- A statement about what may happen if the authorization is not signed.
- A warning that once information has been released, it may no longer be covered by the Privacy Rule and may be released again without further authorization.

Compensation for Injury

- Outline the plans for compensation and/or medical treatment for research-related injury or illness, including who will be responsible for the costs.
- Explain what will happen if the subject gets injured. Explain how they will get treatment.
- Clearly state who will pay for treatment if the subject is harmed.
- Address what will happen if the subject's insurance is billed for the treatment, but refuses to pay.

Questions

All three of the following specific contacts must be addressed in the consent form.

- Whom subject should contact with research-related questions.
- Whom to call if the subject has a research-related injury or illness (preferably, a physician should be listed as the contact for injury or illness) or study problems.
- Whom to call if subjects have questions about their rights as research subjects (a local or institution IRB contact).

Voluntary Participation/Withdrawal

- State that the subject's participation is voluntary and that a subject may withdraw at any time for any reason.
- State that the subject's decision not to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled.
- State that the subject's participation may be ended by the study doctor or sponsor at any time for any reason without the subject's consent. General reasons for this may be included. *Please note:* the FDA may stop the research, but will not stop the participation of an individual subject.
- Indicate that subjects who withdraw after the start of the study may be asked to return for a final visit and final study procedures, and must return the study drug.

Other

- Explain that significant new information that may be related to the subject's willingness to remain in the research will be provided to the subject.
- Identify the source of funding for the research.

- Disclose conflicts of interest (financial and otherwise).
- State that the subject will receive a copy of the signed and dated consent form.

Consent

This section changes to first person for emphasis; for example, "I voluntarily agree..." or "I have..."

- Include a statement of the subject's consent to participate, as well as an authorization to release medical (or research, as appropriate) records to the parties in the HIPAA authorization (or confidentiality) section, and a statement that the consent form does not waive subject rights.
- State that the subject has read the information in the consent form or had it read to her/him (as appropriate); however, don't include statements which imply a level of comprehension, such as "I understand..."
- State that the subject's questions have been answered.
- State that the subject has not waived any rights by agreeing to participate.

Signatures and Dates

- Include appropriate signature and date lines for assent/consent as applicable
- If appropriate, include a signature block for an impartial witness (if limited or non-readers are not excluded from participation).
- Use the term "subject" ("participant" for some behavioral research), rather than "patient"
- Provide a space for the "Legally Authorized Representative" (LAR) to consent (if allowed) and a place to indicate relationship to the subject.
- Include a space for the person conducting the informed consent discussion to sign (required by ICH).
- Provide a line for the investigator to sign if desired by researcher or sponsor; however, this is not an IRB requirement.
- Where applicable, provide a space to obtain the consent of a caregiver. Please note that this does not replace the signature of an LAR when required.

Improving the Readability of a Consent Form or Assent Form

- Decrease sentence length.
- Limit each sentence to one thought or topic. Avoid run-on sentences.
- Use simpler words (select words with fewer syllables).
- Use common words. Remove technical jargon and medical terms.
- In discussing risks, use the symptoms the subject might experience rather than just the medical terms for the problem.
- Use short, simple paragraphs.
- Use correct basic grammar and form.

When evaluating a proposed word or phrase, consider whether a reader with no college education, no science background, and little or no exposure to the medical professions would easily understand it. Most words or concepts can be explained in simple language; however, the reader can be directed to ask the study doctor for an explanation of a complex item.

When drafting a consent form, frequently ask "Does the reader need this information in order to make an informed decision?" Avoid including excess technical information that would only confuse or intimidate a reader.

Special Considerations for Subjects Who Do Not Speak English

All consent forms and other subject materials must be in a language easily understood by the subject, and all translations must be approved by the IRB.

If a non-English speaking subject may receive benefit from study participation, and that benefit is not available outside of the study, the IRB may allow an ad hoc translation of the consent form if time or financial restraints exist. Please request IRB review of these situations.

Sponsor/CRO/Site Translations:

The IRB-approved version of the consent form may be translated and submitted along with a Certification statement signed by the translator (see sample format below). The IRB will request that the form be translated by a certified translator. The translation must correspond to the IRB approved version; therefore, a translation of the sponsor template is not acceptable.

The translated consent form must be submitted electronically (disk or e-mail) for final verification by the IRB. If the Certification statement is not available electronically, then it should be sent by mail along with a copy of the English document from which the form was translated. If the translation is acceptable, the approval date will be affixed by the IRB staff and an approved copy sent to the site. Other documents (e.g., subject diaries, subject instructions) need not be submitted electronically, but copies submitted must be legible (faxed copies often are not legible).

Sample Certification Statement:

CERTIFICATION

I hereby certify that I am fluent in English and (name of language) and that I have, to the best of my knowledge and belief, made a true and complete translation from English to [name of language] of the IRB approved [name of document; e.g., Research Subject Information and Consent Form, Advertisement] for [sponsor / protocol number], [IRB protocol number] this _____ day of _____, 2007.

(Signature of Translator)

Name of Certification (ATA, DSHS) _____
Certified by the State of _____
Certificate No. _____