

Informed consent process and procedures

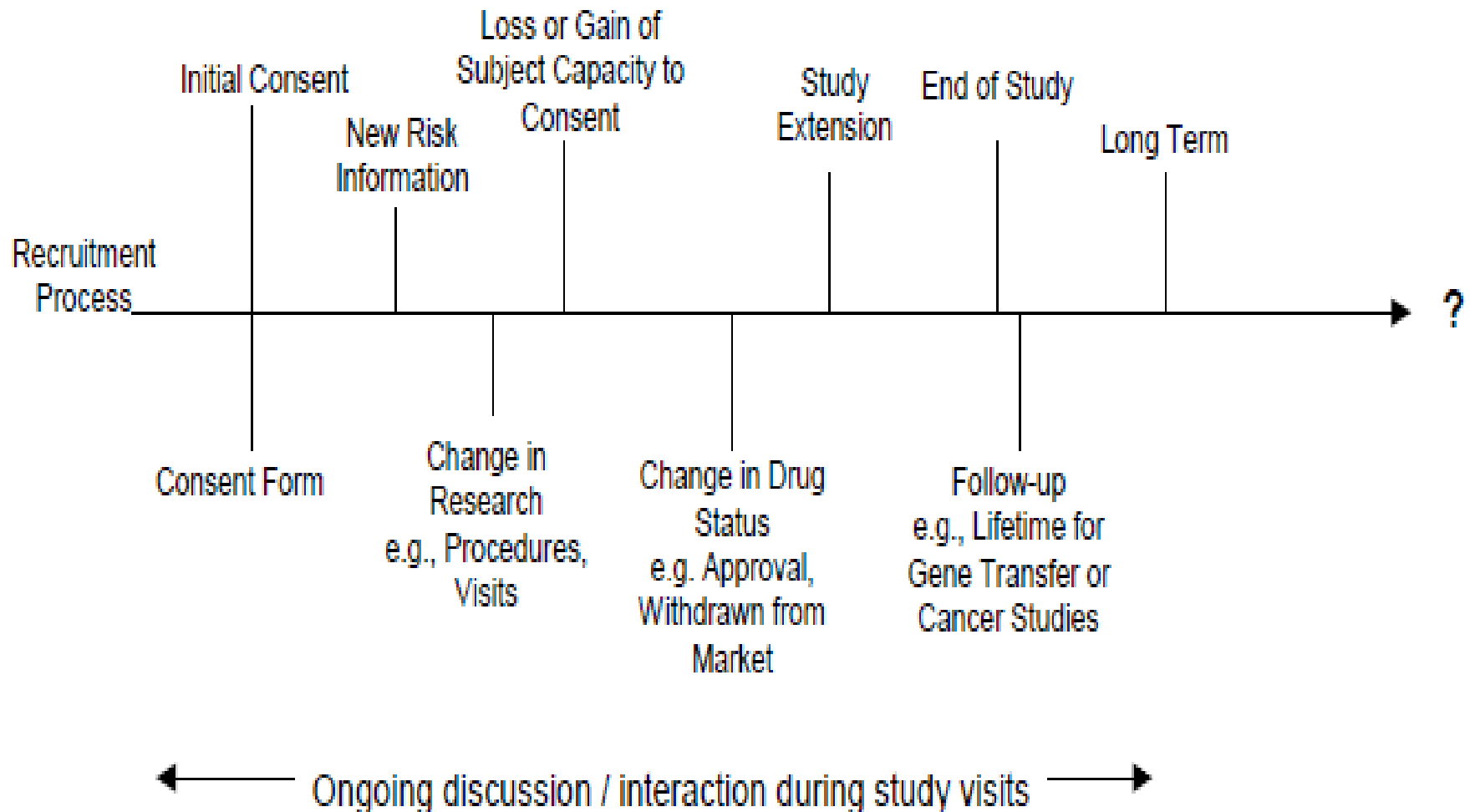
Informed Consent Process

- The informed consent process is central to the ethical conduct of research.
- It is an ongoing conversation between the human research subject and the researchers that 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**

Consent process diagram



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

Investigator responsibilities in regard to informed consent

- Obtain consent before initiating study-specific procedures.
- 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 WIRB 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 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?
- 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?

- 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?
 - ✓ 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?

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 WIRB 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 multi-center 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 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.
 - Use the term “subject” rather than “patient” (the term “participant” may be used in some behavioral research).
 - 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,
 - 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.
 - Try to avoid the use of the terms “treatment,” “therapy” or “therapeutic” (because these words may imply effectiveness).

Consent by Legally Authorized Representatives

- The laws regulating who can consent for *adults who lack the capacity to consent for themselves* are defined at the state level and vary from state to state.
- Persons who can consent for adults who lack the capacity to personally provide informed consent are known as Legally Authorized Representatives (LARs).
- Such trials, unless an exception is justified, should be conducted in individuals having a disease or condition for which the investigational product is intended.

Consent by Subjects Who Cannot Physically Sign the Consent Form (due to physical impairment)

- WIRB does not require a Legally Authorized Representative to provide consent for subjects who are *cognitively capable of consenting, but physically unable (for example, due to paralysis)*.
- In those cases, obtaining consent from the subject with the assistance of a witness is usually sufficient.
- WIRB can provide additional guidance for these situations upon request.
- 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 while the consent form is being read to the subject, 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.

Waivers of Consent for *non-FDA studies*

- If you are requesting a waiver of consent and the research is not an FDA regulated study, then criteria from 45 CFR 46.116(d) must be met:
 1. The research involves no more than minimal risk to the subjects.
 2. The waiver or alteration will not adversely affect the rights and welfare of the subjects.
 3. The research could not practicably be carried out without the waiver or alteration.
 4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.
- WIRB applies this standard to all requests for waiver of consent for non-FDA regulated research.

Waivers of Consent for *FDA studies*

- For FDA regulated studies, waiver of consent must meet requirements of either waiver of consent for individual emergency use or emergency research without consent.
- For individual emergency waivers of consent, prospective IRB approval is not always necessary if a patient's life can be saved.

Waiver of Documentation of Consent

- A waiver of documentation of consent is a waiver of the requirement for a signature on a consent form. The regulations allow the Board to approve this type of waiver if:
 - The research is of minimal risk and involves no procedures for which written consent is usually required; or
 - The only record linking the subject and the research would be the consent document and the principal risk of the research is the risk of breach of confidentiality.

Assent

- "Assent" means a subject's affirmative agreement to participate in research. An investigator should not interpret a subject's failure to object as "assent" unless the subject has also affirmatively agreed to be in the research.
- When a subject may not be able to legally consent to research participation, a Legally Authorized Representative provides the consent for the subject.
- However, WIRB usually also requires 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*.

ASSENT SECTION:

Statement of person conducting assent discussion:

1. I have explained all aspects of the research to the subject to the best of his or her ability to understand.
2. I have answered all the questions of the subject relating to this research.
3. The subject agrees to be in the research.
4. I believe the subject's decision to enroll is voluntary.
5. The study doctor and study staff agree to respect the subject's physical or emotional dissent at any time during this research when that dissent pertains to anything being done solely for the purpose of this research.

Signature of Person Conducting
Assent Discussion

Date

Statement of Parent or Guardian:

My child appears to understand the research to the best of his or her ability and has agreed to participate.

Signature of Parent or Guardian

Date

Consent form elements

- **Introductory Information and Purpose**
- **Description of Study/Procedures**
- **Risks and Discomforts**
- **Expected Benefits**
- **Alternatives**
- **Costs**
- **Payment for Participation**

Introductory Information and Purpose

- Explain 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, 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 (in agreement 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. It is not necessary to list the procedures visit by visit, as detailed descriptions can result in an unnecessarily long consent form.
- 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, layperson's language.
- Provide the risks related to all drugs required by the protocol, 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, including protocol- required biopsies.
- 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 childproof 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.
- 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.”
- The section on alternatives should 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, hospitalization and treatment for possible side effects.
- 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 the planned prorated payment for participation, if any.
- Any money or other incentive of monetary value should be listed in this section rather than 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. Consider whether any aspects of the total amount or the proration plan may be coercive or unduly persuasive (WIRB does not routinely 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.