



Informed Consent Process

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National Institutes
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Agenda

- Guiding principles of the informed consent process
- Required and additional elements of the informed consent document
- Appropriate procedures for consenting an adult, child, and a non-English speaking individual
- Capacity and competency

What is Informed Consent (IC)

- Having the capacity to agree for one's self to participate in a given situation (e.g., research) and, once the risks and benefits of participation are understood, agreeing to potential consequences
- Ongoing process of communication and mutual understanding between an individual and investigator which is then demonstrated by the individual's voluntary agreement to enter a clinical trial
- Participant's initial agreement is evidenced by signing an IC document.

IC is **NOT** just a piece of paper, or a moment in time, or a contract.

Guiding Principles of IC

Nuremberg Code	Belmont Report
<ul style="list-style-type: none">• Voluntary consent• Subject is free to stop at any time	<ul style="list-style-type: none">• People are autonomous agents and should be treated with respect• Informed consent must be freely and voluntarily given• Those of diminished capacity require additional protections

Key Elements of Ongoing Informed Consent Process

- Disclosure of relevant information
- Subject's comprehension of the information
- Voluntary agreement free from coercion



Informed Consent Process

Step 1

- Investigator verbally explains the study to the individual providing all required information. The individual is then given enough opportunity to ask questions.

Step 2

- A copy of consent is given to the individual for further review before they make a decision to participate. The individual is given sufficient time to discuss with family, friends, and other physicians. Sufficient time means hours to days depending on the type of study.

Step 3

- After allowing the individual time to read the consent form, an investigator should meet with the individual and answer any additional questions.

Step 4

- After all questions are answered and the individual agrees to participate, the individual signs and dates the IC document. Other signature(s) may be required based on organization's policy.

Step 5

- A copy of the signed IC document is given to the individual and the original goes in the individual's medical record or research chart.

Step 6

- Individual who obtains the consent will document the process in medical record.

Waiver of Informed Consent for Minimal Risk Research Studies

- IRB can approve consent procedure which does not include, or which alters, some or all of the elements of IC
- IRB may waive the requirement to obtain IC from some or all of the research subjects
- All of the following criteria are met:
 - Research involves no more than minimal risk to the subjects;
 - Waiver or alteration will not adversely affect the rights and welfare of the subjects;
 - Research could not reasonably be carried out without the waiver or alteration; and
 - Whenever appropriate, subjects will be provided with additional pertinent information after participation.

Beginning the IC

- Begins with the development of recruitment materials and a recruitment plan
- Both the Federal Regulations and GCP require that subject recruitment procedures be reviewed and approved by the IRB before use
 - Advertisements
 - Other written information given to participants

IRB and Review of Recruitment Materials

- IRB reviews recruitment materials ensuring that there is:
 - No misleading text,
 - No claims of safety, efficacy, equivalence, or superiority,
 - No overemphasis of payment,
 - No overstatement of benefits.

Informed Consent Document

Written tool used by the Investigator to guide the discussion with a patient about a clinical trial

- Explains subject's rights of participation
- Written in language understandable to the subject (appropriate reading level)
- Contains no exculpatory language
 - OHRP and FDA consider *exculpatory language* to be language which has the general effect of freeing or appearing to free an individual or an entity from malpractice, negligence, blame, fault, or guilt.

8 Basic Elements of the IC Document...

(per 21 CFR 50 & 45 CRF 46)

- A statement disclosing that the study involves research including:
 - explanation of the purpose of the research
 - invitation to participate
 - expected duration of participation
 - description of procedures to be followed
 - identification of any procedures that are experimental (e.g., MRI that would not be done as part of standard of care, but for research only)
- Description of any foreseeable risks/discomforts
- Description of any benefits to individual or others
- Disclosure of any appropriate alternatives to study participation (e.g., standard comfort measures)

...8 Basic Elements of the IC Document

- How will the individual's confidentiality be maintained
- For research that involves more than minimal risk, an explanation regarding compensation if injury occurs, what that compensation is and how to obtain further information
- Contact persons for questions related to research and research subject's rights
- A statement regarding the voluntary nature of participation including that refusal to participate won't involve any penalty or loss of benefit to the subject

6 Additional Elements

(per 21 CFR 50 and 45 CFR 46)

- Intervention or procedure may cause unforeseeable risks (e.g., risk to fetus if subject should become pregnant)
- Circumstance for termination of participation by the investigator (e.g., non-compliance with protocol's safety assessments, sponsor terminates an Investigational New Drug application)
- Additional costs to the subject from participation
- Consequences of the subject's decision to discontinue research participation
- Statement that the subject will be notified of significant new findings that may impact their decision to continue participation
- Approximate number of subjects

Tips to Improve Readability and Comprehension

(See handout)

IRB IC Template

- Each IRB will have an informed consent document template that you will need to use.
- When working on industry sponsored trials, multi-site trials or cooperative group trials, a sample IC document will be provided. This will need to be formatted using the IRB's template.

Office of Human Subjects Research Protection Applicable SOPs

- [HRPP SOP 12 Requirements for Informed Consent](#)
- [HRPP SOP 14A - Research Involving Vulnerable Subjects \(General Considerations\)](#)
- [HRPP SOP 14B- Research Involving Pregnant Women, Human Fetuses and Neonates v2 10-1-13](#)
- [HRPP SOP 14C- Research Involving Prisoners v2 10-1-13](#)
- [HRPP SOP 14D- Research Involving Children v2 10-1-13](#)
- [HRPP SOP 14E - Research Involving Adults Who Are or May Be Unable to Consent](#)
- [HRPP SOP 14F - Research Involving NIH Staff as Subjects](#)

Responsibilities of the Principal Investigator...

- It is the responsibility of the Principal Investigator (PI) to ensure that informed consent is obtained consistent with the requirements of SOP #12
- As appropriate, SOP #15 “Research Regulated by the Food and Drug Administration (FDA): General Procedures for Both IND and IDE Applications”.

...Responsibilities of the Principal Investigator

- PI may designate other qualified persons to obtain consent from prospective subjects
- Those designated must be identified in the protocol application (or subsequent protocol amendment) and noted on the delegation of authority log.

PI Delegation

- The PI is responsible for assuring that the individuals:
 - have thorough knowledge of the protocol, enabling them to answer questions from potential subjects
 - receive appropriate training in obtaining proper informed consent related to the protocol
 - have appropriate training in human subjects research protections (see SOP #25 *Training Requirements for the NIH HRPP*)
 - Have appropriate conflict of interest clearance, for NIH Employees this is from their Institute's ethics office (see SOP #21 *Conflict of Interest Requirements for Researchers and Research Staff*)

Who Gives Consent/Assent for Research Participation?

- Informed consent is valid only with adults age ≥ 18
- Assent is obtained from children and adults who are unable to make their own decisions regarding research participation when possible
- Surrogate “One appointed to act in place of another”
 - Legally Authorized Representative (LAR)
 - Guardian (court-appointed)
 - Durable Power of Attorney (DPA)
 - few states allow specific use of DPA for research

Capacity vs. Competence: What is the difference?

Capacity:

a one time clinical judgment of a client's ability to give informed consent

Competence:

the ability to understand legal rights and responsibilities and the possession of authority to make legal decisions

Participant Vulnerability and Factors Which May Compromise Capacity:

Panic

Delirium

Psychosis

Medical illness

Substance abuse

Cognitive difficulty

Dependency upon those who provide treatment

A cognitive impairment or a psychiatric condition doesn't *automatically* remove capacity.

Determining Capacity to Give Informed Consent:

- A subject must have capacity in order to provide informed consent
- The higher the risk in research, the higher the level of capacity required
- There is no single test of capacity
- There is an array of practices of documentation tools used, domains assessed and level or training

Facets of Capacity

- Capacity assessments are based on a modified MacCAT-CR. The four domains assessed are:
 1. understanding of disclosed information about the nature of the research project and its procedures
 2. appreciation of the effects of research participation (or failure to participate) on subjects' own situation;
 3. reasoning about participation; and
 4. ability to communicate a choice

Appelbaum, PS & Grisso, T (2001). MacCAT-CR MacArthur Competence Assessment Tool for Clinical Research.

Help with capacity assessments?

- NIH Ability to Consent Assessment Team (ACAT)
 - Determine individual's ability to consent
 - Can be reached at 301-496-9675 or 301-496-2429
 - Members of NIMH Human Subjects Protection Unit (HSPU) and Bioethics Department
- Resources
 - NIH [Medical Administrative Series Policy 87-4](#) (Research Involving Adults Who Are or May be Unable to Consent)
 - [MAS 77-2](#) (Informed Consent)

When & How Will Consent be Obtained?

When

- Initial protocol consent is to be obtained prior to any protocol specific activities
- As new information relevant to the subject's continued participation becomes available, should be provided to that person / Legally Authorized Representative (LAR)

How

- Consent is typically done as a discussion using the IRB approved IC document as the guide
- Setting should be quiet and private
- Discussion needs to include a summary of:
 - Purpose of the research
 - Procedures involved
 - Potential risks and benefit
 - Alternatives to participation
 - Other information necessary for individual to make informed decision

Signatures on the Document...

- Per the regulations (21 CFR 50.27, 45 CFR 46.117) , signature of participant/LAR is required
 - By signing the informed consent document, the participant/LAR is indicating his/her willingness to participate **after** receiving information regarding the study
- Per GCP guidelines (ICH GCP E6, 4.8), signature of witness is required
 - The witness attests that information explained accurately and understood by the subject/LAR AND that consent freely given.

...Signatures on the Document

- NIH [MAS 77-2](#) requires 2 additional signatures over that of the participant:
 - PI or designee obtaining the consent
 - Witness who attests only to the validity of the signature not to the validity or quality of consent.
 - Any adult other than the person obtaining or providing consent may be a witness to the signature.

Documentation of Informed Consent Process

- Specific statement should be written in the medical record addressing the informed consent process.
- Should be done by all who discussed the study with the subject
- Typically note will include a statement that:
 - A discussion occurred
 - All questions were reviewed and answered to individual's satisfaction
 - A copy of the signed IC document was given to the subject
- CRIS has an IC process template progress note

Children, Research and Assent

- Federal regulations state that parents and guardians must participate in an informed consent process just as they would do if they themselves were considering enrolling in a clinical trial.
- LAR must give legal permission
- Process must follow the guidelines established for the general requirements of informed consent

Assent...

- Assent is the child's affirmative agreement to participate in research
- Failure to object to participation should not be construed as assent
- IRB's may waive the requirement for assent (capacity-based waiver)
 - 45 CFR 46.408, 21 CFR 50.55
 - Insufficient capacity to participate in the decision
 - Direct benefit to the child

...Assent...

- Age appropriateness needs to be considered including:
 - Maturity level
 - Psychological state
 - Disease
 - Level of comprehension and reasoning can be altered by:
 - Anxiety
 - Physical disturbances
 - Emotional disturbances
- Child's verbal assent needs to be indicated on the IC document

Assent Template

- IRB determines if a separate assent document is required rather than a verbal assent
- Decision based on the expected level of comprehension
 - Assent document is typically used if the child is over 14 years of age but consult with the IRB
- Check with your IRB for assent template

Assent Signing

- IRB determines if a separate assent document is required rather than a verbal assent
- Child's verbal assent needs to be indicated on the IC document
 - Parent's signature is also required next to a statement the child did assent to participate.
 - This means the parent would sign twice

COMPLETE APPROPRIATE ITEM(S) BELOW:			
A. Adult Patient's Consent I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby consent to take part in this study.		B. Parent's Permission for Minor Patient. I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby give permission for my child to take part in this study. (Attach NIH 2514-2, Minor's Assent, if applicable.)	
Signature of Adult Patient/Legal Representative	Date	Signature of Parent(s)/Guardian	Date
C. Child's Verbal Assent (If Applicable) The information in the above consent was described to my child and my child agrees to participate in the study.			
Signature of Parent(s)/Guardian		Date	
THIS CONSENT DOCUMENT HAS BEEN APPROVED FOR USE FROM MAY XX, 1998 THROUGH MAY XX, 1999.			
Signature of Investigator	Date	Signature of Witness	Date

- For written assent, child signs assent

Consenting Non-English Speaking Subjects

Expected Enrollment

- Full protocol consent translated in participant's/LAR's native language
- Interpreter used to facilitate discussion

Consenting Non-English Speaking Subjects

Unexpected Enrollment

- Federal regulations allow use of short form in participant's native language after approval by IRB
 - Short form states that 8 required elements of IC document have been presented orally
- Need prior IRB approval
- Written summary used by investigator and interpreter

Translation

- Should be done by a certified translator fluent in subject's native language and in English
- [NIH Library Translation Services](#) offer fee-based translation services

Interpreter...

- Unless the person obtaining consent is fluent in the patient's language
- Preferable to have someone independent of the subject (e.g., not a close family member, significant other, partner, etc.)
- Contact the Social Work Department to secure an interpreter

...Interpreter

- If possible, provide the interpreter with the consent documents ahead of time for their review (24-48 hours)
- Language Line can only be used if your IRB-approved protocol has included a phone consent process
 - how the IC document will be sent to the interpreter (e.g., fax or mail),
 - how the process will be documented and by whom, and
 - how the interpreter will return the signed IC document so that it becomes part of the record

Expected Enrollment...

- PI expects non-English speaking patients to be screened or enrolled
 - Screening protocol
 - Tissue acquisition protocol
 - Protocol studying disease or condition that is likely to attract someone who does not speak English
- Must have translation and IRB approval of the long form consent document is required
 - **DO NOT USE THE SHORT FORM PROCESS**

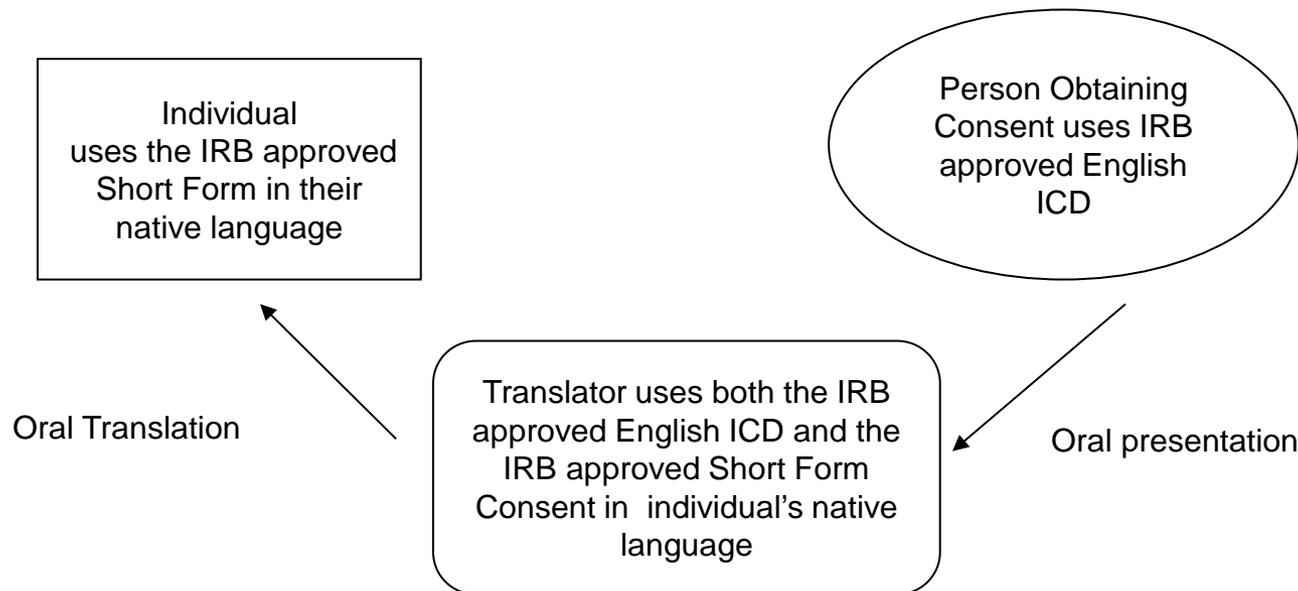
...Expected Enrollment

- IRB may choose to have a back translation or review of the document by an IRB member or other person who is fluent in that language
- Signatures per SOP
 - Subject
 - Person obtaining consent (i.e. Investigator or designee)
 - Witness

Unexpected Enrollment

“Short Form” Consent Process

(21 CFR 50.27, 46 CFR 46.117)



Note: IRB may request translated full English version if a few subjects have been through the “short form” process

Signatures on the Consent Documents

“Short Form” Process

- “Short form”, (21 CFR 50.27, 46 CFR 46.117), IRB approved
 - Signed by subject
 - Signed by witness/translator
- English version, IRB approved
 - Signed by investigator
 - Signed by witness/translator

Short Form Process	Long Form Process
Need IRB approval before consenting (see M2P2 #24)	N/A - Already have IRB approval
Interpreter needed unless the person obtaining consent is fluent in the prospective patient's language (see M2P2 #24)	Same
Discussion between person obtaining consent and the patient via an interpreter if applicable (see M2P2 #25)	Same
Signatures required on <u>English long form</u> : Person obtaining consent (Investigator line) and the witness to the oral presentation is often the interpreter (see M2P2 #25)	Signatures required on <u>non-English long form</u> : Person obtaining consent (Investigator line), the patient, and the witness to the oral presentation is often the interpreter <i>Note:</i> <ul style="list-style-type: none"> • <i>The English long form is not used.</i> • <i>Since there is an English version and often a back translated English version, the person obtaining consent may sign on the non-English long form.</i>
Signatures required on the <u>short form</u> : Person obtaining consent (Investigator line) and the patient (see M2P2 #25)	N/A

Whole Genome, Exome and Other Whole Genomic-Related Analysis

- Description of the research related to whole genome, exome or other whole genomic-related analysis
- Purpose of [whole genome, exome sequencing or other whole genomics-related analysis research]
- Data Sharing
- Benefits
- Risks
- Whether to include GINA
- Disclosure of research results
- Certificates of Confidentiality
- Withdrawal from study

IC for gene transfer studies

- For additional information related to informed consent and gene transfer studies, see the NIH Office of Biotechnology Activities (OBA)'s [guidance document](#).

Consent Considerations

- Informed consent *should not* be considered a one time signing of a document, but rather an ongoing dialogue between clinician and subject and a process that is revisited and re-evaluated through out the study for two reasons:
 - Nature of treatment may change with time
 - Subject's capacity to give informed consent may fluctuate

Re-consenting Study Subject: Signing a New IC Document

- Investigator is required to inform subject of new findings (e.g., toxicities) and to ensure that they are still willing to participate on clinical trial
 - Document this process in medical record, including willingness of subject to continue
- IRB or sponsor may require that the subject sign the IRB approved updated IC document
 - *Never hurts to obtain anyway*
- For children who were *assented*, they will need to be *consented* when they become 18 years of age

Where to find IRB Approved IC/Assent Documents

All IC documents are posted by the NIH Clinical Center's Office of Protocol Support on the following website:

- NIH Clinical Research Studies Active Consent/Assent Documents search:
http://clinicalstudies.info.nih.gov/protocol_consents/search.html
- Short forms (translations for approximately 43 languages) : <http://www.cc.nih.gov/protocolconsents/>

TIP: Bookmark both sites!

NIH Clinical Research Studies Active Consent/Assent Documents

Information Page



[Perform A Search](#)

Information Page

The collection of consent and assent documents available, have been approved for use by a National Institutes of Health (NIH) intramural research Institutional Review Board (IRB) for use with an active protocol at the NIH Clinical Center. The documents are available as Adobe Acrobat Portable Document Format (PDF) files that may be reviewed or printed using a PDF viewer. PDF viewers are available at no cost for a variety of operating systems at [Adobe.com](http://adobe.com). On-line revisions are not permitted.

The "Perform a Search" feature provides by Sponsoring Institute, Principal Investigator, protocol number or words(s)/phrases from the protocol title. [need to verify where the word/phrase is retrieving from]

Short Form Consents - Version Differences

Short Form Consents are used for the enrollment of a non-English speaking subject. When the PI uses the English version of the informed consent document as the written summary, the version of the short form consent must match the required informed consent elements in the protocol consent document as required by 45 CFR 46 and the Food and Drug Administrative Amendments Act (FDAAA). Below is an explanation for each version as well as the 3 versions translated into the languages most common at the NIH Clinical Center

Version 1: Reflects the required elements of informed consent required by 45 CFR 46, mirroring the NIHCC protocol consent template.

Version 2: Reflects the required elements of informed consent required by 45 CFR 46, in addition to the Food and Drug Administrative Amendments Act (FDAAA) when the protocol is known to meet the definition of an "applicable clinical trial". The following sentence is generally located on the English consent at the end, but before the last page containing "Other Pertinent Information."

A description of this clinical trial will be available on <http://www.Clinicaltrials.gov>, as required by U.S. Law. This web site will not include information that can identify you. At most the Web site will include a summary of the results. You can search this Web site at any time.

Version 3: Reflects the required elements of informed consent required by 45 CFR 46, in addition to the Food and Drug Administrative Amendments Act, however the language is preceded with a sentence to indicate that the protocol "may" meet the definition of an "applicable clinical trial".

The following sentence is generally located on the English consent at the end, but before the last page containing "Other Pertinent Information" and used when it is unclear if the protocol meets the definition of an "applicable clinical trial." If this trial is an applicable clinical trial, the following statement applies: A description of this clinical trial will be available on <http://www.Clinicaltrials.gov>, as required by U.S. Law. This web site will not include information that can identify you. At most the Web site will include a summary of the results. You can search this web site at any time.

Amharic

- o [Amharic Version 1](#)
- o [Amharic Version 2](#)
- o [Amharic Version 3](#)

Arabic

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Documents are available as Adobe Acrobat Portable Document Format (PDF) files. They may be reviewed and printed using a PDF viewer. However, on-line revisions are not permissible. PDF viewers are available at no cost for

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- Technical questions about Adobe Acrobat, PDF format, or this Web Server, please contact the [Department Clinical Research Informatics \(DCRI\), CC.](#)

Questions????