INFORMED CONSENT

This unit defines informed consent and outlines the elements that should be included in an informed consent document. It reviews conditions that may affect a person's capacity to consent and the responsibilities of the researcher in seeking consent from the research participants. The legal aspects of Informed Consent vary internationally. Each Principal Investigator must make themselves aware of their country's law.

Background

Informed consent as a legal, regulatory, and ethical concept, has become widely accepted as an integral part of research. Current requirements for informed consent owe much to the legal system. Fundamentally, informed consent is based on respect for the individual, and in particular the individual's autonomy or capacity and right to define his or her own goals and make choices designed to achieve those goals for his/her own life. This right is well established in many national laws and medical practice and applies to all types of medical interventions and clinical research.

Informed consent in research means more than simply obtaining the signature of the potential research participant. It is a process that involves conveying accurate and relevant information about the study and its purpose; disclosing known risks, benefits, alternatives and procedures; answering questions; enabling the potential participant to make an informed decision about whether to participate.

Valid Consent

In order for consent to be valid it should be based on the following critical elements:

COMPETENCE: The participant must be COMPETENT to begin the informed consent process. If the participant is not competent because of age, illness, incapacity, or any other reason, special provisions usually apply.

FULLY INFORMED: The research team must DISCLOSE all relevant information to the potential participant. The information must be sufficient to allow the potential participant to decide whether to participate. It is generally accepted that the potential participant must be given the following information: the purpose of the study; nature of the procedure; reasonable alternatives to the proposed intervention; risks, benefits, and uncertainties of each possible intervention.

UNDERSTANDING: The participant must COMPREHEND the information. The research team must evaluate the potential participant's ability to understand the proposed intervention in the study.

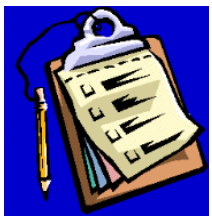
AGREE: The participant must AGREE to the proposed intervention in the research study.

VOLUNTATY: The participant's agreement must be VOLUNTARY and free from coercion.

FREEDOM TO WITHDRAW: Participants must be informed that even after they have made a voluntary agreement to participate in the study, they may WITHDRAW such agreement at any time without penalty.

Planning the Consent Process

Once the researcher has a carefully defined research question, a valid design and protocol for a research project, it is time to plan for the informed consent for those invited to participate. Planning involves deciding:



- **What** information to provide to potential participants, both in writing and in discussions
- **Who** will present the information
- **When**, or at what point in your interactions with participants to provide the information
- **How** to assess the participant's understanding
  Who will obtain the participant's signature or agreement.

This plan must be reviewed and approved by an IRB before approaching potential participants.

Preparing the Information Sheet and Consent Form (ICON)

The first step to take in the process of informed consent is preparing the written consent document for presentation to the IRB. This document should include all the elements listed above as well as any other information prospective participants might need to make an informed decision about participation. ICON documents should be written in non-technical language that can be understood by the proposed participant population, consistent with their educational level, familiarity with research, and cultural views.

The consent document must make clear that participation in research is voluntary, and should not include any language waiving or appearing to waive participants' rights. In some cases, the researcher may want to request the IRB to approve a modification or waiver of the elements of informed consent as spelled out in the regulations.

Advertisements, fliers or brochures that are prepared to recruit and inform potential participants about a study are considered part of the informed consent process and also require review and approval by the IRB.

Approaching Research Participants

Researchers and members of the research team are responsible for making sure that the process of informed consent conforms to the value of respecting individuals' right to make informed and voluntary decisions about research participation, as well as to the regulations guiding research with human participants. In this regard, after receiving approval for the consent plan from the IRB, there are several essential steps to take in the process of informed consent.

The researcher and responsible research team members should:

- Feel confident that the potential participant has the capacity to understand information, make decisions, and provide informed consent for the particular study.
- Provide both written (as described above) and verbal information about the details of the study in a way that is understandable to the participant.
- Be satisfied that the participant understands the information provided, has had an opportunity to ask questions, and an opportunity to deliberate about participation.
- Be satisfied that the participant is in a position to make a voluntary decision, not coerced or unduly influenced by circumstances or other people.
- Be satisfied that the participant affirmatively agrees to participate, as indicated in most cases by signing an informed consent document.

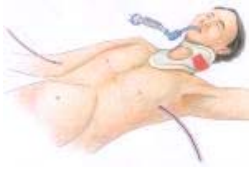
Capacity to Consent

How does the researcher determine if a participant has the capacity to consent?

Adults have the capacity to consent when they possess sufficient mental capability to understand the information provided, appreciate how it is relevant to their circumstances, and make a reasoned decision about whether or not to participate in a particular study.

Children (in most jurisdictions those under 16 years of age) do not have the legal capacity to provide their own consent. Capacity can be affected by several things, including age, cognitive impairment, illness and treatments. Capacity to consent for a study is study-specific. For example, a person may have sufficient capacity to carry out their daily activities and make their own decisions, but not sufficient capacity to appreciate how the particulars of a given protocol might be relevant to them.

For some participants or groups of participants, you or the IRB may decide that an independent capacity assessment is a good idea.



If a person is unable to provide his or her own consent, a legally authorised representative can in some cases give

permission for participation in research. A legally authorised representative is a legal guardian; a parent (for children only); and in some cases a validly designated durable power of attorney for health care (the latter is an evolving area). The researcher should check with national, institutional policies or assurance and the IRB.

Providing Study Information

What should the researcher think about when providing information to potential participants about the study?

The provision of information about a study usually involves more than just providing the written consent document for the potential participant to read. Oral presentation of information and the opportunity to discuss and answer questions and concerns are important parts of the process, usually in addition to giving the person time to read the written consent form. Educational materials about the study or clinical research in general are helpful.

If the researcher delegates the function of verbal presentation and discussion of a study to members of the team, he or she must be sure they have sufficient knowledge of the protocol to answer questions appropriately. Delegation may have to be approved by the institution's IRB.

Assessing Participant's Understanding

How does the researcher assess the participant's understanding?

The researcher should feel satisfied that after the detailed information has been presented and discussed, the potential participant understands it well enough to make a decision. Of course, some studies are more complicated and involved than others. Researchers use many different strategies for determining whether or not a research participant understands. Sometimes it is clear at the end of a discussion, other times having a participant answer questions about the study either informally or even in writing may be appropriate. The best method may depend both on the complexity and risk level of the study as well as on the potential participants. For some studies, time to deliberate or discuss the study with family, trusted friends or other health care providers can be very important.

Voluntary Decisions

How does the researcher know whether or not the participant's decision is voluntary?

Individuals who feel 'coerced' into making a decision about research participation or are in a position where it is impossible or extremely difficult for them to say "no" should not be enrolled into research. Coercion occurs if there is some threat of harm or punishment for refusal to participate. Individuals in relationships of unequal power or dependence have historically been particularly vulnerable to coercion. Examples might include telling students they would fail a course, employees they would not be promoted, or soldiers they would be reprimanded if they refused to participate in research. Coercion in research is rare due to the vigilance of research teams and IRBs.

All decisions, including a decision about research participation, are subject to the influences of one's previous experiences and circumstances. Sometimes understanding the reasons why an individual is considering participation is helpful in assessing how voluntary a decision is. The goal is to be sure that individuals understand research participation as a choice or an option among other – albeit in some cases, limited – options. Being sure that individuals understand that they can freely refuse to participate and/or withdraw at any time without penalty is critical to assuring voluntary consent.

Written Signatures

Must the researcher always obtain an individual's written signature?

In most cases, consent to research participation is documented by obtaining the signature of the participant or the legally authorized representative on the written informed consent document. A copy of this

document should be given to the person signing the form. A signature is required on the written document that contains all the required elements of information, or on a short form and written summary of the information when the information has been presented orally.

In some cases, a signed consent document is inappropriate. The IRB may waive this requirement if it determines:

- there is a confidentiality risk, and the only link between the participant and the research would be the consent document
- the research presents no more than minimal risk of harm and involves no procedures which normally require informed consent outside of research

Consent by Proxy and Implied Consent

Proxy consent, or consent to participate in research by one competent adult on behalf of another, may be appropriate under certain circumstances. All uses of proxy consent must be approved by an institution's IRB.

If the prospective participant is identified as incompetent to provide informed consent, and if the condition of being incompetent is temporary, (if for example, potential participants have received sedating or pain-relieving medications and consent must be obtained before the effects wear off),

the duration of the incompetence is unknown (for example, when a potential subject is in a coma resulting from traumatic injury), or the potential participant is cognitively impaired, the subject's authorised representative is responsible for deciding whether the subject should participate in the research. This person will sign the consent form on behalf of the participant and will indicate his or her relationship to the subject.
Consent from the subject's authorized representative should be obtained by the researcher in person and documented on the approved consent form.

Consent provided by a proxy should never be accepted if the potential participant has indicated refusal to take part in the research.

Research with Children and Assent to Research

Legally, children have not attained an age at which they can consent to research or treatment. This legal age vary internationally, however the minimum is 16 years or over. Most countries provide special provisions for agreement to participate in research (e.g Section 46.408 of the US Federal regulations). This section establishes the requirements for obtaining permission from parents or guardians and assent from children. The parent or guardian may provide "permission" for the child to participate in a study. Permission means the agreement of parent(s) or guardians(s) to the participation of their children or wards in research. Valid permission can be given only following an explanation incorporating the information currently required for informed consent.

In most cases, the child must indicate willingness to participate by assenting to the study. Assent means a child's affirmative agreement to participate in research. By law, failure to object may not be construed as assent. IRBs make the final determination if sufficient protections exist for children and how assent should be documented.

The inclusion of children in research studies poses many ethical and legal questions.

Waiver of Consent Waiver of Consent

Some countries (e.g. US Federal law (see Title 45 CFR 46.116(d)) permits an IRB to waive the requirement of obtaining written prospective informed consent under the following essential conditions:

- The research poses no more than minimal risk to subjects.
- There are no adverse effects as a result of the waiver or alteration.
- Without the waiver or alteration, the research in question could not be carried out.
- Information will be provided after participation is completed, if appropriate.

The ICH/GCP Guidelines allow for trials to be conducted in the emergency situation in such patients and section 4.8.15 states the following:

In emergency situations, when prior consent of the subject is not possible, the consent of the subject's legally acceptable representative, if present, should be requested. When prior consent of the subject is not possible, and the subject's legally acceptable representative is not available, enrolment of the subject should require measures described in the protocol and/or elsewhere, with documented approval/favourable opinion by the IRB/IEC, to protect the rights, safety and well-being of the subject and to ensure compliance with applicable regulatory requirements. The subject or the subject's legally acceptable representative should be informed about the trial as soon as possible and consent to continue and other consent as appropriate (see 4.8.10) should be requested.

Special Issues in Informed Consent

Language Barriers

Information relevant to participation in research must be communicated to participants "in language understandable to the subject". In most situations, such informed consent must be documented in writing and must include all elements necessary for legally effective informed consent in language comprehensible to the intended participants.

Thus, participants who are not native English speakers should be provided with a consent document in their native language, written at a level that makes the information comprehensible.

Community Consent and Cross-Cultural Issues

Researchers conducting studies in multicultural settings have found that it sometimes is not enough to obtain individual consent using traditional concepts and rules. For example, among some ethnic groups, the role of the individual is secondary to the individual's role as part of a community, and there is no distinct concept of individual will or identity. In other groups, women will defer to the decisions of their husbands, fathers, or other male relatives and will not express their own wishes. In still other groups - and depending on the nature of the research - the implications of participating in research extend beyond the individual and affect the entire group or community.

Community may be defined as a group living in proximity, a group related by blood or marriage, or a group with a common religious, ethnic, or racial heritage or identity.

The concept of community consent has developed, largely in response to research involving identifiable groups. Research with these groups, which are sometimes related by blood as well as living in proximity, requires a reconsideration of traditional concepts of consent. Traditionally, consent was a private matter between an individual patient and a treating physician. Today, the implications of participation in research may involve information that affects family and community members as well. For example, members of one group may feel stigmatised if a number of members of that group participate in research that reveals unpopular or dangerous traits. This may be true for behavioural research that indicates certain behaviours (such as alcoholism or violence) that portray others in the community unfavourably. Moreover, the conduct of clinical research may reveal general information that renders a group less desirable genetically, interfering with potential marriage prospects or employment opportunities.

As a result, some believe that community consent should be an additional requirement - or at least an issue addressed as part of education provided to participants - along with individual consent as a requirement for the ethical conduct of research.