

## OBTAINING INFORMED CONSENT FROM HUMAN RESEARCH SUBJECTS

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### **Abstract**

Obtaining appropriate informed consent is necessary before any research is initiated. However, informed consent should not be seen as only a research ethic requirement, but as a moral obligation, designed to protect the basic human rights of research subjects. The primary goals of informed consent are to protect the welfare and the rights of research subjects. As the Belmont report states, the process require three key components to be ethically valid: information, understanding and voluntary agreement. The challenge of informed consent is to provide sufficient information to make an informed decision, while at the same time presenting this information in a manner that is comprehensible to the potential subject. The use of support materials, such as brochures or videos should be considered. In studies where risks may be high, field-testing of the informed consent process should be deemed prior to the study initiation. Informed consent must be obtained without coercion or undue influence. The researcher's special cultural or intellectual status should not play a role in inducing the subject's decision. In some circumstances, informed consent may be better obtained by a neutral party without a direct interest in the research study. In addition, vulnerable subjects may require special protection.

**Key words:** Inform consent, Human research, Ethics

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## การขอความยินยอมจากผู้เข้าร่วมโครงการสำหรับงานวิจัยในมนุษย์

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### บทคัดย่อ

การขอคำยินยอมจากผู้เข้าร่วมโครงการวิจัยที่เป็นเรื่องจำเป็นอย่างยิ่ง ก่อนที่จะเริ่มต้นกระบวนการศึกษาหรือทำการใด ๆ นักวิจัยไม่ควรเห็นว่าคุณยินยอมเป็นเพียงแค่ความจำเป็นทางด้านจริยธรรมเท่านั้น แต่ยังเป็นหน้าที่ทางคุณธรรมของนักวิจัย ที่จะต้องตระหนักถึงการพิทักษ์สิทธิพื้นฐานของผู้เข้าร่วมโครงการ จุดประสงค์หลักของการขอคำยินยอมนั้นเพื่อปกป้องสิทธิและความปลอดภัยของผู้เข้าร่วมวิจัย ดังรายงานของเบลมอนล์ที่ว่า องค์ประกอบหลัก 3 ประการในคำยินยอมคือ ข้อมูลที่เป็นสาระสำคัญของโครงการ นำเสนอด้วยภาษาที่เข้าใจได้ง่าย และความสมัครใจของผู้เข้าร่วมวิจัย กระบวนการขอความยินยอมจากผู้เข้าร่วมโครงการวิจัยจึงเป็นสิ่งที่ท้าทาย เนื่องจากนักวิจัยจะต้องให้ข้อมูลที่จำเป็นเพื่อการตัดสินใจเข้าร่วมโครงการ ขณะเดียวกันข้อมูลที่นำเสนอต้องเป็นข้อมูลที่ผู้เข้าร่วมโครงการวิจัยสามารถเข้าใจได้ การเลือกใช้เครื่องมือต่างๆ เช่น แผ่นพับ วีดีโอ ควรจะมาประกอบการพิจารณาเพื่อเพิ่มความเข้าใจ อย่างไรก็ตามในการวิจัยที่อาจมีความเสี่ยงสูง ควรมีการทดสอบความเข้าใจเกี่ยวกับขั้นตอนการวิจัยกับผู้เข้าร่วมโครงการก่อนเริ่มต้นทำการวิจัย การขอความยินยอมนั้น ต้องกระทำโดยปราศจากการบังคับขู่เข็ญ หรือใช้อิทธิพลต่างๆ นักวิจัยต้องไม่ให้บทบาทของตนเองไปมีอิทธิพลต่อการตัดสินใจของผู้เข้าร่วมโครงการ ในบางสถานการณ์ ผู้เสนอขอคำยินยอมอาจจะเป็นคนกลาง ที่ไม่ได้มีความเกี่ยวข้องใด ๆ กับโครงการวิจัย ขณะเดียวกันผู้เข้าร่วมโครงการวิจัยที่เป็นกลุ่มอ่อนแอควรจะได้รับการปกป้องเป็นพิเศษ

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## Introduction

When doing the research involving human subjects, it is the responsibility of the investigator to protect right and welfare of the research subjects. In the general rule of research involving human subject, every subjects must agree to participate in writing before they can enroll in a research. By giving their consent to be in a research, they are saying that they understand and accept the risks involved. Consent ensures that they take the proper steps to fully understand the clinical trial, which they are volunteering to be subjects. The process of informed consent is not only about signing a piece of paper; **it is a communication process between the researcher and the subjects** that starts before the research is initiated and continues throughout the study<sup>1</sup>. It is essential that the information provided is understood by the potential participant and empowers that person to make a voluntary decision about whether or not to participate in the study. The subjects have to agree to take any medication or intervention available or investigational until they know what to expect. As the consent form is a contract between the subjects and the investigator, in a real sense, informed consent might best be described as the subject's bill of rights. These rights were formally recognized in 1979 in what is known among research professionals as "The Belmont Report"<sup>2</sup>. Informed consent, the report stated, demands three basic things:

1. Research subject are told everything about the study, including risks.
2. The information must be easy to understand.
3. Research subjects who agree to participate must do so voluntarily, they must not be pressured, coercion, undue influence or inducement, or intimidation

This means that subjects are to be granted the right to freely choose what they want to do. The informed consent process is an on-going conversation between the human research subject and the researcher. The process begins before consent is given and continues until the end of subject's involvement in the research.

## Goals of Informed Consent

The primary goals of informed consent are the protection of patient or subject welfare and the promotion of autonomy<sup>3</sup>. According to Western Institutional Review Board (WIRB)<sup>4</sup>, when obtaining the consent form, there are some important feature to process:

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

The consent form spells out the study procedure, how long the study will last, side effect that could happen and how much subjects will be paid for participation, if anything. The form also states the reasons for various research steps, hoped for benefits and others available treatment option<sup>5</sup>. Many other important details are also provided, such as screening tests that will be expected to take and other medication will require to stop (or start) taking. Every foreseeable risk—including the remote possibility of infection from a routine blood draw—is covered.

## Element of Informed Consent

### Basic Elements of Inform Consent

Researches conducted in the States need to follow the Code of Federal Regulations Title 21, Section 50.25 which indicated the element of informed consent, the following information should be provided to each subject<sup>6</sup>:

- a. A statement explaining the **purpose** of the research, the **procedures** to be followed, the **duration** of participation and any investigational treatments or procedures
- b. A description of **foreseeable risks** and discomforts to subjects
- c. A description of **benefits** that the subjects can reasonably expect
- d. A disclosure of any **alternative treatments** or procedures that might be advantageous to subjects
- e. A statement about how subjects **confidentiality** will be maintained
- f. An explanation of **compensation** and whether medical treatments are available if injury occurs
- g. A list of **contacts** to answer study-related questions and to help with research-related injuries

- h. A statement that participation is **voluntary**, that refusal to participate involves no penalty or loss of benefits to the person

### **Additional Elements on Informed Consent Forms When Appropriate**

When appropriate, one or more of the following elements of information shall also be provided to each subject<sup>6</sup>:

- a. A statement of unforeseeable risks to the volunteer, embryo or fetus—if the volunteer is or may become pregnant
- b. A description of circumstances under which the subject's participation may be terminated by the investigator without the subject's consent.
- c. A description of additional costs to the subjects that may result from participation in the research.
- d. An explanation of the consequences and procedures if a volunteer decides to withdraw
- e. A statement about informing subjects of significant new findings that might affect their willingness to participate
- f. The approximate number of subjects that will be involved in the study

### **The Person Who Obtain Consent**

Cynthia McGuire Dunn, and Gray L. Chardwick<sup>7</sup> suggested that the investigator may not always be the one who obtains the informed consent, the study investigator or other team members are charged with this responsibility. In some cases, translators, witnesses, advocates and others can help ensure impartiality and enhance the decision-making process. However, the person or persons obtaining consent must be sufficiently trained and knowledgeable about the study to answer questions posed by subjects. When principle investigators delegate this important task, they need to be sure that those who obtain consent are properly qualified and know when to refer questions that may exceed their expertise.

In addition, an important issue to decide who will obtain consent is whether or not the investigator has a pre-existing relationship with the potential subject. If the investigator is in a position of power such as the subject's teacher or personal physician, etc., it may be appropriate to delegate the consent responsibility to someone else. This technique may help avoid undue influence and the possibility—real or perceived—that the subjects would feel pressured or obligated to agree to participate.

## **Places for Obtaining Consent**

Privacy is an importance to the consent process. The consent process should not be conducted in areas that would permit others to overhear the discussion. The assurance of privacy is of even greater importance when the topic of the research is in sensitive areas of subjects' lives<sup>7</sup>. Typically, a private office or room helps ensure privacy. The consent is often obtained in the investigator's office or laboratory settings may negatively influence the process. For example, a classroom setting may introduce peer pressure and or inattention. The pre-operative area of the surgical suite likely adds an unwanted element of stress and anxiety. Also, the prospective subject may feel pressured to make an immediate decision. The situation reduces both comprehension and voluntariness, thus detracting from the decision-making process.

## **Timing of Consent Process**

The timing of the consent process may also have a negative impact on the potential subject's ability to make a considered decision<sup>6</sup>. For example, if the research procedures follow immediately after the consent form is signed, there will be no time for the subject to reflect on potential consequences or to ask questions that might come to mind later on. This may be acceptable for minimal risk studies, but for those posing greater risk or possible negative consequences, lengthening the time between presentation of the consent and the final agreement to participate can help protect subjects. Investigators should anticipate circumstances in which it would be difficult to have a satisfactory consent discussion. For example, if the investigator wants to evaluate a new drug for the treatment for woman during delivery, one should anticipate that once labor begins it would be relatively difficult to have a satisfactory consent discussion. Therefore, the discussion should occur during one of the prenatal visits. However, allowing subjects sufficient time to consult with family, friends and others may also improve the quality of the process.

## **Technique to Obtain Consent**

The traditional method is to sit with the potential subject and read/discuss a written consent document, this may not be the best technique for all subjects and for all types of studies. Some subjects may respond better to different modes of presentation. The study of Flory J. and Emanuel E.,<sup>8</sup> suggested that having a study team member or a neutral educator spend more time talking one-on-one to study participants appears to be the most effective

way of improving research participants' understanding. However, investigators whose research involves mailed surveys may not actually interact with subjects, so face-to-face consent is not possible. For complex studies, additional aids—such as videotapes, charts or brochures—may enhance the subject's understanding. Under certain circumstances in research involving minimal risk, the consent process—or its documentation—may be waived. This is often the case for telephone surveys and interviews, where the investigator may note in the study records that the subject gave consent, but a signed document is not obtained. **The best method to obtain consent may depend on the complexity and risk level of the study as well as on the potential participant<sup>9</sup>.**

## **Obtaining Consent from Vulnerable Subject**

### **Vulnerable subjects**

Vulnerable subjects refer to group or individual who cannot give informed consent because of limited autonomy (e.g. children, mentally ill and prisoner) or subjects who may be unduly influenced to participate (e.g. student, employee and patient)<sup>7</sup>.

Here is an example to consider when obtaining consent form vulnerable subjects:

### **Research involving Children**

Because children cannot give consent, some Institutional Review Board (IRB) may require the permission of their parents and, with the exception of very young children in some treatment protocol, the assent of the child–subject. Assent means a child's affirmative agreement to participate in research. In general, the considerations for parental permission are same as for consent in adult subjects.

Assent has generally has been divided into three categories depending upon the age of the child–subject<sup>7</sup>. Very young children have not developed decision– making skill, while older children may function at levels equal to that of adults. The commonly rule of thumb is that children under the age of 7 are too young to assent; children between ages 7 to12 should be capable of assenting, but need not provide written documentation; and those who over the age of 12 should be capable of full participation in the consent process. The investigator's professional judgment and expertise have to determine individual variations on this theme to assure an adequate consent process.

### **Adults with limited capacity to consent**

Capacity can be affected by several things, including age, cognitive impairment, illness, and treatments. For some participants or groups of participants, the researcher or 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 authorized representative (LAR) can give permission for participation in research in some cases.

*Legally authorized representative* means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research<sup>6</sup>.

### **Waiver of Informed Consent**

Although it is ideal to have an informed consent document that contains all recommended elements, there may be situations where this is not appropriate for the research. For some types of research, such as anonymous survey methods, some of the elements may not apply. In such cases, the local ethics committee may allow a waiver of informed consent that allows the researcher to delete some or all of the required elements.

*The Common Rule* provides four criteria for allowing a waiver<sup>10</sup>:

- a. Research should involve no more than minimal risk to the subjects.
- b. A waiver will not adversely affect the rights and welfare of the subjects.
- c. The research could not be conducted without the waiver.
- d. Whenever appropriate, the subjects will be provide with additional pertinent information after participation

*Minimal risk* means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests<sup>6</sup>.

However, all requests for waived should be submitted to the ethics committee before implementation of the research.

## The Investigator Responsibilities

According to the Western Institutional Review Board (WIRB), these are the investigator responsibilities in regard to informed consent<sup>6</sup>:

- a. Provide a **quiet, comfortable, and private setting** for the informed consent process whenever possible.
- b. **Explain** the consent process to the subject.
- c. Make sure the subject has **time to consider** all options; allow subject to take the form home before signing (whenever possible).
- d. Consider the **subject's reading abilities**. Some 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.
- e. **Answer all questions**.
- f. To the extent possible, make sure the subject **understands enough information** about the research study to give informed consent.
- g. To the extent possible, make sure the subject can consent **free from coercion or other undue influence**.
- h. Since the informed consent process continues throughout the subject's participation in the study, **consent should be informally verified on a continuing basis**.
- i. **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.

## Special Challenges Issues

### Language Issues

The consent process should be conducted in the language spoken by the subject, and the consent form should be translated into that language. An IRB may require independent confirmation of the accuracy of the translation<sup>11</sup>. Likewise, subjects who are not literate in their language must have an interpreter present to explain the study to the subject and translate questions and answers between the subject and investigator. The studies, which have self-administrative questionnaire, may include the subjects who are able to read and write. The investigator needs to consider whether it is appropriate to enroll limited or non-readers in the research.

### **Cultural Consideration**

In some cultures an investigator may enter a community to conduct research or approach subjects for their individual consent only after obtaining permission from a community leader, a council of elderly, or other designated authority<sup>12</sup>. Besides, some customs must be respected. In some area, the permission of a community leader or other authority substitute for individual informed consent. The investigator may develop culturally appropriate ways to communicate necessary information to subjects.

### **Conclusion**

Informed consent plays major component in ethical principle of respect for persons, of their autonomy, rights. Therefore, investigators must to ensure that the process of consent—the information in the consent form, the setting, the timing and the manner—shows respect for persons and gives subjects the opportunity to choose what is the best for themselves. The Belmont Report presents three basic things regarding to the consent, those are information, understanding, and voluntary. However, there are a variety of methods to present consent form. The best method may depend on the study research and potential subjects. The investigator have to understand that informed consent in research means more than simply obtaining the signature of the potential research subjects. It is a process that involves conveying accurate and relevant information about research study and its purpose; disclosing known risks, benefits, alternatives, and procedures; answering questions; and enabling the potential participant to make a decision whether to participate.

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