

## Informed Consent - Protection of Human Subjects

### Introduction

No clinical investigator may involve a human being as a subject in research unless the investigator has obtained the legally effective informed consent from the subject. Informed Consent is a written notification to human subjects involved in clinical investigations that provides them with sufficient opportunity to consider whether or not to participate in the study. The informed consent document must include all the basic elements of informed consent (outlined below) or it may be a short form written consent document stating that the elements of informed consent have been presented orally (§50.27). If the short form method is used, there must be a witness to the oral presentation.

An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.

The written consent form must be approved by the Institutional Review Board (IRB) and contain the following basic elements (§50.25):

1. A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.
2. A description of any reasonably foreseeable risks or discomforts to the subject.
3. A description of any benefits to the subject or to others which may reasonably be expected from the research.
4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.
5. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained and that notes the possibility that the Food and Drug Administration may inspect the records.
6. For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.
7. An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.
8. A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

## STRP-IRB member and investigator information

Document source: [http://www.fda.gov/cdrh/devadvice/ide/informed\\_consent.shtml](http://www.fda.gov/cdrh/devadvice/ide/informed_consent.shtml)

9. Additional elements of informed consent. When appropriate, one or more of the following elements of information must be provided to each subject:
  - a. A statement that a particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable.
  - b. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.
  - c. Any additional costs to the subject that may result from participation in the research.
  - d. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.
  - e. A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject.
  - f. The approximate number of subject's involved in the study.

The consent form must be signed by the subject or the subject's legally authorized representative. *The consent form must also be signed by the person explaining the consent form.* <sup>STRP-IRB Requirement</sup> Each signed consent must be maintained by the clinical investigator and a copy of the informed consent must be provided to the human subject.

A combination of oral and written consent may be used. The short form method of informed consent includes a written summary and a "short form." A written summary is a document of what is to be said to the subject or representative and must be approved by the IRB. The summary must include all the basic elements of informed consent (discussed above). A short form is a document stating that the elements of informed consent (§50.25) have been presented orally to the subject or the subject's legally authorized representative.

After oral presentation is provided, the summary must be signed by the witness and the presenter (investigator or investigator's representative). The short form must be signed by the subject (or the representative) and the witness. A copy of the summary must be provided to the subject (or the representative) in addition to a copy of the short form. The signed documents must be maintained by the clinical investigator.

### **Exception from Informed Consent Requirements for Emergency Research**

#### Criteria for exception from informed consent

There are special cases under emergency care research in which the human subject is in a life-threatening situation and it is not feasible to obtain informed consent. In order to allow such research to proceed, there are special provisions for exception from informed consent requirements (§50.24).

The IRB responsible for the review, approval, and continuing review of the clinical investigation may approve that investigation without requiring that informed consent of all research subjects be obtained if the IRB (with the concurrence of a licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation) finds and documents each of the following:

1. The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.

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2. Obtaining informed consent is not feasible because:
  - a. the subjects will not be able to give their informed consent as a result of their medical condition;
  - b. the intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; and
  - c. there is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.
3. Participation in the research holds out the prospect of direct benefit to the subjects because:
  - a. subjects are facing a life-threatening situation that necessitates intervention;
  - b. appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and
  - c. risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.
4. The clinical investigation could not practicably be carried out without the waiver.
5. The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review.
6. The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with the elements of informed consent (§50.25). These procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible. The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the clinical investigation as discussed in (7)(e) below.
7. Additional protections of the rights and welfare of the subjects will be provided, including, at least:
  - a. Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn;
  - b. Public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits;
  - c. Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results;
  - d. Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; and

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- e. If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the subject's family member who is not a legally authorized representative, and asking whether he or she objects to the subject's participation in the clinical investigation. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.

### IRB Responsibilities

The IRB is responsible for ensuring that procedures are in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, of the subject's inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document.

The IRB must also ensure that there is a procedure to inform the subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, that he or she may discontinue the subject's participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. If a legally authorized representative or family member is told about the clinical investigation and the subject's condition improves, the subject is also to be informed as soon as feasible. If a subject is entered into a clinical investigation with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the subject's legally authorized representative or family member, if feasible.

If an IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the clinical investigator and to the sponsor of the clinical investigation.

Records of IRB determinations must be retained by the IRB for at least 3 years after completion of the clinical investigation. These records must include the IRB determinations of exemption from informed consent and also the documentation of IRB denial, including documentation of findings and disclosure of the findings to the clinical investigator and the sponsor. The records must be accessible for inspection and copying by FDA [§56.115(b)].

### Sponsor Responsibilities

The sponsor must monitor the progress of all investigations involving an exception from informed consent. When the sponsor receives information concerning the public disclosures under (7)(b) and (7)(c) above from the IRB, the sponsor must promptly submit copies of the information that was disclosed to the IDE file and to Docket Number 95S-0158 in the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1-23, Rockville, MD 20857, identified by the IDE number.

The sponsor also must monitor such investigations to determine when an IRB determines that it cannot approve the research because it does not meet the exception criteria or because of other relevant ethical concerns. The sponsor must promptly provide this information in writing to FDA, investigators who are participating or are asked to participate in this or a substantially equivalent clinical investigation, and other IRB's that have been asked to review this or a substantially equivalent investigation.

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### IDE Application

Protocols involving an exception to the informed consent requirement under this section must be performed under a separate investigational device exemption (IDE) that clearly identifies such protocols as protocols that may include subjects who are unable to consent. The submission of those protocols in a separate IDE is required even if an IDE for the same device already exists. Applications for investigations under this section may not be submitted as amendments to an approved IDE [§812.35].

### References:

#### 21 CFR 50

Information Sheets: Guidance for Institutional Review Boards and Clinical Investigators, 1998  
<http://www.fda.gov/oc/ohrt/irbs/default.htm>

A Guide to Informed Consent  
<http://www.fda.gov/oc/ohrt/IRBS/informedconsent.html>

Frequently Asked Questions on Informed Consent Process and Informed Consent Document Content  
<http://www.fda.gov/oc/ohrt/IRBS/faqs.html>

Declaration of Helsinki  
<http://www.fda.gov/oc/health/helsinki89.html>  
(World Medical Association's recommendations to every physician in biomedical research involving human subjects)

The Belmont Report, April 18, 1979  
<http://www.fda.gov/oc/ohrt/irbs/belmont.html>

Significant Differences in FDA and HHS Regulations for Protection of Human Subjects  
<http://www.fda.gov/oc/ohrt/irbs/appendixe.html>

Guidance on IDE Policies and Procedures  
Text-<http://www.fda.gov/cdrh/ode/idepolicy.html>  
PDF-<http://www.fda.gov/cdrh/ode/idepolicy.pdf>

Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors: Exception from Informed Consent - Requirements for Emergency Research  
<http://www.fda.gov/OHRMS/DOCKETS/98fr/000805GL.pdf>

### Recommended Links

Information for Health Professionals - Clinical Trials and Institutional Review Boards  
<http://www.fda.gov/oc/oha/default.htm#clinical>

Institutional Review Board Guidebook, 1993, National Institutes of Health, Office of Extramural Research, Office for Protection from Research Risks  
[http://ohrp.osophs.dhhs.gov/irb/irb\\_guidebook.htm](http://ohrp.osophs.dhhs.gov/irb/irb_guidebook.htm)