

Waivers and Alterations of Informed Consent

Informed consent is an important component of human subject protection. Unless the IRB approves a waiver of informed consent or approves a waiver of documentation of informed consent (i.e. verbal consent), investigators are responsible for obtaining and documenting informed consent from research subjects or from their legally authorized representatives.

Waiver of Informed Consent:

In accordance with 45 CFR 46.116, the IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent, or may waive the requirement to obtain informed consent provided the IRB finds and documents that:

(1) The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine: (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs; and (2) the research could not practicably be carried out without the waiver or alteration;

or

- (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; and
- (4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Investigators who wish to request a waiver of informed consent for research must address the criteria set forth above in the Recruitment

section of the protocol summary document and indicate a waiver of informed consent is requested in the Consent of Subjects section of the NR-Exp form.

Waiver of Documentation of Informed Consent (Verbal Consent)

In accordance with 45 CFR 46.117, an IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either:

(1) That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or

(2) That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside the research context.

In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.

Investigators who wish to request a waiver of informed consent for research must address the criteria set forth above in the Recruitment section of the protocol summary document and indicate a waiver of informed consent is requested in the Consent of Subjects section of the NR-Exp form.

Exception from Informed Consent for Emergency Research:

Federal regulations allow for an exception to the informed consent requirements for a limited class of research activities involving emergency medicine. These regulations permit enrollment of human subjects who are in need of emergency medical intervention but who cannot give informed consent because of their life-threatening medical condition, and who do not have a legally authorized person to represent them. Protocols involving an exception to the informed consent requirement for emergency medicine research must be performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies the

protocol as including subjects who are unable to consent. The submission of a separate IND or IDE is required even if an IND for the same drug product or an IDE for the same device already exists.

According to 21 CFR 50.24, in order for the IRB to approve the consent waiver under these circumstances, the IRB must find and document each of the following:

1. The human subjects are in a life-threatening situation; available treatments are unproven or unsatisfactory; and 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.
2. Obtaining informed consent is not feasible because: (i) the subjects will not be able to give informed consent as a result of their medical condition; (ii) the intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; and (iii) 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: (i) subjects are facing a life-threatening situation that necessitates intervention; (ii) 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 (iii) 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 Sec. 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 consistent with paragraph (a)(7)(v) of this section.

7. Additional protections of the rights and welfare of subjects will be provided, including, at least: (i) 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 (ii) 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; (iii) 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; (iv) establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; and (v) 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.

8. 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 shall 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.

For more information on Exception from Informed Consent in Emergency Research, see the FDA website at:

<http://www.fda.gov/oc/ohrt/irbs/except.html>