

Guidance and Procedures Number: 35

Title: IRB Approved Research in an Emergency Setting

Date of Last Revision: February 11, 2008

I. Introduction

Proposed research in an emergency setting requires prospective IRB review and approval. Investigators must submit a detailed protocol application and the IRB must review and approve the proposal, informed consent process and/or application to waive informed consent consistent with federal regulations and California law.

Please note that research in an emergency setting is not the same as an emergency use of a test article. For details, please see [HRPP Guidance & Procedures #36: Emergency Use of a Test Article](#).

II. Planned Research in an Emergency Setting

- A. California law provides for the conduct of planned research in an emergency setting without the subjects' informed consent. Please refer to [HRPP Guidance & Procedures #24: Special Subject Populations: Cognitively Impaired](#) for details. If informed consent from the subjects or from the subjects' proxy or surrogate as outlined in California law cannot be obtained, all requirements outlined by the FDA at 21 CFR 50.24 [see (B) below] must be met prior to the conduct of research in an emergency setting without informed consent.
- B. The IRB must determine whether a given project is subject to FDA regulation.
 - 1. DHHS defers to the FDA regulations where applicable. If the project is not subject to FDA regulation, the project is subject to DHHS requirements (see paragraph C below and the accompanying footnote).
- C. FDA regulations at 21 CFR 50.24 permit planned research in an emergency setting without informed consent. All requirements outlined at 21 CFR 50.24 must be met and IRB approval obtained prior to implementation of planned research in the emergency room/setting without informed consent.¹
 - 1. Per FDA regulations, the IRB may approve a clinical 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

¹ The informed consent exception described in this guidance applies to research whether or not the research is FDA-regulated. On October 2, 1996, the FDA and the Secretary of DHHS jointly published Federal Register actions permitting harmonization of DHHS and FDA regulations regarding research in emergency circumstances. For more information, please see *OPRR Reports: Informed Consent Requirements in Emergency Research*, October 31, 1996 (<http://hhs.gov/ohrp/humansubjects/guidance/hsdc97-01.htm>). **DHHS requirements specifically exclude the use of the waiver for research involving fetuses, pregnant women, in vitro fertilization and prisoners.**

who is not otherwise participating in the clinical investigation) finds and documents each of the following:

- a. 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.
- b. Obtaining informed consent is not feasible because: (1) The subjects will not be able to give their informed consent as a result of their medical condition; (2) The intervention under investigation must be administered before consent from the subjects' [legally authorized representatives](#) is feasible; and (3) There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.
- c. Participation in the research holds out the prospect of direct benefit to the subjects because:
 - (1) Subjects are facing a life-threatening situation that necessitates intervention;
 - (2) 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
 - (3) 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.
- d. The clinical investigation could not practicably be carried out without the waiver.
- e. The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the investigator has pledged to try to contact a [legally authorized representative](#) for each subject within that window of time and, if feasible, to ask the [legally authorized representative](#) for consent within that window rather than proceeding without consent. The investigator must summarize efforts made to contact [legally authorized representatives](#) and make this information available to the IRB at the time of continuing review.
- f. The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with 21 CFR 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 (g)(5) below.

- (1) When a project is not FDA-regulated, the informed consent provisions at 45 CFR 46.116 and 117 govern.
- g. Additional protections of the rights and welfare of the subjects will be provided, including, at least:
 - (1) 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;
 - (2) 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;
 - (3) 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;
 - (4) Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; and
 - (5) If obtaining informed consent is not feasible and a [legally authorized representative](#) is not reasonably available, the investigator has pledged, if feasible, to attempt to contact within the therapeutic window a subject's family member who is not a [legally authorized representative](#), and ask whether s/he objects to the subject's participation in the clinical investigation. The investigator must summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.
2. 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.
 - a. Both FDA and DHHS define a "family member" as any one of the following legally competent persons: spouse; parents; children (including adopted children);

brothers, sisters, and spouses of brothers and sisters; and any individual related by blood or affinity whose close association with the subject is the equivalent of a family relationship.

3. The IRB determinations required by paragraph (a) above and the documentation required by paragraph (5) below are to be retained by the IRB for at least 3 years after completion of the clinical investigation, and the records shall be accessible for inspection and copying by FDA in accordance with 21 CFR 56.115(b).
4. Protocols involving an exception to the informed consent requirement under this section must be performed under a separate investigational new drug application (IND) or 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 IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists. Applications for investigations under this section may not be submitted as amendments under 21 CFR 312.30 or 21 CFR 812.35.
5. If an IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided under paragraph (a) above 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. The sponsor of the clinical investigation must promptly disclose this information to FDA and to the sponsor's clinical investigators who are participating or are asked to participate in this or a substantially equivalent clinical investigation of the sponsor, and to other IRB's that have been, or are, asked to review this or a substantially equivalent investigation by that sponsor.

Regulations:

21 CFR 50.24
21 CFR 50.25
21 CFR 56.115(b)
21 CFR 312.30
21 CFR 812.35

References:

OPRR Reports: Informed Consent Requirements in Emergency Research, October 31, 1996.
<http://www.hhs.gov/ohrp/humansubjects/guidance/hcdc97-01.htm>