

**UNIVERSITY OF TENNESSEE GRADUATE SCHOOL OF MEDICINE
INSTITUTIONAL REVIEW BOARD
EMERGENCY MEDICINE RESEARCH EXEMPTION FROM INFORMED
CONSENT REQUIREMENTS**

I. PURPOSE

This document outlines the procedures for University of Tennessee Graduate School of Medicine Institutional Review Board (UTGSM IRB) concerning the review and approval of an exemption from informed consent for emergency medicine research.

II. SCOPE

This SOP applies to all IRB administrative staff, board members and investigators.

Personnel Responsible:

UTGSM IRB members, administrative staff and investigators

III. BACKGROUND

The federal regulations for the protection of human research subjects generally require the informed consent of prospective subjects or their legally authorized representatives, although a few narrow exceptions exist. In October of 1996, FDA published a final regulation to amend its regulations to permit a limited class of research in emergency settings without consent. The Department of Health and Human Services simultaneously published waiver criteria that match the FDA requirements. These documents establish a single standard for this class of research.

The new FDA regulation (21 CFR 50.24) provides a narrow exception to the requirement for informed consent from each human subject prior to initiation of an experimental intervention. The exception applies to a limited class of research activities involving 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 representative available prior to the time when the research interventions must be initiated. The intent of the new regulation is to allow research on life-threatening conditions for which available treatments are unproven or unsatisfactory and

where it is not possible to obtain informed consent, while establishing additional protections to provide for safe and ethical conduct of these studies.

FDA recognizes that persons with life-threatening conditions who can neither give informed consent nor refuse enrollment are a vulnerable population. FDA recognizes that the lack of autonomy and inability of subjects to give informed consent requires additional protective procedures in the review, approval, and operation of this research. The exception from the informed consent requirement permitted by the rule is conditional upon documented findings by an institutional review board (IRB). The required findings by the IRB are delineated in the procedures section below.

The provisions at 21 CFR50.24 for the conduct of emergency medicine research with a waiver of informed consent are distinct from the waiver of informed consent for single patients or subjects as permitted under FDA regulations. The latter regulations apply to situations in which there is a need to use a test article to preserve the life of the patient or subject and it is not possible to secure the consent of the patient or subject prior to its use. Conditions for waiver of consent for emergency use are formulated at 21CFR50.23. Emergency use provisions of FDA regulations are addressed in SOP IRB #23.

In Accordance With:

21 CFR 50.24

Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors: Exception from Informed Consent - Requirements for Emergency Research

<http://www.fda.gov/downloads/regulatoryinformation/guidances/ucm249673.pdf>

FDA Guidance for Institutional Review Boards and Clinical Investigators 1998 Update located at

<http://www.fda.gov/scienceresearch/specialtopics/runningclinicaltrials/guidances/informationalnotices/ucm113709.htm>

Compliance with this policy also requires compliance with state or local laws or regulations that provide additional protections for human subjects.

IV. PROCEDURES

1. The IRB may approve an 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:
- 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:
 - i. The subjects will not be able to give their 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.
 - c. 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.
 - 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 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.
 - f. The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with 21CFR50.25. 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 (1)(g)(v) of this section.
- g. Additional protections of the rights and welfare of the 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.
 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.

3. The IRB determinations required by paragraph (1) of this section and the documentation required by paragraph (5) of this section 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 812.35.
5. If the IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided under part (1) of this section or because of other relevant ethical concerns, the IRB will 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 IRBs that have been, or are, asked to review this or a substantially equivalent investigation by that sponsor.
6. The following recordkeeping requirements will be observed:
 - a. IRB decisions will be communicated to the investigator in writing.
 - b. Should the IRB not approve a waiver of consent, documentation will be provided to the investigator in writing.
 - c. All correspondence and documentation will be kept in the files for the study.