SOP 6.04 – Informed Consent: Emergency Research under FDA 50.24

1. Objective

In accordance with FDA regulation 21 CFR 50.24, this SOP is intended to discuss the exceptions from informed consent requirements allowable in emergency research.

2. General Description

This SOP reiterates FDA Regulation 21 CFR 50.24. This regulation describes the allowable conditions for research on life-threatening conditions for which available treatments are unproven or unsatisfactory and in situations where obtaining informed consent is not possible.

There are two situations for allowing a waiver of informed consent in emergency research under this regulation: 1) the research involves an investigational intervention that falls under FDA jurisdiction (i.e. drugs, devices, biologics that are not approved for marketing, or are not approved for the desired emergency situation), 2) the emergency research is sponsored by a federal agency (i.e. where federally funded, an innovative emergency surgical procedure, or the evaluation of an approved treatment in an emergency situation).

3. Roles & Responsibilities

Execution of SOP: Principal Investigators (PI)/Study Personnel (SP), IRB Chair, IRB, Office of Research Integrity (ORI) Staff.

Emergency research, by its very nature is greater than minimal risk and must always be reviewed by the fully convened IRB. When one of the two situations discussed in Section 2 are applicable, or where best practice dictates the use of 21 CFR 50.24 as guidance, the process discussed below will be used to make the necessary determinations prior to approval of emergency research.

Researchers are advised to work closely with the IRB during the review process due to the additional requirements for approval of emergency research with which researchers will likely require guidance and direction from the IRB to achieve approval and compliance.

4. Procedures

The necessary determination discussed below will be documented appropriately during the Full Board Review process:

(a)The IRB responsible for the review, approval, and continuing review of the clinical investigation described in this section 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.

(2) 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.

(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 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 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.

(b) 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.

(c) The IRB determinations required by paragraph (a) of this section and the documentation required by paragraph (e) 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 56.115(b) of this chapter.

(d) 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 312.30 or 812.35 of this chapter.

(e) 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) of this section 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.

Community Consultation
Providing the opportunity for discussion with, and soliciting opinions from, the communities in which the study will take place and from which the study subjects will be drawn. These communities may not always be the same; when they are not the same, all affected communities should be consulted.

This stipulation is often difficult to abide by and warrants additional discussion. It is advisable that the IRB request that the researcher(s) draft a plan and document their consultation with the community. To aide this process the IRB should 1) define "community" for the purposes of the research, 2) identify the best approach for consulting the community, and 3) the IRB and researcher(s) should agree on a set of goals to be achieved by consulting with the community.

ORI-HS staff serves as intermediaries between the PI and the IRB. However, the IRB, or IRB Chair on behalf of the IRB may contact the PI directly. The PI may also be invited to the convened meeting (in-person, or by phone). Issues discussed with the PI will be documented in the IRB meeting minutes and/or study file as appropriate.

5. References

21 CFR 50.24
UNLV Rules and Procedures for Conducting Human Subjects Research 4.1, 5.1.4
Bankert & Amdur Chapter 4-4 (p.109)