THE UNIVERSITY OF MICHIGAN

Medical School Institutional Review Board (IRBMED)

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Position Statement of the Medical School Institutional Review Board for Human Subject Research (IRBMED) on Allowing Exception From Informed Consent For Emergency Care Research. January 11, 2007

In 1997, the IRBMED appointed a group to review 21 CFR §50.24 and determine if the IRBMED ought to review research protocols which include exception from informed consent in emergency care research settings. The group concluded that the IRBMED should not review any such protocols until there was more experience with the rule throughout the research community. (See attached 1997 report). In 2005, an appropriately constituted review committee was formed to reevaluate the IRBMED policy that prohibits the review of those research protocols that meet the criteria contained in 21 CFR §50.24.

21CFR§50.24, which took effect on 10/26/1996 (the "Amendment"), created a narrow exception to the requirement to obtain and document informed consent from a person or his/her legally authorized representative prior to enrollment in a clinical research project. Accordingly, the Federal government allows Institutional Review Boards ("IRBs") to approve certain research protocols in which investigators reserve the option to enroll subjects who, due to their medical condition, are unable to consent to participate at the time of enrollment.

The IRBMED must find and document the following prior to approving a research protocol that includes a request for an exception from the informed consent requirement:

(1) The human subjects are in a life-threatening situation, available treatments are unproved or unsatisfactory, and the collection of valid scientific evidence 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 (LAR) 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;

(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 benefits of the proposed intervention or activity.

(4) The clinical investigation could not practicably be carried out without the exception;

(5) The proposed investigational plan defines:

(i) The length of the potential therapeutic window based on scientific evidence;

(ii) An attempt by the investigator to contact a LAR for each subject within that window of time and, if feasible, to asking the LAR for consent within that window rather than proceeding without consent;

(iii) The investigator will summarize efforts made to contact a LAR and make this information available to the IRBMED at the time of continuing review; If obtaining informed consent is not feasible and a LAR is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window a subject's family member who is not a LAR, and asking whether he/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 IRBMED at the time of continuing review.

(6) The IRBMED has reviewed and approved an informed consent document and an informed consent process that meets all other statutory requirements.

(7) The IRBMED has reviewed and approved procedures and information to be used when providing an opportunity for a family member/LAR to object to the subject's participation in the investigation;

(8) Additional protections of the rights and welfare of the subjects will be provided, including:

(i) Consultation 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

(9) If obtaining informed consent is not feasible and a LAR 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 LAR, 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.

(i) 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 LAR 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 incapacitate, a LAR 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 LAR 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 LAR or family member can be contacted, information about the clinical investigation is to be provided to the subject's LAR or family member, if feasible.

(ii) The IRB determinations required by paragraph (i) of this section and the documentation required by paragraph (vi) 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 Sec. 56.115(b).

(iii) 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 Secs. 312.30 or 812.35.

(iv) If an IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided 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.

Based on a review of current scientific literature and common practices of the research community at-large in undertaking emergency research, as well as a careful review of the feasibility of complying with the regulatory requirements, the review committee believes that IRB review of emergency research is now appropriate.

Send your questions and comments to the IRBMED Office:

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