| Wayne State University<br>Human Investigation Committee | |
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| Subject | Planned Emergency Research |
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| Approvals | Office of the General Counsel 12/04/06, Steering Committee 1/17/07, Administrative Approval 03/19/07, Administrative Approval 09/30/10, Administrative Approval 03/07/11 |

## Background

The Food and Drug Administration (FDA) and the Department of Health and Human Services (HHS) permit "planned emergency research" as long as Institutional Review Board (IRB) approval and extensive community consultation [21 CFR 50.24; VHA Handbook 1200.5 14(h)] (OHRP Guidance 97-01) has occurred. This exception under FDA regulations permits planned research in an emergency setting when human subjects (participants) who are in need of emergency medical intervention cannot provide legally effective informed consent and their legally authorized representatives (LARs) are unable to give informed consent as well.

The Secretary of Health and Human Services (HHS) has implemented an Emergency Research Consent Waiver under 45 CFR 46.101(i) with provisions identical to those of the FDA except that there is no IND/ IDE requirement and the definition of family member includes spouses of brother/sisters. The waiver is not applicable to research involving prisoners because of the limitation at 45 CFR 46.101(i) & 46.306(b).

The Human Investigation Committee (HIC) adheres to the FDA Planned Emergency Use requirements and the requirements for HHS Emergency Research Consent Waiver for studies where the FDA does not apply. Most planned emergency research involves the use of a FDA regulated test article and therefore is subject to FDA regulations [21 CFR 50.24].

Principal Investigators who are planning emergency research should contact the HIC office for assistance at least 6 months before the desired start date. The requirements are very complex and include consultation within the institution, in the community in which the research is to be conducted, and with the FDA, the Department of Health and Human Services (DHHS).

Planned emergency research is prohibited at the VA.

## Scope

This policy and procedure applies to planned research that is not covered in the Emergency Single Time Use of a Test Article Policy and Procedures [21 CFR 56.104(c)].

## Definitions

*Planned Emergency Research* - Research that involves participants (subjects) who, because of their condition (e.g., unconsciousness) are in a life-threatening situation that makes intervention necessary, are unable to give informed consent, and to be effective, the intervention must be administered before informed consent from the subject's legally authorized representative is reasonably possible.

## HIC Policy/Procedures

The IRB that initially reviews and approves the planned emergency research may approve the study without requiring informed consent of all research subjects prior to initiating the research intervention if the IRB Committee (that includes a member who is a licensed physician and who is not otherwise participating in the clinical trial) ***finds that the following criteria have been met*** [21 CFR 50.24]:

1. The subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence is necessary to determine the safety and efficacy of certain interventions.

2. Obtaining informed consent is not possible because:
    a. The subjects will not be able to give informed consent because of their medical condition;
    b. The study intervention needs to be administered before consent from the participant's legally authorized representative is possible; and
    c. 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:
    a. Subjects are facing a life-threatening situation that requires intervention;
    b. The potential for the planned emergency intervention providing a direct benefit to the individual subjects is supported by evidence including information and data derived from appropriate animal and preclinical studies; and
    c. The risks associated with the planned emergency research are reasonable in relation to what is known about the medical condition of the potential participants, and when the risks and benefits of standard therapy, if any, are balanced against what is known about the risks and benefits of the proposed planned emergency intervention or research.

4. The planned research could not practicably be conducted without a waiver of informed consent.

5. There is a proposed investigational plan defining 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 potential 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. If the LAR is not available, the PI must have a plan for contacting the subject's family member who is not a LAR within the therapeutic window to ask whether or not he/she objects to the subject's participation in the research study. Documentation of these efforts should be provided to the IRB in writing in summary format at the time of continuing review.

6. The IRB must review and approve the informed consent procedures and the informed consent document which are consistent with 21 CFR 50.25. These procedures and the document are to be used with potential subjects or their LAR, when feasible.

7. The IRB has reviewed and approved the procedures used to provide information about the study to the subject's family member and the family member has had an opportunity to object to the subject's participation in the research.

8. Consultation with representatives of the community in which the study will be conducted and from which the participants will be drawn has occurred.

9. There has been public disclosure to the community prior to the beginning of the study regarding the plans for the research and its risks and expected benefits.

10. There has been public disclosure of information after the completion of the research to inform the community and research participants of the study, including demographic characteristics of the research population and the results of the study.

11. An independent data monitoring committee has been established to provide oversight for the emergency research study.

12. A plan must be in place to ensure that the participant will be informed, or the LAR, if the patient remains incapacitated, or the family member, if the LAR is not available, of the participant's inclusion in the research study. Information that is included on the informed consent document must be included in this explanation. In addition, any of the parties cited above should be notified that they can discontinue participation at any time without penalty or loss of benefits to which the participant is entitled. If the LAR, or family member, is told about the research and the participant's condition improves, the participant is to be informed as soon as practicable. Refer to the HIC Policy and Procedure "Obtaining Permission from Legally Authorized Representative or Family Members (When Subjects Themselves are Unable to Give Consent)" for additional guidance.

13. If a participant is entered into a clinical investigation with waived consent, and the participant dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the participant's legally authorized representative or family member, if feasible.

14. Per ICH-GCP guidance (E6), the participant or the participant's legally authorized representative or family member must be informed about the clinical trial as soon as possible and provide consent if the participant wishes to continue.

15. When following a Department of Defense (DoD) Addendum, an exception from consent in emergency medicine research is prohibited unless a waiver is obtained from the Secretary of Defense.

A new IND or IDE must be provided to the IRB in order for this research to be approved by the IRB. These exemptions must specify that the planned emergency research protocol may include participants who are unable to consent. An existing IDE or IND for the same drug or device will not be sufficient for this planned emergency research.

## Community Consultation

This is one of the most important requirements for conducting planned emergency research, and it must be met prior to full approval by the IRB. The community in which the research is to take place and the persons that would likely be affected by the research must be informed and must agree that it is acceptable to begin the planned emergency research prior to obtaining informed consent.

Depending on the nature of the research, community consultation consists of any number of the following activities: survey(s); questionnaire(s), focus groups and community meetings. The content of these activities/meetings must be approved prior to initiation by the Assistant Vice President of Research (AVPR). Every effort must be made to engage a representative sampling of persons or organizations in the affected community consultation process in order to educate them regarding the research and obtain their input and agreement that the research should go forward. The IRB cannot approve Planned Emergency Research without this part of the process being completed in a thorough manner.

All community meetings must include the Principal Investigator and the Education Coordinator or a representative from the AVPR. The proposed meeting agenda must be approved by the AVPR.

After the community consultation process is complete, the PI must present a written report to the AVPR citing any and all issues raised through the process and conclusions. The AVPR will determine if there is community support based on the report.

## Documentation

The HIC office will keep and maintain detailed documentation that all of the above required procedures for planned emergency research and emergency waiver of consent are met. The documentation will be included in the research protocol and the meetings of the IRB responsible for review and approval of the protocol.