TITLE: Institutional Review Board Special Considerations
SC 510 Prospective Research in Emergency Settings

ORIGINATOR: Institutional Official

APPROVAL: Institutional Official

POLICY STATEMENT: This policy provides an outline of the requirements for review of the conduct of prospective research in an emergency setting.

GENERAL PROVISIONS:
The conduct of prospective research in an emergency setting must be carefully planned and properly reviewed taking into account the risks of the research and the protection of the human research participant with the utmost care. The Food and Drug Administration (FDA) and the Department of Health and Human Services (DHHS) permit "planned emergency research" as long as Institutional Review Board (IRB) approval and extensive community consultation (21 CFR 50.24) 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.

Research in an emergency setting is not the same as an emergency use of a test article.

The Secretary of Health and Human Services (DHHS) has implemented an Emergency Research Consent Waiver under 45 CFR 46.101(j) 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(j) & 46.306(b).

The Mercy Health IRB adheres to the FDA Planned Emergency Use requirements and the requirements for DHHS 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 Mercy Health Office of the IRB for consultation and assistance at least 6 months before the desired start date. The requirements are very complex and include consultation with the institutions Research and Innovation department, representatives of the community in which the research is to be conducted, the FDA and the Department of Health and Human Services (DHHS).

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]: (see SC 510-A)
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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:
   - The subjects will not be able to give their informed consent as a result of their medical condition.
   - The intervention under investigation must be administered before consent from the subject's legally authorized representatives is feasible; and
   - 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:
   - Subjects are facing a life-threatening situation that necessitates intervention;
   - 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
   - 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 of informed consent.

5. The proposed investigation 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 a legally authorized representative 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. 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 information below.

7. Additional protections of the rights and welfare of the subjects will be provided, including, at least:
   - 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;
   - 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;
   - 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;
   - Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; and
   - 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.
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There are also seven requirements that must be met in order to grant IRB approval. These points will need to be carefully considered and documented in the materials submitted to the IRB:

1. Documentation in the Protocol:
The issues raised in the sections below will need to be documented in the appropriate sections of the application. The five points are summarized as follows:

- The human research participants 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 effectiveness of particular interventions;
- Obtaining informed consent is not feasible;
- Participation in the research holds out the prospect of direct benefit to the subjects;
- The study could not practicably be carried out without the waiver of informed consent; and
- The study defines the length of the potential therapeutic window and the investigator has committed to attempting to contact a legally authorized representative to ask for consent for each subject within that window of time.

2. Community Consultation:
Consultation with appropriate community representatives will need to occur before the research begins. 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 Executive Director of Research and Innovation. 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 a representative from the Mercy Health Department of Research and Innovation. The proposed meeting agenda must be approved by the Executive Director of Research and Innovation.

After the community consultation process is complete, the PI must present a written report to the Executive Director of Research and Innovation citing any and all issues raised through the process and conclusions. The Executive Director of Research and Innovation will determine if there is community support based on the report. The Executive Director of Research and Innovation will notify the Office of the IRB of the determination of support of the research and the institutions support in moving forward with the research project.

3. Public Disclosure:
Appropriate public disclosure will need to occur prior to the initiation of the study as well as at the completion of the study.

4. Ongoing Attempts to Obtain Consent:
Consenting is an ongoing process. All applicable criteria that would trigger re-consenting a subject in any study also applies to subjects whose consent has been provided by a surrogate. In addition:

- A subject who regains the cognitive ability to consent must be re-consented using standard consenting procedures.
- In the event a surrogate provides consent for a subject, and a surrogate of higher priority subsequently notifies the investigator of his/her relationship to the subject, the investigator must defer to the higher priority surrogate’s decision regarding whether the subject will continue to participate or to withdraw from the study. This is accomplished by conducting the consent process with the surrogate of higher priority.
- In the event that the surrogate dies, the subject must be re-consented subsequent to any event that would otherwise trigger reconsenting the subject.

Thus, the following versions of consent forms will be needed:

- One for the surrogate
- One for the participant if he or she regains capacity to consent. This one should allow for:
  - Person to continue in study
  - Person not to continue in study but to allow data collected so far to be used for research purposes
  - Person not to continue in the study and not to allow data already collected to be used
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In addition to the situations described above, if a subject is entered into research with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the research should be provided to the subject's legally authorized representative or family member, when feasible.

5. Summaries of Attempts to Obtain Consent:
Investigators will need to document and summarize their attempts to contact family members to obtain their consent if obtaining informed consent is not feasible and a legally authorized representative is not reasonably available. This information will need to be submitted to the IRB at the time of continuing review.

6. Separate IND or IDE:
A separate IND or IDE will be needed for the study.

7. Independent Data Monitoring Committee:
An independent data monitoring committee will need to be established.

Documentation
The Office of the IRB 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 Office of the IRB study specific records and will be made available to regulatory reviewers upon request.

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.

Legally Authorized Representative (LAR): an individual who is authorized under applicable law to grant permission on behalf of a prospective participant for their participation in research.

Family Member: 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.

REFERENCE:
21 CFR 50.24 (b-e)
45 CFR 46.101(i)
45 CFR 46.306(b)
FDA Guidance: Exception from Informed Consent for Studies Conducted in Emergency Settings: Regulatory Language and Excerpts from Preamble - Information Sheet
http://www.fda.gov/RegulatoryInformation/Guidances/ucm126482.htm

http://www.hhs.gov/ohrp/humansubjects/guidance/hsde97-01.htm

ATTACHMENTS:
SC 510-A Worksheet for Review of Prospective Research in Emergency Settings-Exception from Informed Consent

PROCEDURE: All Mercy Health Campuses

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<th>Responsibility</th>
<th>Action</th>
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<td>IRB Specialist/IRB Coordinator</td>
<td>1. Review incoming submissions and determine if they include a proposal for prospective research in an emergency setting.</td>
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<td>2. Notify IRB Chairperson of the new submission and provide the IRB Chairperson with needed materials for review.</td>
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3. Issue correspondence as advised by the IRB Chairperson.

1. Review incoming submissions that include proposals to conduct prospective research in emergency settings.
2. Ensure all requirements of review, consultation and consent and are met and documented.
3. Advise IRB Clinical Research Associate/IRB Coordinator of the correspondence to be issued during the review and consultation process.

1. Review proposals for prospective research in emergency settings as outlined in this policy.
2. May request consultation of experts in the area of study to address questions.

1. Be involved in the community consultation as outlined in this policy.

CONCURRENT CONSENTS:

Institutional Official ______________________

[Signature]