THE UNIVERSITY OF ARIZONA Research & Partnerships

Exception from Informed Consent (EFIC) & Planned Emergency Research

Background

Planned emergency research involves the systematic investigation of a condition experienced by individuals "…in a setting where the emergency circumstances require prompt action and generally provide insufficient time and opportunity to locate and obtain consent from each subject's legally authorized representative (LAR)" (FDA 2013). Because informed consent cannot be obtained prior to initiating research procedures, there are many additional participant protections that must be in place before the Institutional Review Board (IRB) can approve planned emergency research.

Planned emergency research is different than the emergency use of an investigational drug or device in a single patient. Planned emergency research involves the prospective identification and enrollment of participants into a study. Emergency use of an investigational drug or device involves the treatment of a patient using an investigational drug or device outside of the research setting. For more information about emergency use of an investigational drug or device, visit Emergency Use of a test articles.

For a planned emergency research study to proceed, the IRB must grant an "Exception from Informed Consent (EFIC)" waiver.

Guidance

EFIC studies require specific submissions requirements to the IRB:

1. **Justification for Planned Emergency Research Design**
   The IRB considers the following criteria for justifying a planned emergency research design. Researchers must provide justification in the IRB application to address these criteria:
   - 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.
   - 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 involved in the research must be administered before consent from the subjects' LAR is feasible; and
     - there is no reasonable way to prospectively identify the individuals likely to become eligible for participation in the research.
   - 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 research 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.

2. Informed Consent Process for Planned Emergency Research

Though informed consent is not feasible prior to inclusion in planned emergency research, a consent process must be conducted as soon as reasonably possible, based on the ability to locate a patient's LAR or the participant's regained capacity to provide informed consent. The consent document and process used must comply with normal informed consent requirements described in 21 CFR 50.25 (for FDA regulated research) or 45 CFR 46.116 – 46.117 (for non-FDA regulated research).

The consent process must include the following elements:

- The proposed research protocol defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a LAR for each participant within that window of time and, if feasible, asking the LAR contacted for consent within that window rather than proceeding without consent.
- The investigator has summarized efforts that will be made to contact and obtain consent from LAR as soon as possible upon identification of an eligible participant and make this information available to the IRB at the time of continuing review.
- If obtaining 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 participant's family member who is not a LAR, and asking whether he or she objects to the participant'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.
    - "Family member" means any one of the following legally competent persons: spouses; 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 participant is the equivalent of a family relationship.
- If a LAR or family member is told about the clinical investigation and the participant's condition improves, the participant is also to be informed as soon as feasible.

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

3. **Community Consultation and Public Disclosure Plan**

Researchers are required to complete community consultation and public disclosure activities prior to beginning the study. Full information about community consultation and public disclosure can be found in FDA Guidance, April 2013, including a list of the minimum requirements for each activity. Researchers describe the following in the IRB application:

- An appropriate plan for consultation with representatives of the communities in which the clinical investigation will be conducted and from which the participants will be drawn.
- An appropriate plan for public disclosure to the communities in which the clinical investigation will be conducted and from which the participants will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits.
- An appropriate plan for 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.

Use the FDA Guidance to ensure that the minimum necessary requirements are included in these plans.

According to FDA 2013, community consultation means providing the opportunity for discussions with, and soliciting opinions from, the community in which the study will take place and the community from which the study subjects will be drawn. These communities may not always be the same; when they are not the same, both communities should be consulted. The goals of community consultation are to:

- show respect for persons by informing the community about the study in advance;
- inform community members about the trial in advance and provide a means for affected communities to provide meaningful input to the IRB before its decision to approve, require modifications to, or disapprove the study;
- show respect for the community by allowing representatives of the community to identify potential community-level concerns and effects of the research; and
- show respect for subjects' autonomy. Respect may be shown by including in community consultation activities individuals who may have, or be at risk for, the condition under study (and thereby obtain input from a group that is expected to be similar to the eventual study subjects).

According to FDA 2013, public disclosure means dissemination of information (i.e., one-way communication) to the community(ies), the public, and researchers about the emergency research.

The goal of public disclosure prior to initiation of the study is to provide sufficient information to allow a reasonable assumption that the broader community is aware of the plans for the investigation, its risks and expected benefits, and the fact that the study will be conducted without obtaining informed consent from most study subjects.

The goal of public disclosure after the study is completed is to ensure that the communities, the public, and scientific researchers are aware of the study's results. Disclosure to researchers of the results, both positive and negative, of studies conducted under 21 CFR 50.24 is particularly important because such disclosure may help FDA and researchers learn from these studies involving vulnerable subjects who are unable to consent.

4. **Establish an Independent Data Safety Monitoring Board (DSMB)**
   An independent DSMB must be established for the study. Review the FDA guidance on Establishment and Operation of Clinical Trial Data Monitoring Committee.

5. **Obtain an Investigational New Drug (IND) or Investigational Device Exemption (IDE) for Planned Emergency Research**
   For FDA regulated studies, an IND or IDE must be in place for the study, even if the drug or device is already FDA approved for a specific indication.

IRB Review and Approval

When determining whether the community consultation and disclosure process is adequate for an EFIC study, the IRB must consider the community's opinions and concerns, assess the adequacy of the consultation and disclosure process, and incorporate the results of community consultation and discussion into its decision making. At initial review, the IRB will review and consider the Community Consultation Plan. If the IRB determines that the proposed Community Consultation plan is sufficient, approval will be granted for a specified amount of time so Community Consultation activities can proceed. This initial approval generally does NOT grant approval to begin enrolling participants in the study. When the IRB determines that adequate community consultation has occurred, the study will be approved to enroll participants.

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:

• The application clearly identifies the protocols that will include participants who are unable to consent.
• If an IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly (no longer than within 30 days) in writing to the clinical investigator and to the sponsor of the clinical investigation.

Resources

For FDA Regulated Research:

- 21 CFR 50.24 EFIC requirements for emergency research
- Exception from Informed Consent Requirements for Emergency Research
- 21 CFR 50.25 Elements of informed consent

For Non-FDA Regulated Research:

- OHRP Informed Consent Requirements in Emergency Research
- 45 CFR 46.116 General requirements for informed consent
- 45 CFR 46.117 Documentation of informed consent