

DEPARTMENT: Yale University Human Investigation Committee
POLICY NUMBER: XX.BB
SECTION: Planned Emergency Research
REVIEW RESPONSIBILITY: IRB Leadership Committee and HIC Policy Review
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Yale University School of Medicine HIC Policy Regarding: Planned Emergency Research

I. Introduction

FDA regulations at 21 C.F.R. § 50.24 recognize a very narrow exception under which an Institutional Review Board (IRB) may approve a study with no subject informed consent: this exception is limited to planned research in emergency situations in which subjects cannot give informed consent due to a life-threatening medical condition and in which the legally authorized representative cannot be reached within the therapeutic window. Investigators should be aware that such planned emergency research involves an extensive approval process that involves community consultation and submission of a separate protocol to the FDA under a new IND or IDE number. This policy describes the process for conducting planned emergency research at Yale.

II. Definitions

Community Consultation: Community Consultation means providing the opportunity for discussion with, and soliciting opinions from, the community(ies) 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, both communities should be consulted.

Data Monitoring Committee (DMC): A data monitoring committee, sometimes called a data and safety monitoring board (DSMB), is an independent group of experts without Yale affiliation, established by the sponsor of a research protocol to assess periodically the progress of a clinical trial (the safety data and the critical efficacy endpoints), and to recommend to the sponsor whether to continue, modify, or stop a trial. In some instances, the HIC may permit people with Yale affiliations to be members of a DMC so long as the majority of the membership is not affiliated with Yale.

Family Member: For purposes of this policy, 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. [21 C.F.R. § 50.3(m)]

Legally Authorized Representative: An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedures involved in the research.

Public Disclosure: (a) Before a planned emergency research protocol begins, the

dissemination of information in the community(ies) in which the study will take place and from which the subjects will be drawn sufficient to allow a reasonable assumption that the communities are aware that the study will be conducted, and its risks and benefits; and (b) after the study has been conducted, the dissemination of information to the community(ies) in which the study was conducted and to scientific researchers sufficient to describe the study's demographic characteristics and the study's results.

Test Article: Any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under 42 U.S.C. §§ 262 and 263b-263n.

Therapeutic Window: The time period, based on available scientific evidence, during which the intervention under investigation in the planned emergency research might reasonably produce a demonstrable clinical effect.

III. Policy

Investigators may conduct planned emergency research at Yale in accordance with the regulatory requirements of 21 C.F.R. § 50.24, the approval of the Yale HIC, community consultation, and pursuant to an IND/IDE specific to the planned emergency research.

A. Separate Investigational New Drug Application (IND) or Investigational Device Exemption (IDE)

Protocols under this policy require a separate IND or IDE (as applicable) submitted to the FDA, even for products that have current INDs or IDEs, because of the exception to the informed consent requirement. This submission may not be an amendment to an existing IND/IDE, and must clearly identify the study as including subjects who are unable to consent. Investigators should provide a copy of the separate IND/IDE to the HIC.

B. Required HIC Findings

The HIC will approve a protocol for planned emergency research only after review of the protocol and finding each of the following elements:

1. *Concurrence by an Independent Physician*

The HIC must obtain the documented concurrence of a physician, licensed in the state where the research will occur, who is a member of or consultant to the HIC but who is not otherwise connected to the study or involved in the research before approving an exception to informed consent for planned emergency research.

2. *Life-Threatening Situation*

The HIC must find that the subjects will be in life-threatening situations, which means, for purposes of this policy, diseases or conditions in which the likelihood of death is high unless the course of the disease or condition is interrupted. An

individual is *not* considered to be in a life-threatening situation when the situation is not emergent. For example, research involving an individual who has been in a coma for a long period of time and whose condition is not rapidly deteriorating is not considered planned emergency research. In that case, the research intervention requires consent by a legally authorized representative of the subject.

The HIC must also find that available treatments are unproven or unsatisfactory, and that the collection of additional valid scientific evidence is necessary to determine the safety and effectiveness of particular interventions and/or test articles.

3. *Informed Consent Not Feasible*

The HIC must find that informed consent is not feasible because:

- (a) the subjects will not be able to give their informed consent as a result of their medical conditions;
- (b) the intervention under investigation must be administered before obtaining consent from a subject's legally authorized representative is feasible; and
- (c) there is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the research.

4. *Prospect of Direct Benefit*

The HIC must find that participation in the research holds out the prospect of direct benefit to the subjects because:

- (a) they are in life-threatening situations that necessitate intervention;
- (b) data from animal and preclinical studies support the potential for direct benefit to individual subjects; and
- (c) risks associated with the investigation are reasonable in relation to what is known about the medical conditions 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.

5. *Research Impracticable in Absence of Waiver*

The HIC must find that the clinical investigation could not practicably be carried out without the waiver.

6. *Therapeutic Window*

The HIC must find that the proposed investigational plan defines the length of the potential therapeutic window based on available scientific evidence.

7. *Plan to Contact Legally Authorized Representative*

The HIC must find that the investigator has committed to attempting to contact a legally authorized representative within the therapeutic window 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 the legally authorized representative and make this information available to the HIC at the time of continuing review.

8. *Informed Consent Procedures and Documents*

The HIC must review and approve informed consent procedures and informed consent documents. These procedures and documents are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible.

The HIC must also review and approve 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 (see Paragraph 9(e) and Section C below).

9. *Additional Protections*

The HIC must find that additional protections for subjects will be provided, including the following:

- (a) consultation with representatives of the community(ies) in which the clinical investigation will be conducted and from which the subjects will be drawn;
- (b) public disclosure to the community(ies) in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the research, of plans for the research and its risks and expected benefits;
- (c) public disclosure of sufficient information following completion of the protocol to apprise the community(ies) and researchers of the study, including the demographic characteristics of the research population, and its results;
- (d) establishment of an independent DMC to exercise oversight of the research;
and
- (e) 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 research. The investigator will summarize efforts made to contact family members and make this information available to the HIC at the time of continuing review.

C. Required Information for Subject (or Legally Authorized Representative or Family Member)

The HIC is responsible for ensuring that the investigator has procedures in place:

1. 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:
 - (a) Of the subject's participation in the research, the details of the research protocol, and other information contained in the informed consent document; and
 - (b) That the subject may discontinue participation in the study at any time without penalty or loss of benefits to which the subject is otherwise entitled;
2. to inform the subject as soon as possible, if a subject's condition improves, and if a legally authorized representative or family member is informed of the above;
3. to provide information about the research protocol to the subject's legally authorized representative or family member, if feasible, if a subject is entered into a planned emergency research protocol and dies before a legally authorized representative or family member can be contacted; and
4. to obtain signed informed consent from the subject, or if the subject remains incapacitated, the subject's legally authorized representative, when research interventions are required after the emergency intervention and/or when subsequent data is collected for longitudinal purposes.

D. The HIC Must Notify the Investigator and the Sponsor if It Does Not Approve the Planned Emergency Research

If the HIC disapproves the proposed planned emergency research protocol, the findings must be documented in writing and provided promptly to the investigator and the sponsor of the study (if different from the investigator). The sponsor must promptly disclose the disapproval to the FDA, to other investigators who have been asked to participate in this or a substantially similar study by the sponsor, and to other IRBs that have been asked to review this or a substantially similar study by the sponsor.

IV. Record Retention

All documentation identified above must be retained by the HIC for 3 years after a study under this policy has been completed or terminated.