
Yale University Institutional Review Boards

IRB Policy 620 Planned Emergency Research Which Necessitates Waiver of Informed Consent

Responsible Office	Office of Research Administration	Effective Date:	November 19, 2009
Responsible Official	IRB Director	Last Revision:	November 19, 2009

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Scope

This policy applies to all investigators conducting planned emergency research involving human participants at Yale and addresses an exception from informed consent requirements for planned Emergency Research.

Policy Statement

The Institutional Review Board (IRB) will only approve planned emergency research at Yale in accordance with the applicable regulatory requirements of the Food and Drug Administration (FDA) at 21 CFR 50.24 and the Department of Health and Human Services (DHHS) Emergency Research Consent Waiver effective November 1, 1996 pursuant to 45 CFR 46.101(i). Research that is subject to FDA regulations will be carried out under an FDA IND application or an FDA IDE, and will be reviewed by the IRB in accordance with FDA regulations. Research that is not subject to FDA regulations but is federally funded or supported will be reviewed under the DHHS Waiver provisions.

Reason for the Policy

Federal regulations recognize a very narrow exception under which an IRB may approve a study which is greater than minimal risk or which involves FDA regulated products in which informed consent will not be obtained. 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 for which the legally authorized representative or other appropriate surrogate cannot be reached within the therapeutic window. Investigators should be aware that such planned emergency research involves an extensive application process that involves prior community consultation and, when applicable, submission of a separate protocol to the FDA under a new IND or IDE number before the research can be approved.

An important distinction must be made between **Planned Emergency Research** and **Emergency Use of an Investigational or Unlicensed Drug or Device**. The Emergency Use IND or IDE is not for research purposes; it allows the FDA to authorize **clinical use** of an experimental drug in an emergency situation that does not allow time for submission of an IND or IDE in accordance with the regulations. It is also used for patients who do not meet the criteria of an existing study protocol, or if an approved study protocol does not exist. **For more information on Emergency Use of an Investigational or Unlicensed Drug or Device, see IRB Policy 600 Use of Investigational New Drugs and Devices in Human Research, and Procedure 600 PR.1 Emergency Use of an IND or IDE.**

Definitions

Community Consultation

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.

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) and DHHS Waiver under 45 CFR 46.101(i)]

Independent Data Monitoring Committee (DMC)

A data monitoring committee, sometimes called a data and safety monitoring board (DSMB), that is an independent group of experts, 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.

Legally Authorized Representative (LAR)

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.

Surrogate Permission

Permission for an individual to participate in research given by an appropriate surrogate (e.g., next of kin – spouse, parent, child, sibling) when an individual is assessed as not capable of providing fully informed and legally effective consent.

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.

Policy Sections

620.1 Separate Investigational New Drug Application (IND) or Investigational Device Exemption (IDE) Required

Protocols under FDA oversight will not be approved by the IRB without a separate IND or IDE (as applicable) as required by the FDA. Products that have current INDs or IDEs must also provide a separate IND/IDE for the purpose of the planned emergency research, because of the exception to the informed consent requirement. Hence the IND/IDE 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 IRB.

620.2 Required IRB Findings

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

1. Concurrence by an Independent Physician

The IRB 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 IRB 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 IRB 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 or appropriate surrogate of the subject.

The IRB 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 study interventions and/or test articles.

3. Informed Consent Not Feasible

The IRB 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 treatment window does not allow time to get prospective consent, and the intervention under investigation must be administered before obtaining consent from a subject's legally authorized representative or appropriate surrogate 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 IRB 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 of Informed Consent

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

6. Therapeutic Window

The IRB 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/Surrogate

The IRB must find that the investigator has committed to attempting to contact a legally authorized representative (LAR) or appropriate surrogate within the therapeutic window and, if feasible, to asking the LAR/surrogate contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact the LAR/surrogate and make this information available to the IRB at the time of continuing review.

8. Informed Consent Procedures and Documents

The IRB must review and approve informed consent procedures and informed consent documents. These procedures and documents are to be used with subjects or their LARs/surrogates in situations where use of such procedures and documents is feasible.

The IRB 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 620.3 below).

9. Additional Protections

The IRB 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 LAR is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the subject's family member/appropriate surrogate who is not a LAR, 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 IRB at the time of continuing review.

620.3 Required Information for Subject (or Legally Authorized Representative or Family Member/Surrogate)

The IRB 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 LAR 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 LAR or family member is informed of the above;
3. To provide information about the research protocol to the subject's LAR or family member, if feasible, if a subject is entered into a planned emergency research protocol and dies before a LAR 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 LAR/surrogate, when research interventions are required after the emergency intervention and/or when subsequent data is collected for longitudinal purposes.

620.4 IRB Notifications of Disapproval

If the IRB 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 is responsible for promptly disclosing the disapproval to the FDA (if applicable), 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.

Special Situations/Exceptions

Planned Emergency Research may not be conducted in research populations covered by Subparts B (pregnant women, fetuses and neonates) and C (prisoners).

Related Information

IRB Policy 200: Informed Consent for Human Research

References:

21 CFR 50.24

45 CFR 46 Waiver of Informed Consent Requirements in Certain Emergency Research (Federal Register, Vol. 61, No. 192, pp. 51531-51533, October 2, 1996)

FDA Guidance for Investigators: <http://www.fda.gov/OHRMS/DOCKETS/98fr/06d-0331-gdl0001.pdf>

Harmonized Rule: <http://www1.va.gov/oro/apps/compendium/Files/emergency%20waiver%201996.htm>

OPRR Reports: <http://www.hhs.gov/ohrp/humansubjects/guidance/hcdc97-01.htm>

Contacts

Subject	Contact	Phone
Biomedical Studies Involving Human Subjects in Planned Emergency Research	Human Investigation Committee	203-785-4688 ysmhic@yale.edu
Surrogate or Legally Authorized Representative	Office of the General Counsel	203-432-4949

Roles and Responsibilities

[Human Investigation Committee](#)

HIC I, HIC II, HIC III and HIC IV serve as the four Institutional Review Boards or IRBs for biomedical human research conducted at Yale University.

Office of the General Council

The OGC serves as legal advisor to the Yale community.