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Manager
Department Research
Applicability Boston Children's
Hospital- Policies
& Procedures

Exception from Informed Consent Requirements for Emergency Research Policy/Procedure

Internal Approval

SVP, Research

EVP & Chief Scientific Officer, Research

Scope

This policy describes the circumstances and criteria that must be met in order to conduct emergency research without informed consent

Policy Statements

Researchers who plan to conduct their research protocols in an emergency setting when they know that it will not be possible to obtain consent from the patient or legally authorized and the research involves an US Food & Drug Administration (FDA) regulated product are required to conduct the research in accordance with the FDA regulations 50.24 and US Department of Health & Human Services (HHS) regulations 45.CFR 46.101(i) as referred to a "Emergency Research Consent Waiver".

The HHS and FDA regulations have been harmonized with small differences noted.

Researchers are encouraged to consult with the Institutional Review Board (IRB) administrative staff and IRB Chair in preparing their applications.

Pertinent Regulations: FDA CFR 50.24 and HHS 45 CFR 46.101(i)

FDA CFR 50.24

The IRB responsible for the review, approval, and continuing review of the clinical investigation described in this section may approve that investigation without requiring that informed consent of all subjects be obtained if the IRB (with the concurrence of a licensed physician who is a member of the IRB and who is not otherwise participating in the clinical investigation, if subject to FDA regulations) finds and documents each of the following:

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:
 - a. The subjects will not be able to give their informed consent as a result of their medical condition.
 - b. The intervention under investigation must be administered before consent from the subject's legally authorized representatives is feasible; **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 necessitates intervention;
 - b. 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**
 - c. 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.
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 ask 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 paragraph (7)(v) below.

7. Additional protections of the rights and welfare of the subjects will be provided, including, at least:
 - i. 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;
 - ii. 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;
 - iii. 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;
 - iv. Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; **and**
 - v. 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.
 - a. The IRB is responsible for ensuring that procedures are in place 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, of the subject's inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document. The IRB shall also ensure that there is a procedure to inform the 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, that he or she may discontinue the subject's participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. If a legally authorized representative or family member is told about the clinical investigation and the subject's condition improves, the subject is also to be informed as soon as feasible. If a subject is entered into a clinical investigation with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the subject's legally authorized representative or family member, if feasible.
 - b. The IRB determinations required by § 50.25(a) of this section and the documentation required by § 50.25(e) of this section are to be retained by the IRB for at least 3 years after completion of the clinical investigation, and the records shall be

accessible for inspection and copying by FDA in accordance with § 56.115(b).

- c. Protocols involving an exception to the informed consent requirement under this section must be performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies such protocols as protocols that may include subjects who are unable to consent. The submission of those protocols in a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists. Applications for investigations under this section may not be submitted as amendments under § 312.30 or 812.35.
- d. If an IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided under § 50.25(a) of this section or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the clinical investigator and to the sponsor of the clinical investigation. The sponsor of the clinical investigation must promptly disclose this information to FDA, when the project is under the jurisdiction of the FDA and to the sponsor's clinical investigators who are participating or are asked to participate in this or a substantially equivalent clinical investigation of the sponsor, and to other IRBs that have been, or are asked to review this or a substantially equivalent investigation by that sponsor.

Additional HHS requirements: HHS 45 CFR 46.101(i):

- a. In accordance with HHS regulations the "Emergency Research Consent Waiver" does not apply to research involving prisoners, fetuses, pregnant women and human in vitro fertilization.
- b. The IRB must approve the research, waiver, and document that the research activity is subject to regulations codified by the FDA Title 21 CFR part 50 and will be carried out under an FDA investigational new drug application (IND) or an FDA investigational device exemption (IDE). The application for which has clearly identified the protocols that would include subjects who are unable to consent, and
- c. That:
 - i. The requirements for exception from informed consent for **emergency** research detailed in title 21 CFR section 50.24 have been met relative to those protocols, or
 - ii. The IRB responsible for the review, approval, and continuing review of the research has approved both the research and a waiver of informed consent and has found and documented that the research is not subject to regulations codified by the FDA at Title 21 CFR part 50 and found and documented and reported to the Office for Protection from Research Risks, HHS, that all the above mentioned conditions have been met relative to the research.

*In accordance with HHS and for the purposes of this waiver, "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 subject is the equivalent of a family relationship.

Procedures

The following is a summary of the justifications and steps that need to be taken in order to conduct

emergency research protocols with a waiver of informed consent:

1. **Protocol justification:** Researchers must provide a detailed description in their protocol that:
 - a. The human subject is 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;
 - b. Obtaining informed consent is not feasible, for three reasons:
 - i. Participation in the research holds out the prospect of direct benefit to the subjects,
 - ii. The study could not practicably be carried out without the waiver of informed consent; and
 - iii. 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
3. **Public disclosure:** Appropriate public disclosure will need to occur prior to the initiation of the study as well as the completion of the study
4. **Ongoing attempts to obtain consent:** Researchers planning to conduct research that does not include the informed consent of all subjects must provide information and attempt to obtain the consent from the subjects and/or the appropriate relatives or legally authorized representatives on an ongoing basis throughout the conduct of the research and at the conclusion of the research.
 - a. It is also required that information be provided about the clinical investigation to the subject's legally authorized representative or to a relative, if feasible, if the subject dies before consent has been obtained
5. **Summaries of attempts to obtain consent:** If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, investigators must document and summarize their attempts to contact family members to obtain their consent.
 - a. This information will need to be submitted to the IRB at the time of continuing review.
6. **A separate Investigational New Device (IND) or Investigational Device Exemption (IDE) - if subject to FDA regulations:** Protocols involving an exception to the informed consent requirement under this FDA regulation must be performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies such protocols as protocols that may include subjects who are unable to consent.
 - a. The submission of those protocols in a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists.
 - b. Applications for investigations under this section may not be submitted as amendments under 312.30 or 812.35.

7. **Independent Data Monitoring Committee:** An independent data monitoring committee will need to be established.
- a. Requests for research that fall within this emergency informed consent exemption often take longer periods of time to review, therefore investigators should plan ahead.
 - b. Often, it will be necessary to arrange for meetings with the IRB Chair and administrative staff in addition to the IRB meetings. Other representatives from Boston Children's Hospital, such as public affairs may also need to be contacted and involved.

Related Content

- Department of Health and Human Services Regulations: HHS 45.CFR 46.101
- U.S. Food & Drug Administration CFR - Code of Federal Regulations Title 21 CFR 50.24: Exception from informed consent requirement
- IRB Policy: Community Consultation and Public Disclosure Guidance for Exception from Informed Consent Research (EFIC)

Approval Signatures	Approver	Date
Step Description		

Applicability

Boston Children's Hospital- Policies & Procedures