

The Carle Foundation IRB Policy 502

Subject	Emergency Use and Other Special Situations in Research		
Approval	Dec 2006	Review	Sep 2010
Revision	Dec 2009		
Scope	These policies and procedures apply to all research under the jurisdiction of the Carle IRB.		
Purpose	To provide guidance for reviewing the emergency use and other special situations in research.		

Statement of Policy

Certain types of research use methods that require additional evaluation, or are subject to additional requirements for IRB review. These types of research include, but are not limited to:

1. Clinical research involving devices
2. Genetic research
3. Prospective research in emergency settings
4. Emergency use of an investigational article
5. Medical records and chart review
6. Protocols lacking plans for human involvement

Emergency Use of Investigational or Test Articles (Retrospective Review) Definitions

Emergency use – The use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available and where there is not sufficient time to obtain Carle IRB approval. [21 CFR 56.102(d)]

Test article – Any investigational drug, biological product, or medical device for human use. [21 CFH 56.102(1)]

Life threatening – for the purposes of section 56.102(d), includes the scope of both life-threatening and severely debilitating, as defined below.

Life-threatening – diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the Carle IRB is feasible.

Severely debilitating – diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

Significant risk device – an investigational device that: (1) Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject; (2) Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject; (3) Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or (4) Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

Carle IRB approval is required prior to conducting human subject research. An exception to this is in the one-time use of an investigational drug or device (*test article*) for a single participant in a life-threatening (*emergency use*) situation.

An emergency use of a test article is exempt from prior Carle IRB review and approval, **provided that the emergency use of a test article is reported to the IRB within 5 working days of date of the emergency use.** [21 CFR 56.104(c)]

The Carle IRB may be notified prior to an emergency use; however, *this notification should not be construed as an IRB approval.* Notification is used by the Carle IRB to initiate tracking to ensure that the investigator files a report within the five day time-frame required. The Carle IRB may choose to request additional information.

Any subsequent use of the test article is subject to Carle IRB review and approval. **Only one use of the test article is permitted** under the emergency use Carle IRB exception and **any** subsequent use needs to be done under a Carle IRB approved protocol - however, the FDA acknowledges that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the Carle IRB has not had sufficient time to convene a meeting to review the issue ["Emergency Use of an Investigational Drug or Biologic," FDA Information Sheet, 1998 Update].

Emergency Use of Investigational or Test Articles (Retrospective Review) Definitions (cont.)

Criteria for Emergency Use

All the following must be satisfied:

- Existence of a life-threatening/severely debilitating condition where no standard acceptable treatment is available
- No current IRB approved protocol covering the situation and no time to obtain prior FDA and Carle IRB approval
- Availability of an investigational agent or device which in the opinion of the physician might be beneficial, and
- Availability of an investigational agent or device from a sponsor or elsewhere.

The Emergency Use of a Test Article is **not** a systematic investigation designed to develop or contribute to generalizable knowledge.

Specific Policies

1. **Clinical Research Involving Devices.** In accordance with the other Carle IRB policies, Carle IRB (or Chairperson if the review is expedited) will determine whether, in the context of the study or by the nature of the investigational medical device (see significant risk devices definition below), the study presents a significant risk (SR) or a non-significant risk (NSR) of harm to study subjects. This assessment will be based on the information provided by the Investigator and/or the Sponsor. The Carle IRB's device risk determination must be documented in the Carle IRB meeting minutes.

If an Investigator submits a NSR device research protocol that is determined by the Carle IRB to be a significant risk device study, the Investigator and the Food and Drug Administration (FDA) will be notified in writing. No further action will be taken by the Carle IRB on the research until the Sponsor or Investigator has met the requirements for an SR study described in 21 CFR 812 (Investigational Device Exemption regulations).

2. **Genetic Research.** Genetic research may require special considerations. Because there is still little regulatory guidance and relatively few ethical precedents, genetic research will require close scrutiny, and the input of experts in this area. The Carle IRB will refer to the OHRP Guidance on the Genetic Information Nondiscrimination Act dated April 6, 2009.
3. **Prospective Research in Emergency Settings (Prospective Review).** When the Carle IRB has reviewed and approved informed consent procedures and informed consent documents consistent with 21 CFR 50.25, these procedures are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is applicable. The Carle IRB, with the concurrence of a licensed physician who is either a member of the Carle IRB or a consultant and who is not participating in the research being reviewed, may waive the requirement for informed consent in certain emergency research if it finds and documents the following:
 - a. 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.
 - b. 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.
 - c. 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 pre-clinical 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.
 - d. The clinical investigation could not practicably be carried out without the waiver.
 - e. The proposed investigational or research plan includes:
 - Investigator 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,

Specific Policies (cont.)

- 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 legally authorized representatives and make this information available to the Carle IRB at the time of continuing review.
- f. 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 Carle 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 Safety Monitoring Board (DSMB) 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 Carle IRB at the time of continuing review.

The study plan must ensure that, 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 is informed of the subject's inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document.

The study plan must 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, if permitted by law, 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.

If the Carle IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exceptions provided above, or because of other relevant ethical concerns, the Carle IRB will document its findings and provide these findings promptly in writing to the Investigator and to the Sponsor of the clinical investigation. It is the investigator's responsibility to meet the requirements of IND, IDE and to obtain FDA approvals for any new IND or IDE when such applications are warranted.

5. Consent Requirements

- a. Informed consent of the patient or the patient's legally authorized representative is required, **unless both the investigator and a physician (not otherwise participating in the investigation) certify in writing** that
- The patient is confronted with a life-threatening situation;
 - That informed consent cannot be obtained from the patient (because patient cannot communicate or is incompetent to give consent);
 - Consent cannot be obtained from the legally authorized representative (unavailable or unknown); and
 - No alternative approved treatment/therapy is available that provides an equal or greater likelihood of saving the patient's life.

Specific Policies (cont.)

6. Drugs and Biologics - Reporting Requirements to the Carle IRB (and FDA)

- a. The Principal Investigator must submit the following materials to the Carle IRB **within five (5) working days** following the use of the test article:
- Emergency Use of a Test Article – Notification to the Carle IRB which includes:
 - information about the patient
 - indication of the life-threatening or severely debilitating nature of the situation
 - explanation as to why this drug or treatment was necessary
 - **and** if the emergency use occurred **without obtaining prior informed consent**, Independent Physician Certification - Emergency Use of a Test Article Without Informed Consent
 - **Written permission from the manufacturer** for the use of the test article under their Investigational New Drug (IND) application. Generally the investigator will contact the manufacturer and determine if the drug or biologic can be made available for the emergency use under the company's IND. If the company declines permission or cannot be reached, the investigator should contact the FDA for authorization of the shipment of the drug in advance of the IND submission. In such a case the FDA may authorize shipment of the test article in advance of the IND submission. The Carle IRB may request that the investigator contact the FDA to obtain an IND.
 - Signed Consent Form from the subject or the legally authorized representative, and applicable HIPAA documents.

7. Devices - Reporting Requirements to the Carle IRB (and FDA)

- a. The Principal Investigator must submit the following materials to the Carle IRB **within five (5) working days** following the procedure:
- Emergency Use of a Test Article – Notification to the Carle IRB which includes:
 - information about the patient
 - indication of the life-threatening or severely debilitating nature of the situation
 - explanation as to why this drug or treatment was necessary
 - **and** if the emergency use occurred **without obtaining prior informed consent**, Independent Physician Certification - Emergency Use of a Test Article Without Informed Consent
 - **Written permission from the manufacturer** for the use of the test article under their Investigational Device Exemption (IDE). Generally the investigator will contact the manufacturer and determine if the device can be made available for the emergency use under the company's IDE. The IRB may request that the investigator contact the FDA to obtain an IDE. If the company declines permission or cannot be reached or an IDE does not exist, the FDA expects the investigator to:
 - Determine whether the criteria for emergency use have been met;
 - Assess the potential for benefits from the unapproved device and to have substantial reason to believe that benefits exist;
 - Assure that the decision of the investigator that an emergency exists is not based solely on the expectation that IDE approval procedures may require more time than is available.
 - Obtain an independent assessment by an uninvolved physician.In addition, if the device is used and **there is no IDE**:
 - The use must be reported to the FDA within 5 working days (to Center for Devices and Radiological Health or Center for Biologics Evaluations and Research). This report should contain a summary of the conditions constituting the emergency, patient outcome information, and the patient protection measures that were followed.
 - Signed Consent Form from the subject or the legally authorized representative, and HIPAA documents.

8. **Medical Records and Chart Review.** Studies involving the use of existing public or privately held records only may qualify for exempt status or expedited review. However, if the nature of the research could put subjects' confidentiality at risk, the study will be reviewed by the full Carle IRB. Studies that involve only chart and record review can sometimes pose significant risk to patients.

The most common breach of confidentiality is disclosure of possibly embarrassing information without the knowledge or consent of the patient. Such studies may also lead to recruitment of patients into future non-therapeutic studies in a manner, which may provoke the patient to ask how his/her record was revealed to someone not part of his/her therapeutic team. The present policy is to require Carle IRB review of studies involving chart review or data collection and analysis.

Specific Policies (cont.)

If identifiers were to be recorded, the research would require Carle IRB review to ensure that, among other things, procedures for protecting privacy and confidentiality are adequate. Furthermore, the Investigator studying cancer risk factors may propose to contact the subjects (if still living) or family members (if the subject is deceased) to gather additional information, which may or may not be subject to the federal regulations.

9. **Research requiring the use of Residual Human Body Fluids, Tissues and Recognizable Body Parts:** Research protocols planning the use of existing specimens ("on the shelf" or frozen) without identifying information (e.g., no names, initials, hospital number, etc.) may be submitted to the Carle IRB. These studies may qualify for the use of HIPAA waiver/documentation other than the use of a HIPAA Authorization Form.

Reference

<http://www.hhs.gov/ohrp/humansubjects/guidance/gina.html>

<http://www.genome.gov/Pages/PolicyEthics/GeneticDiscrimination/GINAInfoDoc.pdf>

<http://www.hhs.gov/ohrp/policy/> , [21 CFR 56.102(d)], [21 CFR 56.104(c)], [21 CFR 56.102(1)],

"Emergency Use of an Investigational Drug or Biologic," FDA Information Sheet, 1998 Update

21 CFR 812 Investigational Device Exemptions

Electronic Approval On File

*Approved by IRB Board Aug 2010

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