

The Carle Foundation

IRB Policy 409

Subject	Clinical Investigations Involving Drugs, Devices, and Biological Products				
Approval	Dec 2006	Review	Jun 2009	Revision	Jun 2009
Scope	These policies and procedures apply to all human subjects research that involves a clinical investigation and is conducted under the jurisdiction of the Carle IRB.				
Purpose	To provide information about investigations involving drugs, devices and biological products.				

Statement of Policy

1. All human subjects research utilizing investigational drugs, devices, or biological products, or research in which it is reasonably anticipated data will be provided to the Food and Drug Administration (FDA) will also be known as clinical investigations and will be conducted in accordance with both HHS and FDA regulations, and policies of Carle Foundation Hospital and the Carle IRB. The regulatory requirements for studies involving drugs, devices, and biological products are specific and complex; contact the Carle IRB for assistance with this process. Failure to comply with this or any Carle IRB policy can result in termination of research privileges; see IRB General Administration Policy 101 Compliance with Policies and Procedures Mandate.

Specific Policies

1. **Definitions** – Consistent with federal regulations, the following definitions apply to this policy:
 - a. Under FDA regulations, the terms “research” and “clinical investigation” are synonymous and are defined as any experiment that involves a test article and **one or more** human subjects, **and** that is one of the following:
 - Subject to requirements for prior submission to the FDA under section 505(i) or 520(g) of the Federal Food, Drug, and Cosmetics Act as amended (the FDCA); or
 - Not subject to the requirements for prior submission to the FDA under the Act, but the results of which are reasonably anticipated to be later submitted to, or held for inspection by the FDA.
 - b. A “test article” is defined as any drug, 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 the Act or under relevant sections of the Public Health Service Act. [21 CFR 50.3]
Test articles include articles approved for marketing but which are undergoing evaluation (a) for different indications; (b) in a different population; (c) using different dosages; (d) in combination with other drugs or devices, the use of which has not previously been approved by the FDA; (e) for different means of administration (e.g., IV versus p.o.); or (f) for any other change in use that would, if accepted and approved by the FDA, lead to changes in labeling, advertising, or promotion.
 - c. The term “sponsor” means a person who takes responsibility for and initiates a clinical investigation. The sponsor may be an individual or company, governmental agency, academic institution, private organization, or other organization. The sponsor does not actually conduct the investigation unless the sponsor is a sponsor-investigator.
 - d. The term “sponsor-investigator” means an individual who both initiates and conducts an investigation, and under whose immediate direction the test article is administered or dispensed. The requirements applicable to a sponsor-investigator include those applicable to both an investigator and a sponsor.
 - e. The term “investigator” means an individual who actually conducts a clinical investigation. In the event an investigation is conducted by a team of individuals, the investigator is the responsible leader of the team.
2. **Applicability of FDA and HHS Regulations** Clinical investigations shall comply with all relevant FDA and HHS regulations.
3. **IRB Review**
 - a. Except as otherwise provided in these policies, all clinical investigations must be reviewed and approved by the Carle IRB prior to commencement of research activities. Exemptions permitted under 45 CFR 46 do not apply to clinical investigations.
 - b. **For drug studies**, a clinical investigation is any experiment in which a drug is administered, dispensed to, or used involving **one or more** human subjects. [21 CFR 312.3(b)]
 - An investigational new drug (IND) application must be filed when a sponsor wishes to test a new drug; generate data for a new advertising claim, a new clinical indication, or a new formulation of a drug; or modify a study design, subject group, or clinical indication for a drug under study but not yet marketed. The IND rules apply to all clinical investigations of products subject to sections 505 or 507 of the FDCA or to the licensing provisions of the Public Health Service Act.

Specific Policies (cont.)

- The use of an experimental (nonmarketed, non-FDA-approved) drug in clinical practice, even on a single patient, qualifies as a clinical investigation and requires an IND and prior IRB approval. This helps ensure quality control and centralized data and safety monitoring.
 - An “emergency use IND” allows the one-time use of an experimental drug under prescribed circumstances. See IRB Policy 410 for details.
 - A “treatment IND” is a special IND that allows the use a drug currently undergoing FDA review for serious or immediately life-threatening conditions for which no alternative therapy exists, with the aim of accelerating access to the drug. [21 CFR 312.34 and 312.35]
 - The “off-label” use (for an indication other than the approved one) of a marketed (FDA-approved) drug, by a physician treating a single patient is permitted without an IND. However, if a physician uses a drug off-label in a systematic way with intent to generalize the results, this would constitute human subjects research requiring an IND and prior IRB approval.
- c. **For device studies**, a clinical investigation is research involving **one or more** subjects to determine the safety or effectiveness of a device. [21 CFR 812.3(h)]
- An investigational device exemption (IDE) application must be approved by the FDA prior to a clinical investigation with a device. The device must be categorized as either significant risk or nonsignificant risk; this determination is initially made by the sponsor and must be approved by the IRB. A significant risk device [21 CFR 812.3(m)] is one that is
 - Intended to be used as an implant; or
 - To be used in supporting or sustaining human life; or
 - For a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health; or that
 - Otherwise presents a potential serious risk to the health, safety, or welfare of a participant.If the IRB determines that a device previously characterized as a nonsignificant risk device is to be characterized as a significant-risk device, the IRB shall inform the investigator and the sponsor in writing of such determination.
- d. When reviewing a protocol, the IRB shall determine whether investigational new drug (IND) or investigational device exemption (IDE) requirements must be met. If it is determined that IND and/or IDE requirements apply, the protocol shall not be approved until such time as the IRB is provided a copy of a valid IND and/or IDE, as appropriate.
- e. Any change in an investigational plan or protocol shall be approved by the IRB prior to implementation. Deviations from protocol for emergency purposes or to avoid imminent harm to a participant must be promptly reported to the Carle IRB in sufficient detail to permit the IRB to evaluate the event and any need for a change in protocol. No other deviations from the protocol are permitted without prior approval.
- f. The IRB shall oversee and monitor all clinical investigations in accordance with federal laws and regulations and these policies, and may require continuing review at any appropriate interval.
4. **Conduct of Clinical Investigations**
- a. **General Principles** A clinical investigation shall be conducted in accordance with the investigational plan/protocol approved by the IRB, the signed agreement with the Sponsor, and applicable regulations.
- b. **Control of the Test Article**
- **The investigator is responsible** for assuring control of the test article in accordance with federal regulations, other applicable laws (e.g., the Controlled Substances Act), sponsor requirements, and the IRB-approved protocol. Research staff at Carle may be involved with storing, handling, dispensing, accounting, accessing, and securing test articles, as appropriate. The investigator is ultimately responsible for assuring that the procedures followed are in compliance with all applicable policies, regulations, laws, and guidelines.
 - **Administration and/or Implantation of a Test Article** Investigational drugs shall be administered only by or under the personal supervision of the investigator, or under the direct supervision of an approved sub-investigator, and then only to individuals who are participating in the study and have signed a study informed consent form, unless a waiver of documentation of consent or waiver of consent has been approved by the Carle IRB. An investigational device shall be implanted only under the investigator's supervision.
 - **Disposition of Unused Test Articles** The sponsor shall assure the return of all unused supplies of an investigational drug or device from each individual investigator whose participation in an investigation is discontinued or terminated.

Specific Policies (cont.)

- c. **Recordkeeping** All investigators, sponsors, and sponsor-investigators conducting research with test articles under the Carle Foundation Hospital Federal Wide Assurance shall maintain and retain complete and accurate records and reports in accordance with these policies and federal regulations. This includes but is not limited to
- All correspondence with other investigators, IRBs, sponsors, monitors, the FDA, and others, including required reports;
 - Records related to the receipt, use, disposition, or return of test articles;
 - Records of each subject's case history;
 - Documents evidencing informed consent;
 - Observations and records concerning adverse effects and events, whether anticipated or not;
 - The research protocol with amendments, addenda, and updates;
 - Complete records and documents related to deviations from protocol;
 - Any other records required under these policies, FDA regulations, or HHS regulations.
- d. **Reports to Sponsor** Investigators shall provide timely, accurate, and complete information to the sponsor regarding the conduct of a clinical investigation, to permit the sponsor to prepare and submit required reports to the FDA. Upon completion of the clinical investigation, investigators shall submit timely, accurate, and complete reports regarding their conduct of the clinical investigation, as required by applicable laws, regulations, and these policies.
5. **Interactions with FDA** For clinical investigations falling under the jurisdiction of the FDA, investigators shall upon request from any properly authorized officer or employee of FDA, at reasonable times, permit such officer or employee to have access to, and copy and verify any records or reports relating to the clinical investigation. This includes inspection of any establishment where devices are held, manufactured, processed, packed, installed, used, or implanted or where records of results from use of devices are kept. If the clinical investigation is being conducted, or if records are retained, at a Carle Foundation Hospital facility, the investigator shall advise the appropriate research coordinators and the Carle IRB of the FDA's request, and cooperate with them to facilitate the appropriate scheduling and coordinating of the inspection. If the FDA requests review of any records or information held by the Carle IRB, the investigator shall promptly notify the Carle IRB of that request and cooperate with the IRB to facilitate the appropriate scheduling and coordinating of the inspection.

Reference

45 CFR 46, 21 CFR 56, ICH – Good Clinical Practices

Approval On File

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