

The Carle Foundation

IRB Policy 404

Subject	Continuing Review				
Approval	Dec 2006	Review	Apr 2011	Revision	Apr 2011
Purpose	To provide guidance in conducting continuing reviews of approved research under the jurisdiction of the Carle Institutional Review Board (Carle IRB).				

Statement of Policy

1. The Carle IRB conducts continuing review of research taking place within its jurisdiction at intervals appropriate to the degree of risk, at least once per year.
2. Interval for Review for Purposes of Renewal
 - a. The Carle IRB must conduct continuing review of protocols, for purposes of renewal, of the Carle IRB approval period, at intervals appropriate to the degree of risk. All human subject research studies which are conducted at The Carle Foundation or any other entity for which the Carle IRB serves as the reviewing IRB shall be subject to continuing review, regardless of type of study or funding. The frequency of continuing review will be determined at the initial review. Each study will be reviewed at least once per year. Continuing review must occur within one (1) year of the date of the last approval of the study. The Carle IRB may increase the frequency of review at any time. In determining the frequency of review, the Carle IRB shall take into consideration:
 - The experience of the Investigator(s)
 - The risk posed by the study
 - The vulnerability of study participants
 - Other concerns, as identified by the Carle IRB.
 - b. The frequency of continuing review shall be indicated in the Carle IRB approval or re-approval letters. Frequency of review may be modified by the Carle IRB based on:
 - Number and type of serious adverse events
 - Number and type of unexpected adverse events
 - Number and type of unanticipated problems
 - Reports of concerns regarding the study of the Investigator
 - Changes to the protocol
 - Significant new information, including reports related to similar research at other facilities.
 - c. Principal Investigators or qualified designees are required to submit a Continuing Review Form prior to the expiration of the study or as specified by the Carle IRB, but at least annually. The Continuing Review Form should normally be filed two Carle IRB meetings before the study approval period ends. No study shall be accepted for continuing review unless all required forms and information has been submitted. The Human Subject Protection Office staff shall document and track a study's initial approval and expiration dates.
3. Criteria for Renewal
 - a. Continuing Review must be substantive and meaningful. When discussing whether or not to approve a continuing study, the proper quorum of the Carle IRB at a convened Carle IRB meeting considers the same criteria used to grant initial approval and reviews the appropriate documentation (see Section 4 below). The type of review the protocol will undergo (Full committee or Expedited review) will be determined once a complete Continuing Review submission is received.
 - The Carle IRB must approve **each version** of the protocol, and during Continuing Review, at least one member of the Carle IRB should receive a copy of the complete protocol, including any modifications previously approved by the Carle IRB.
Because it may be only after research has begun that the real risks can be evaluated and the preliminary results used to compute the actual risk/benefit ratio; after reviewing information regarding the conduct of the study to date, Carle IRB can then determine whether or not the risk/benefit ratio is substantially the same, or if new information has changed that determination.
 - Designation of Primary Reviewer(s): The Carle IRB may approve designation of primary reviewer(s) for continuing review of each protocol in accordance with Carle IRB Policy 302--IRB Meeting Administration. Although the primary reviewer(s) may present to the Carle IRB an initial, detailed review of the proposed continuing study, the Carle IRB must independently approve such protocol (e.g., the Carle IRB members cannot merely accept the recommendations of a subcommittee). Prior to the meeting, all Carle IRB members

Statement of Policy (cont.)

must receive and review at least the documents listed at Section 4.a. below, and other research documents must be made available if requested. A proper quorum of the Carle IRB must review the materials received and make a determination with recorded vote, documenting the full Carle IRB meeting discussion and vote.

4. Information to be Reviewed

- a. In order to evaluate a study for renewal of approval, the Continuing Review Form and all required supporting documents must first be submitted and such documentation must be maintained in accordance with Carle IRB Functions and Operations Policy 303 Documentation and Document Management.
 - Consent Document. The currently approved consent document shall be reviewed to ensure that the information is still accurate and complete. The Investigator shall advise the Carle IRB in writing whether he/she believes new findings that may relate to the subject's willingness to continue participation have developed, and whether any additional or revised information should be provided to subjects in an updated consent document.
 - Current approved protocol including any amendments to the protocol since initial review: Amendments and addenda to a research protocol must be approved prior to implementation. A separate cover letter describing in detail each change and all appropriate documentation (a copy of an approved consent form and Carle IRB approval letter, as well as any documentation explaining the reason for the change(s)) must accompany the continuing review application.
 - Continuing Carle IRB review is required as long as individually identifiable data are collected or analyzed. This remains the case even after a protocol has been closed at all sites and protocol-related treatment has been completed for all subjects.
 - Continuing review of Data Safety Monitoring Board/Data Monitoring Committee ("DSMB/DMC")-monitored clinical trials: When a clinical trial is subject to oversight by a DSMB or DMC whose responsibilities include review of adverse events, interim findings and relevant literature, in conducting continuing review, the Carle IRB may rely on a current statement from the DSMB/DMC indicating that it has reviewed study-wide adverse events, interim findings and any recent literature that may be relevant to the research, in lieu of requiring that this information be submitted directly to the Carle IRB. However, the Carle IRB must still receive and review reports of local, on-site adverse events, serious adverse events, or unanticipated problems involving risks to subjects or others and any other information needed to ensure that its continuing review is substantive and meaningful. The Carle IRB has the right and authority to decline to approve a renewal or continuation application regardless of the conclusions of the DSMB/DMC.
 - Progress Report. Each Carle IRB member shall receive and review a protocol summary and a progress report prepared and submitted by the Investigator which sets forth clearly:
 - The number of subjects accrued to date and since the last review;
 - Adverse event experience summary [HSP Office staff shall verify the number of adverse events reported by the investigator];
 - Unanticipated problems involving risks to subjects or others;
 - Withdrawal of subjects since last review;
 - Complaints about the study since the last review;
 - A summary of recent literature relevant to the research;
 - Amendments, changes in personnel, training of personnel and new COI disclosure as applicable;
 - Updated assessment of the risk-to-benefit ratio which takes into account the above factors.
 - Grant applications will be reviewed by the HSP Office to verify that there have been no changes.
 - Documentation of appropriate Investigator training which meets the requirements of these Policies and any applicable grant requirements must be submitted with the continuing review materials.
 - Significant New Findings. Any statements of significant new findings provided to subjects during the course of the study will be reviewed.
 - Checklists. Checklists will be used to assist the Carle IRB in the Continuing Review process.

5. Expedited Continuing Review

- a. Expedited continuing review is permitted for the continuing review of minimal risk research as described in Office for Human Research Protections Guidance on the Use of Expedited Review Procedures dated August 11, 2003. Expedited review categories 1 through 9 as described in Carle IRB Policy 401 apply to continuing reviews and the applicability of one or more of these category (ies) shall be documented in the review procedures used.
- b. Category 8 for continuing review of research: research previously approved by the Carle IRB, even if the research was greater than minimal risk, if:

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- The research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or
 - No subjects have been enrolled and no additional risks have been identified at the local or another site; or
 - Remaining research activities are limited to data analysis.
- c. Category 9 for continuing review of research: research not conducted under an investigational new drug application or investigational device exemption, where the categories 2 through 8 do not apply but the Carle IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.
- d. Expedited continuing review of research/treatment involving Humanitarian Use Devices (HUD): Expedited continuing review of research involving HUD is permitted when the study is initially approved by the full IRB and the IRB has determined that expedited review is appropriate for subsequent reviews and approvals.

6. Possible Outcomes of Continuing Review

As an outcome of continuing review, the Carle IRB may renew approval of the study, or require that the research be modified or halted altogether. The Carle IRB may impose special precautions or relax special requirements it had previously imposed on the research protocol. Future continuing review may be required annually or more frequently, based on an evaluation of the risks. Investigators shall permit audits of the approved research by auditors, HSP staff or agents thereof. Refusal to permit access to research-related documents will be grounds for suspension and possible termination of the Carle IRB's approval of the research. Any decision of the Carle IRB to suspend or terminate the study shall be reported in accordance with Carle IRB policies.

7. Lapsed Study

When a study has lapsed, research activity may occur on the date of expiration as granted on the previous approval letter; however, all research activity must stop from the day after the date of expiration. Conducting research activities on a lapsed study constitutes noncompliance with these policies and other applicable regulations. Continued and/or serious noncompliance is a reportable offence and will be reported to the Institutional Official and then to the Office for Human Research Protections as required. The expiration notifications sent out via IRBNet or from the Carle Human Subject Protection Office are only to serve as reminders and it is the responsibility of the Principal Investigator to ensure that Carle IRB approvals for their studies do not lapse. If an Investigator wishes to pursue the lapsed study, he/she must complete an initial review form and submit all necessary documents to the Carle IRB for review.

Definitions

Human Subjects Protection Office (HSP) – Human Subjects Protection office at Carle, which supports the Carle IRB administratively.

Institutional Review Board (IRB) – Means any board, committee, or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodic review of, biomedical research involving human subjects. The primary purpose of such review is to assure the protection of the rights and welfare of the human subjects.

Principal Investigator – The investigator/researcher who is responsible for the conduct of a research study at an institutional site.

Procedures

1. All human subject research under the oversight of the Carle IRB must be submitted to the Carle IRB via IRBNet for continuing review at the interval determined by the Carle IRB, at least once a year.
2. Extensions of Approval Period – **There is no grace period** extending the conduct of the research beyond the expiration date of Carle IRB approval if the Continuing Review Form and other requested documents are not received as scheduled. Extensions beyond the expiration date **will not** be granted and a previously approved study for which Carle IRB approval has expired will be a lapsed study and will be closed by the Carle. The Principal Investigator **must stop all non exempt research activities**. If a Principal Investigator wishes to pursue the study, he/she must complete an initial review form and submit all necessary documents to the Carle IRB.
 - a. Once approval of a study has lapsed, the Principal Investigator must cease all non-exempt research activities involving human subjects related to that study. Prospective research data cannot be collected, and no protocol-specific procedures may be performed.
 - b. The Principal Investigator may determine that it is in the best interest of previously enrolled study subjects to continue participation and promptly recommend that the Carle IRB continue the study; but the Carle IRB must review and approve such recommendation. Exceptions to this policy must include all of the items listed below to ensure patient safety:
 - The Principal Investigator is in communication with the Carle IRB;
 - Sufficient information regarding renewal and the risks and benefits of continuing the intervention is provided;
 - The Continuing Review Report or other report is forthcoming; and

Procedures (cont.)

The Carle IRB determines, after considering all the facts, that it is in the best interest of subjects participating in the study to continue participating in the research interventions or interactions either one at a time or as a group. The intervention may continue for the shortest possible time until:

- The study is re-approved.
 - The study is suspended or terminated; or
 - An alternative Investigator is identified and the conduct of the study under the supervision of that Investigator is approved by the Carle IRB.
 - In the event the study is terminated or suspended, the Investigator shall cooperate with the Carle IRB in assuring a safe transition of care for study subjects, including, if appropriate, weaning from the study intervention. In no event may new subjects be enrolled if approval has expired, suspended or terminated.
- If the Carle IRB determines that it is not in the best interests of already enrolled subjects to continue to participate, investigators must stop all human subjects research activities, including intervening or interacting with subjects, or obtaining or analyzing identifiable private information about human subjects.

3. Review of Continuing Review Submissions by the Carle IRB

a. Intake and Pre-Review by HSP Office

- The HSP staff reviews the continuing review submission for completeness according to HSP procedure 100 and 101. If necessary, the HSP staff may contact the Principal Investigator for further explanation for incomplete submission or those requiring modification or additional information.
- Once the HSP staff has determined that a continuing review submission is complete, they may complete the “pre-reviewer’s checklist” section of the “Reviewer’s Worksheet for Research Study” in order to document their pre-review of study materials.
- The HSP staff then shares the continuing review with the Carle IRB chair or designee for all expedited reviews (HSP Procedure 102) and with all IRB members for full board reviews (HSP Procedure 103) via IRBNet.

b. Conducting Expedited Review for Continuing Review Submissions

- Continuing Review submissions that qualify for expedited review will be reviewed in accordance with Carle IRB Policy 401—Expedited Review.

c. Conducting Full Board Review for Continuing Review Submissions

- Continuing Review submissions that must be reviewed by the convened Carle IRB will be reviewed in accordance with applicable HHS and FDA regulations as well as applicable Carle IRB policies, given the type of study that will be reviewed. Additionally, the HSP office will follow its internal procedure for assisting the Carle IRB in its conduct of full board reviews.

References

OHRP Guidance on the Use of Expedited Review Procedures dated August 11, 2003

www.hhs.gov/ohrp/humansubjects/guidance/expedited98.htm

www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/default.htm

45 CFR 46

21 CFR 56

Carle IRB Policies

Electronic Approval on File

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