

The Carle Foundation Research Policy 104

Subject	Carle Scientific Review Committee				
Approval	Apr 2008	Review	Aug 2009	Revision	Aug 2009
Purpose	The Scientific Review Committee reviews all research proposals for studies which will be conducted in part or in whole at Carle Foundation Hospital. Protocols include, but are not limited to research in the areas of translational, aging, oncology, cardiovascular, gastroenterology, genomics, and medical informatics.				

Abbreviations

CFH – Carle Foundation Hospital

IRB – Institutional Review Board

SRC – Scientific Review Committee

Primary responsibilities of the Scientific Review Committee at CFH

1. Evaluate new research proposals for its scientific quality and merit including, but not limited to experimental design, statistical analysis, number of subjects, frequency of these subjects enrolled, and potential scientific impact.
2. Evaluate new research study proposals for the utilization of CFH resources and services.
3. Evaluate if the new research study proposals are within the priority research areas of CFH.
4. Evaluate the potential long-term beneficial impact of the new research proposals on patient care at CFH.
5. Evaluate ongoing research studies annually, or more frequently if needed, to ensure continued scientific quality and feasibility of continuation of the study at CFH.

Composition of the Scientific Review Committee

1. The Scientific Review Committee (SRC) is composed of a broad range of scientific and clinical specialties as well as administrative areas to ensure a thorough review and proper use of resources and services for all research studies conducted at CFH.
2. The core of the SRC consists of
 - a. Chair
 - b. Co-Chair (a Research Office member)
 - c. Administrative Coordinator (Research Office Office Coordinator)
 - d. Data and Safety Monitor(s)
 - e. Biostatistician(s)
 - f. Nurse(s) in Research
 - g. Basic Scientist(s)
3. Depending on the focus of the proposed research study, at least one expert member from a clinical specialty area below will be required to review the proposed study and attend the SRC meeting when that proposed study is discussed:
 - a. Oncology/Hematology
 - b. Gastrointestinal
 - c. Genetics/Genomics
 - d. Stem cells
 - e. Cardiovascular
 - f. Imaging
 - g. Medical Informatics
 - h. Pathology
 - i. Database
 - j. Other: as required, see below
4. Other expert members with specific areas of expertise may be invited to selected meetings by the Chair to review study protocols involving subspecialty areas not adequately represented in the regular SRC composition.
5. A list of current SRC members will be available upon request and will be posted on the Research Institute website at CFH.

Criteria for Selection of Membership to the Scientific Review Committee

1. The SRC will consist of many areas of specialties. Members can be affiliated with CFH, Carle Clinic Association, the University of Illinois or other institutions as needed for the SRC to conduct a thorough review of the proposed research studies. Members will be appointed by the Executive Director of the Research Institute at the CFH. Before a member can serve on the SRC, he/she will need to go through basic training and sign a personal Appointment Agreement. For each specified research area there will be at least one member but aiming to have two or more members in each area so that not all members have to attend each monthly meeting.
 - a. **Voting Members**
 - The SRC will contain members from a variety of specialty areas and the representative(s) of each specialty area may vote on the proposed study if present at the meeting. Only the person(s) who does the statistical analysis can be absent from voting as long as a written evaluation including a vote of each protocol is submitted no later than the Friday before the monthly meeting.
 - In order for quorum to be achieved, at least four voting members need to be present along with the written statistical evaluation at each SRC monthly meeting. Voting cannot take place on the proposed research studies reviewed that month without a quorum.
 - The Chair or a designee assigns each protocol a primary and a secondary reviewer among the members. A statistical analysis is always done for a full board scientific review, and if the statistician cannot be present at the meeting, a written review and vote needs to be submitted to the Chair prior to the meeting. At the meeting the primary reviewer gives a brief overview of the study and its strengths and weaknesses followed by the secondary reviewer before the protocol is open for discussion. Each study protocol is voted on individually. If any of the SRC members are involved in that research he/she cannot vote on that protocol since that would be considered a conflict of interest.
 - b. **Non-voting Members**
 - The Chair, Co-Chair, Database expert, and Administrative Coordinator are non-voting members of the Research Office, and the Data and Safety Monitor is from the Compliance Office. The Chair cannot vote regarding the approval of a protocol unless required to break a tie. Other staff at the Research Office and the Human Subject Protection may become members of the SRC as non-voting members if appointed by the Executive Director of the Research Institute at CFH.
 - c. **Length of Term**
 - For all voting members the term consists of two years. There is no limitation to the numbers of terms one member can serve. Appointments and re-appointments are done by the Executive Director of the Research Institute at CFH. If the Chair determines that a member is not following the Appointment Agreement, he/she will address it with the member and give him/her the option to continue or terminate the Appointment Agreement. The termination letter should be sent to the Chair on letterhead. If the Chair feels that a member is not capable of doing his /her job as a member, the Chair can terminate the Appointment Agreement in writing after consultation with the Executive Director of the Research Institute.
 - d. **Criteria for Selection and Duties of the Chair**
 - The Chair of the SRC is appointed by the Executive Director of Research Institute at CFH. The Chair cannot be assigned as a primary reviewer for a research protocol, and he/she does not vote regarding the approval of a protocol unless required to break a tie. The Chair oversees the SRC meetings to ensure consistent and fair operation and deliberations. He/she communicates with the principal Investigators regarding outstanding issues from the protocol review to protect the anonymity of the reviewers.
 - e. **Selection and Duties of the Co-Chair, Database Expert, Data and Safety Monitor, and the Administrative Coordinator**
 - Except for the Chair, all non-voting members are appointed by the Executive Director of Research Institute at CFH. The Co-Chair, Database Expert and Data and Safety Monitor cannot be assigned as a primary reviewer for a research protocol. The Co-Chair does not vote except when he/she assumes the role as the Chair in a tiebreak when the Chair is unable to attend (see above for the role of the Chair). The Administrative Coordinator is a non-voting member and cannot review research proposals. The Administrative Coordinator is responsible for making the agenda and recording the minutes at the SRC meetings. Minutes of each meeting are sent out via email to the voting members present at that meeting. The voting members vote and/or makes suggested corrections and send the email back to the SRC chair or designee. The Database Expert will provide his/her expertise on creating database when requested by the Chair. The Data and Safety Monitor is a non-voting member who will attend all convened meetings and provide compliance input, as needed, to help the reviewers understand the relative risk of conducting the proposed study.
 - In the event that the Chair and Co-Chair are unable to attend, an Acting Chair is designated among the voting members.

Criteria for Selection of Membership to the Scientific Review Committee (cont.)

f. Education

- All members of the SRC must have a basic understanding of scientific and clinical research design, procedures, and how a research study is conducted. A basic training will be completed by each member before they can sign the Appointment Agreement and serve on the SRC. Continuing education will be required by the members when the Chair determines it necessary.

g. Appointment Agreement

- Before serving as a voting member of the SRC, each person must sign a personal Appointment Agreement. By signing the agreement they agree to thoroughly review an assigned protocol. Only after they fully understand the proposed research will they recommend this study feasible or not to conduct at CFH. If the voting member is reappointed after two years, a new contract must be signed. Non-voting members must also sign an Appointment Agreement to be able to serve as a member on the SRC.

h. Compensation

- Voting members will be compensated at a rate of \$200.00 for each meeting attended. The biostatistician(s) will be compensated for the reviews submitted.

Types of Reviews

1. Regardless of the study protocol type, no research proposal that qualifies for review by the SRC will be submitted to the Carle Institutional Review Board (IRB) until the SRC approves the study. There are two types of review, full or expedited review.
2. Some studies qualify for expedited review by the SRC. Expedited review is conducted by the Chair or a designee. Below are the types of studies that qualify for expedited review:
 - a. Retrospective research that is IRB – exempt.
 - b. Retrospective research that is IRB – expedited and does not require CFH resources other than by the investigators.
 - c. Studies that do not use any CFH Resources.
 - d. NIH Cooperative Group Studies that will be completely conducted at the Carle Cancer Center with no involvement of CFH resources.
3. Approved federal grants, already peer-reviewed such as NIH funded studies, will only undergo Carle feasibility review by the full SRC.
4. All other studies require a full scientific and feasibility review by the SRC. In some cases, an exception can be granted by the Chair of the SRC to enable a concurrent IRB submission, see section “Grant Submission- special circumstances for select protocols”, section 16.

Criteria and Process for Submission of New Protocols for Review

1. The review process, criteria for approval, process for submission of study protocols for review, and approval, varies depending on whether the study protocol has been previously externally peer-reviewed or not. Other types of protocols may be exempt from a full SRC review depending on the scope and purpose of the study.
2. **Externally Peer-Reviewed Study Proposals** – This includes study proposals which have gone through peer-review by a federal granting agency such as all NCI Cooperative Group studies (SWOG, RTOG, NSABP, etc) and other federal granted studies:
 - a. **Cooperative Group Studies**
 - National cooperative group studies undergo exhaustive scientific review with regard to background and biostatistical design. As a result, formal full review by the SRC at CFH is unnecessary. However, the study proposal must be submitted to the SRC so that it can undergo a review focusing on the feasibility of conducting the study at CFH. If the Cooperative Group Study will be completely conducted at Carle Cancer Center the study will go through expedited review by the Chair. All other Cooperative Group Studies will be reviewed by the SRC, with the review focused on utilization of CFH resources, anticipated accrual to the study, and whether the study competes with open or pending studies. The reviewers recommend approval for the study where no direct competition exists or in situations where the Cooperative Group study will replace an existing closing study. Studies that fail to gain approval by this mechanism may be submitted for formal scientific review as a process of appeal.

Criteria and Process for Submission of New Protocols for Review (cont.)

b. Federal Granted Studies, already Peer-Reviewed

- Per National Cancer Institute guidelines, clinical protocols incorporated as part of a federal agency-sponsored research do not require additional review by the SRC for scientific merit or biostatistical design. In order to meet these criteria, clinical protocols must be peer-reviewed by a federal agency where review of the *clinical protocol* is included in the review, for example, R01 grants awarded specifically for clinical research. *Clinical protocols that are not reviewed as part of the study section review process must undergo full SRC review.* For example, P01 or P50 grants awarded for disease-oriented research that generate clinical trials as a Specific Aim of the project(s). Study protocols from federal grants that meet this peer review criteria will only go through feasibility review by the SRC, with the review focused on utilization of CFH resources, anticipated accrual to the study and whether the study competes with open or pending studies. The reviewers recommend approval for study where no direct competition exists or in situations where the study will replace an existing closing study. The study approval is incorporated into the minutes at the next scheduled SRC meeting. Studies that fail to gain approval by this mechanism may be submitted for formal SRC review as a process of appeal.

c. Non-Externally Peer-Reviewed Study Proposals

- Protocols without external peer-review may include investigator-initiated studies or sponsor-initiated studies. All non-federal peer-reviewed research study protocols require full review by the SRC for scientific design, integrity, research value and feasibility.
- Project Protocols Exempt from Scientific Review Committee Review
 - *Protocols Intended for Treatment Only:* Research protocols commonly referred to as "treatment protocols," in which the purpose of the protocol is simply to provide a standardized treatment plan are not reviewed by the full SRC. An example of this type of protocol includes standard-of-care protocols for bone marrow transplants where data collection in terms of numbers of patients and survival are needed for National Marrow Donor Program registration.
 - *Single Patient Use (Compassionate Use) Protocols:* Single patient (compassionate) use of a test agent is allowed by the Carle IRB under certain circumstances. Review of these non-research proposals are not under scope of the SRC.

3. **Grant Submission-special circumstances for select protocols:** It is recognized that submission of research grants for peer-reviewed funding may require Carle IRB review and approval prior to the planned initiation of the study. For these studies, full SRC review must be undertaken since use of the shared facilities will be utilized. However, at the discretion of the SRC Chair, studies may be forwarded directly to the Carle IRB prior to SRC review when an unreasonable deadline for Carle IRB approval has been imposed by a granting agency. Concurrent SRC review will commence at the next available opportunity. All protocols that require Carle IRB approval must still be routed through the Research Office and have an assigned Research Coordinator.

a. Submission Process

- The SRC meets on the fourth Wednesday of the month. Exceptions to the regular meeting schedule will be announced in advance on the SRC website. A listing of SRC submission deadlines and meeting dates are circulated on an annual basis and are posted on the SRC website. That website is located under Research Institute on the CFH website. There is no full review of study proposals outside the scheduled meetings. ***The submission deadline for review of new protocols and revisions is noon on the second Friday of the month.***
- The principal investigator must submit a complete study protocol package via the IRBNet (with assistance by an assigned Research Coordinator from the Research Office) to the SRC for review of any new protocol. The following documents are needed before a scientific review can occur:
 - Study Protocol (including final budget* and budget justification)
 - Informed Consent Form*
 - IRB Application
 - IRB Registration Form

*All submitted protocols must be in final format. No drafts or pre-finalized versions are accepted. If a submission does NOT include a completed Study Protocol, Informed Consent Form (when applicable) or Scientific and Feasibility Review Form it might be rejected.

- The assigned Research Coordinator from the Research Office will provide the following to the SRC:
 - Approval from Carle departments to participate in the proposed project

Criteria and Process for Submission of New Protocols for Review (cont.)

b. Review and Approval Process

- The submitted Study Protocol, Informed Consent Form, and Application for Scientific and Feasibility Review are held on IRBNet. All members assigned to the upcoming meeting can access this website to see what study proposals are up and coming. A primary and a secondary reviewer are assigned to each study by the Chair; the reviewers will be notified via email from the IRBNet website. Every study is also reviewed by a biostatistician. A member with conflict of interest regarding a specific study (such as being a study investigators or co-investigators in that study) cannot serve as reviewer nor can he/she vote on that study proposal.
- The primary reviewer is responsible for presenting and facilitating discussion of the study. Additional comments and critique are supplemented by the secondary reviewer and other committee members during the next SRC meeting. Minutes of the meeting, comments, and project review evaluation forms are submitted by all reviewers for official files.
- Areas reviewed on the Scientific and Feasibility Review Form includes:
 - PI and Co-PIs Training and Experience
 - Scientific and Medical Information
 - Study Design
 - Statistical Analysis
 - Study Methods
 - Benefit to Society as a result of Conducting this Study
 - Resources
 - Budget
 - Is there a Reason this Study should not Move Forward?
 - Overall Rating
- Voting Rules:
 - Quorum must be met before any voting can take place.
 - A priority score is calculated from the completed Scientific and Feasibility Review Form that is used as reference for allocating shared resources of the CFH.
 - The Principal Investigator is encouraged to attend the SRC meeting during the discussion of his/her protocol but must leave before deliberation and voting.
 - A majority vote rules for all SRC decisions.
 - Should a voting member also be an investigator on the protocol up for vote, he/she must leave the room before voting, and his/her vote is recorded as an abstention.
- Each principal investigator is notified of the outcome of the study protocol review within 2-4 working days, to facilitate response to specific criticisms or questions detailed in the written report.

c. Approval Categories

- **Approved for IRB Submission:** Comments may or may not be included in the letter sent to the Principal Investigator. Response from the Principal Investigator is not required. The study package with all documents is forwarded to the Carle IRB by the SRC Chair or a designee.
- **Revise and Resubmit:** Required specific changes to the study protocol or study documentation are indicated in detail in the letter sent to the Principal Investigator. The response from the Principal Investigator is reviewed by the SRC if the study was reviewed by the full committee or by the Chair, or a designee, if the study qualified for an expedited review or if the SRC determines that any modifications required do not warrant a full board review. The outcome is fully dependent on the re-review but comments will be limited to items in the initial review unless significant additional deficiencies are discovered. Upon approval, the study package with all documents is forwarded to the Carle IRB by the SRC Chair or a designee.
- Examples of deficiencies leading to this outcome include:
 - Insufficient justification information in the "Background" section of the protocol to support conduct of the study. If the SRC determines that this information is incomplete or that there is insufficient preclinical or clinical data to warrant conduct of the study being proposed, the protocol is tabled until required material is provided.

Criteria and Process for Submission of New Protocols for Review (cont.)

- Insufficient justification in addressing primary objectives of the study: This could be a result of inadequate biostatistical design, faulty study design or an improper/inadequate data collection design.
- Significant scientific and/or regulatory revisions. This outcome necessitates a second full review by the SRC.
- **Not Approved:** Permanent rejection with specific reasoning provided in the letter to the Principal Investigator. This protocol is ineligible for usage of shared resources. The investigator's departmental chair is notified of the SRC's decision. A rejected protocol can be appealed by resubmission of the study with strong justification for the appeal. Factual errors or omissions will be considered as grounds for appeal. "Strong feelings" by the Principal Investigator are not considered adequate grounds for appeal.

Protocol Monitoring

1. Protocol Monitoring

a. Continuing Review of Approved Study Proposals

- The approval for each study by the SRC is reviewed annually, often via expedited review by the Chair or a designee if the study design has not been altered greatly or if the recruitment is progressing well. This review occurs simultaneously with the Carle IRB's annual review of this same study and can therefore vary some in time. The SRC reserves the right to request review of a protocol on a more frequent basis. Annual reviews for all protocols are reviewed by the Chair of the SRC Chair or a designee. If, in the opinion of the Chair, the study up for continuing review has NOT been significantly altered in regards to the scientific validity of the study, the annual review is forwarded directly to the Carle IRB. If the Chair determined that the study design has been altered greatly, the recruitment is slow or any other major concerns, the study is assigned a primary, secondary and biostatistical reviewer and sent to full SRC review at the next convened meeting. Only protocol reviews whose continuing approval is in question will be brought to a vote before the full committee. By a majority vote, the protocol is either re-approved or termination recommended. A written letter is forwarded to the principal investigator stating questions or criticisms concerning the progress of the study.

b. Amendments of Study Protocols

- For studies that have previously undergone full board review, amendments that significantly alter the study design must be reviewed by the full SRC primarily to evaluate adherence to the original study scientific design, scientific quality and feasibility of conducting the altered study at CFH. After the amendment is received by the Research Office, amendments are forwarded to the SRC Chair, who determines whether the amendment alters the scientific merit of the study. If the Chair decides that, in his/her opinion, the amendment significantly changes the scientific validity of the study, the amendment is forwarded to the full SRC for review. If, in the opinion of the Chair, the amendment does NOT significantly alter the scientific validity of the study, the amendment is forwarded directly to the Carle IRB. For those amendments forwarded to the full SRC, protocols that are "not externally peer-reviewed" are circulated to all members and assigned a primary, a secondary and a biostatistical reviewer. Amendments to protocols that are "externally peer-reviewed" are assigned to a primary reviewer only. In both cases, a majority vote rules, and the outcome is reported to the principal investigator via a written letter. The possible outcomes are identical to those listed in the "Approval Categories" section for new research protocols.

c. Serious Adverse Event Reports

- All serious adverse event reports for all protocols will be primarily managed by the IRB. Following review of the submitted serious adverse event reports, the Carle IRB may request that the SRC take action on the protocol, which may include termination of the study. No communication regarding review of serious adverse event reports is forwarded to the principal investigator, unless sufficient safety concerns exist to warrant a change, suspension or termination of the research study protocol.

Criteria and Process for Terminating a Research Study Protocol

1. On majority vote, the SRC may suspend, recommend discontinuance or terminate approval of a research study for reasons including, but not limited to:
 - a. Accrual goal met
 - b. Insufficient accrual rate (following adequate principal investigator notice and based on the projected accrual at annual review)
 - c. Poor protocol performance (following principal investigator notice)
 - d. Patient safety concerns
 - e. Emergence of new information that diminishes the scientific importance of the study

Criteria and Process for Terminating a Research Study Protocol (cont.)
<p>2. Research studies (excluding cooperative group studies and multi-center phase I trials) that are expected to accrue low numbers of patients (≤ 5/year) are assessed critically for overall scientific value and feasibility of accrual. It should be recognized that in instances where an over-riding reason for approval does not exist, disapproval of such studies shall be considered. Such studies, if approved, are subject to evaluation of accrual at the time of their annual review. Studies that have not met $\geq 60\%$ of their anticipated accrual in that period may be closed by the SRC. In addition, studies with zero accrual six months after activation might receive a SRC warning letter. If zero accrual occurs by twelve months, the study will be evaluated for closure and outcome determined by majority vote. An appeals process incorporating a letter from the principal investigator to the SRC is available. Reactivations of appealed studies are considered by the full SRC review. Conflicts regarding SRC decisions will be arbitrated by the Executive Director of the Research Institute at CFH or another designated person.</p>
Relationship with the Carle IRB
<p>1. The SRC at CFH functions independently of the Carle IRB and is considered to have a separate and distinct role. The primary role of an IRB is patient rights and safety, while that of a SRC is to maximize the scientific quality of research and the utilization of shared resources. SRC approval letters are forwarded to the IRB with the formal submission of the research study by the Research Coordinator at the Research Office. Since review by the SRC is required prior to IRB submission, only approved studies are forwarded to the IRB. Exceptions are specific grant-related submissions and some times other submissions that require simultaneous IRB and scientific review because of funding and other deadlines. No current member of the SRC can be a current member of the IRB to prevent any possible conflict of interest.</p>
Appeal
<p>1. Studies that fail to gain approval by the SRC may send in a written appeal letter to the Chair within 30 days of the date on the non-approval letter sent to the investigators.</p>
Revision of this Policy
<p>1. The policy of the SRC may be changed or revised on an annual basis with approval of the Executive Director of Research Institute at CFH.</p>
Approval on File

Anna Keck, PhD
Executive Director of the Research Institute

William Schuh, MD, PhD
Medical Director of the Research Institute