PROSpect
The PRone and OScillation Pediatric Clinical Trial

http://www.PROSpect-network.org/

Ancillary (Associated) Studies Guidelines

An ancillary study is defined as an investigation involving *PROSpect* subjects using any technique, medication, procedure, questionnaire, or observation other than those set forth in the parent study protocol. *PROSpect* coinvestigators are encouraged to consider ancillary studies and to involve other coinvestigators, within and outside of the *PROSpect* network.

Participation in an ancillary study is subject to the approval of the (1) *PROSpect* Ancillary Study Committee, (2) *PROSpect* Steering Committee, and (3) National Heart, Lung, and Blood Institute (NHLBI).

Support for ancillary studies must be derived from non-*PROSpect* funding sources. Examples include studies funded by investigator-initiated National Institutes of Health (NIH) research awards, grants from academic institutions, private sources (e.g., foundations or pharmaceutical companies), or those performed at no cost (generally because of the special interest of a researcher). Sufficient funding for all aspects of the ancillary study, including cost incurred by *PROSpect*, the Data Coordinating Center (i.e., tasks such as sample selection, tracking consents and samples from ancillary study participants, preparing and documenting analysis files, participating in statistical analysis, and integrating the new ancillary data into the combined *PROSpect* database), the Clinical Sites for personnel (i.e., tasks such as obtaining consent and collecting and transmitting data and/or samples), and any other related expenses must be provided by the ancillary study investigators.

Ancillary studies are subject to the same policies, reviews, and approvals as the parent protocol. Ancillary studies will be evaluated by the *PROSpect* Ancillary Study Committee (ASC) and *PROSpect* Steering Committee with the highest priority given to studies of high scientific merit. In addition, **no** ancillary study will:

1. Cause a deviation from the defined study protocol.
2. Complicate the interpretation of the study results.
3. Potentially affect subject cooperation or interest in the study.
4. Jeopardize the public image of the study.
5. Create a significant diversion of study resources locally or at the Data Coordinating Center.
6. In any way, negatively influence the cooperative spirit of the collaborating investigators.
7. In any way, compromise the scientific integrity of the study.

I. OBJECTIVES

This document describes the procedures for application, submission, review, and approval/rejection of ancillary studies, as well as guidelines for publications and presentations resulting from ancillary studies. Ancillary study data, collected under separate funding but utilizing and dependent on the public resource of *PROSpect*, are required to become part of the *PROSpect* study data set.

II. REVIEW PROCESS

To protect the integrity of *PROSpect*, all ancillary studies are subject to the same policies and procedures as the parent protocol. The *PROSpect* ASC will assure the protection of the *PROSpect* research participants, assure the integrity of the main goals of the parent clinical trial, and facilitate the review of ancillary studies of high scientific merit. The *PROSpect* Steering Committee will take into consideration the ASC evaluation and use the ancillary study application to assign priority of the proposed study according to the evaluation criteria stated above and, in addition, determine its potential impact on *PROSpect* operations.

The review process is as follows:

A. Application Process

Completed ancillary study proposals should be sent to the *PROSpect* Clinical Project Manager, who will then review the proposal to ascertain that it has been completed satisfactorily and establish a file. If incomplete, the Principal Investigator (PI) of the ancillary study proposal will be notified within five (5) working days after receipt by the *PROSpect* Project Manager.

B. Ancillary Study Proposal Form

The proposal must be fully completed by the PI of the proposed ancillary study. The completed proposal should follow SF 424 guidelines. The ancillary study proposal should include the following:

- Title of ancillary study
- Name and contact information for the Principal Investigator
- Statement of relationship between ancillary study and parent study. If the project is time-sensitive, compelling rationale for the proposed ancillary study, supported by an integrated timeline for the parent and ancillary studies
- List of anticipated key personnel and their institutions; Biosketch for key personnel who are not *PROSpect* investigators
- Sponsor information, including budget
- Data safety and monitoring plan
- Draft consent form – layered or separate from *PROSpect*
- Answers to the following questions:
    - How many participants are required?
    - When will additional data be collected?
    - Are blood or other biologic samples required?
    - What, if any, subject follow-up is needed? Specify length of time and events to be ascertained.

- What is the expected burden to the research subjects? What are the time burdens, discomfort, and expected participation rates?
- What collaboration with *PROSpect* investigators is planned? With whom? Include a statement that all collaborating investigators have approved the proposal.
- How will the ancillary study be funded? NOTE: We will not review an ancillary study that does not reimburse the *PROSpect* study for work and/or personnel time.
- What are the data management and data entry plans, including plans to coordinate with other *PROSpect* investigators and the Data Coordinating Center?
- Draft a complete data analysis plan. A detailed list of variables from the *PROSpect* Case Report Forms is required. What core *PROSpect* data and/or analyses are needed for the ancillary study? What resources are needed from the Data Coordinating Center? What additional data and/or analyses are needed for the ancillary study? What funds will be provided to reimburse Data Coordinating Center effort?
- How will confidentiality and other aspects of protection of human subjects be maintained?
- When and in what form will a complete ancillary data set be returned to the *PROSpect* study? (see III.D)

C. Initial Inquiry and Submission

Electronic inquiries and submission of proposals are required. Completed ancillary study proposals should be submitted in one unified document to the Clinical Project Manager, Amy Cassidy at acassidy@nursing.upenn.edu. Initial inquiries about ancillary studies should be directed to one of the multiple *PROSpect* PIs:

Dr. Martha A.Q. Curley at Curley@upenn.edu
Dr. Ira M. Cheifetz at Ira.Cheifetz@duke.edu
Dr. Martin C.J. Kneyber at m.c.j.kneyber@umcg.nl

D. ASC Review

The ASC will review the ancillary study proposal for scientific merit and to assess potential impact on the parent trial. In addition, the ASC will review the safety implications for participants. The recommendation of the ASC, if approved, will be sent directly to the *PROSpect* Clinical Project Manager for Steering Committee review.

E. Steering Committee Review

The Steering Committee will review whether the proposed study duplicates existing *PROSpect* research, whether it is feasible, and whether the impact of the proposed study on *PROSpect* operations and resources is justified by its scientific merit. Approval/disapproval will be made by the Steering Committee.

F. National Heart, Lung, and Blood Institute Review

A Steering Committee approved ancillary study proposal will be sent to the National Heart, Lung, and Blood Institute (NHLBI) Project Office for review by the *PROSpect* DSMB to judge the ancillary study protocol for the protection of human subjects from a safety perspective.

Ancillary study investigators must agree not to enter into any verbal or written agreement or contract with industry or private individuals that will provide funding for any activity related to the *PROSpect* data without prior review and written approval of the *PROSpect* Steering Committee and the NHLBI.

G. Site Participation will be optional. Ancillary studies will not, in any way, negatively influence the cooperative spirit of the collaborating investigators.

III. PROCEDURES

A. Funding

An investigator applying for an ancillary study must supply all additional funds needed to successfully complete the study. The Steering Committee will be concerned with both obvious and hidden costs to the *PROSpect* study entailed by an ancillary study. Provisions of funds for these expenses are essential – an ancillary study cannot begin without such fiscal support to the core study. The need for such support must be stressed in research grant applications since this support is a mandatory ingredient. Such costs include, but are not limited to:

a. The data coordinating and biostatistical staff for coordinating the additional data collection, data set creation, and any required statistical analyses. In general, *PROSpect* biostatisticians should review and sign off on all ancillary study analyses. It is encouraged that investigators contemplating ancillary studies involve *PROSpect* biostatisticians as soon as feasible during the process.

b. The *PROSpect* study expenses involved in altering key identifying data so that subject confidentiality will be protected.

c. Costs for notification of alert values.

d. Personnel, equipment, and supplies necessary to complete the project.

B. Informed Consent and Institutional Review Board Approval

If separate informed consent is necessary, this must be obtained from all participants of the ancillary study. This should clearly identify the ancillary study as one being performed in addition to the main study and inform participants that their participation in the ancillary study is not necessary for them to continue in *PROSpect*. Institutional Review Board (IRB) approval and annual renewals of IRB protocols for the ancillary study are the responsibility of the PI of the ancillary study in conjunction with the *PROSpect* Administrative Project Manager and must be obtained prior to initiation of the study with documentation of same provided to the *PROSpect* Data Coordinating Center. Further, the ancillary study investigators are to provide documentation that they have current certification of IRB and HIPAA training by their institution.

C. Confidentiality of Individually Identifiable Data

Confidentiality of individually identifiable data about *PROSpect* participants must be assured. No personal identification will be provided to ancillary study staff. Further, it is unlikely that ancillary study investigators will be able to identify and contact participants in the future, as participants will be identified only by *PROSpect* patient study ID number.

D. Data and Materials Distribution Agreement
On completion of the parent study, previously specified data from the main *PROSpect* database will be distributed to the ancillary study PI. Ancillary study PIs will be given the first and exclusive opportunity to analyze and publish data collected under the auspices of their ancillary study. After 12 months, ancillary study data are to be provided to the *PROSpect* Data Coordinating Center for integration into the main *PROSpect* database and potentially, for use in the publication and presentations of other investigators. Requests for exceptions must be communicated formally to the Steering Committee in writing.

E. Inclusion of *PROSpect* Coinvestigators in Ancillary Studies
At least one *PROSpect* Investigator (Curley, Cheifetz, or Kneyber) must be involved as a coinvestigator in every ancillary study proposal and is responsible for assuring the study's continuing compatibility with *PROSpect*. In addition, each manuscript and abstract derived from an ancillary study must include this *PROSpect* Investigator(s) and the following statement requiring authorship " for the *PROSpect* Study Investigators". The list of the PROSpect Study Investigators will be identical to that provided in the primary *PROSpect* paper.

If Data Coordinating Center resources are to be used, arrangements must be made with the PI of the Data Coordinating Center. Separate funding will be required for ancillary study related expenses, such as data management, programming, and support staff. To avoid misunderstandings, all communication regarding resources with the *PROSpect* Data Coordinating Center must include Drs. Curley and Wypij.

F. Protocol, Data Request, and Funding Source Changes
Once an ancillary study is approved by the Steering Committee, there can be no changes in the protocol or type or amount of data requested from the Data Coordinating Center. If changes are made, a revised ancillary study proposal must be submitted. Also, if a previously approved ancillary study is to be submitted to a different organization for funding, a revised application must be submitted for approval by the *PROSpect* Steering Committee.

G. Time Requirement for Review of Ancillary Studies
Ancillary studies should be submitted for review at least 45 days prior to the deadline for the funding application. This will provide time for circulation to appropriate committees, the incorporation of *PROSpect* ASC and Steering Committee recommendations into the ancillary study application and budget, and NHLBI approval prior to submission to a funding agency.

H. Criteria Used to Assess Priority of Ancillary Studies
The Steering Committee will review the proposal primarily to determine whether it does not compromise, complicate, or jeopardize the conduct of *PROSpect*. Review of proposed ancillary studies for scientific merit is not the primary responsibility of this review process, but is a necessary consideration for allocating access to *PROSpect* resources. All ancillary study proposals approved by the Steering Committee will also be sent to the NHLBI Project Officer for DSMB review and comment. Ancillary studies that include an intervention must be approved by the DSMB.

The ASC will record the progress of approved ancillary studies since the composite impact of the total number of active studies will be difficult to assess without central monitoring. Investigators with approved ancillary studies will provide a written progress report to the Chair of the ASC annually regarding the status of study funding, initiation and termination dates, success of data collection (including any significant hurdles encountered and mechanisms used to address them), all documentation to and from their IRB, status of the *PROSpect* sites' IRBs, and any presentations and publications derived from the ancillary study. This written report will be submitted to the Steering Committee via the ASC Chair.

I. Guidelines for Publications and Presentations from Ancillary Studies

Authors of ancillary study manuscript proposals, abstracts, manuscripts, and slide presentations must submit these documents to the *PROSpect* PI/Chair of the Publications and Presentations Committee (PPC). All abstracts, publications, and presentations from ancillary studies must be approved by the *PROSpect* PPC prior to presentation/submission. Further, the *PROSpect* PPC must be informed of journal submission details (e.g., dates and journal name) and preliminary/final results of reviews (e.g., acceptance, rejection, or request for revision).

ASC Standing Members

Ira Cheifetz MD (*PROSpect* PI), David Wypij PhD (*PROSpect* DCC PI), and 4 representatives from the Steering Committee that are appointed by the *PROSpect* Executive Committee.