RADIANT Ancillary Studies

1.1. Introduction

Ancillary studies will be evaluated with careful consideration of their potential impact on the objectives and performance of the RADIANT Study. Studies that complement the objectives and thereby enhance the value of the RADIANT Study are strongly encouraged. These studies however, must not interfere with the continued interest and participation of the study subjects and investigators. To protect the interests of the RADIANT Study, each ancillary study must be individually reviewed by the RADIANT Ancillary Studies Committee and approved by the RADIANT Steering Committee before its initiation. All approved ancillary studies will be reviewed by the Ancillary Studies Committee yearly for progress and impact on the RADIANT Study as a whole.

1.2. Ancillary Study Definition

An ancillary study is defined as research or data collection involving RADIANT Study subjects, or the samples collected from those subjects, to enhance and expand knowledge of atypical forms of diabetes beyond what can be gained from the main RADIANT Study protocol. The investigator for the conduct of the ancillary study is a partner in the RADIANT Study and is therefore obliged to follow the rules and regulations governing the study as defined in the study protocol and by the Steering Committee.

1.3. Reasons for Required Approval of Ancillary Studies

RADIANT investigators and subjects are entitled to prior assurance that all ancillary studies are of high scientific merit and that no ancillary study will:

1. Cause a deviation from the defined study protocol.
2. Complicate the interpretation of the study results.
3. Potentially adversely affect subject cooperation or interest in the study.
4. Jeopardize the public image of the study.
5. Create a significant diversion of study resources at the RADIANT study clinical centers, administrative cores, data coordinating center, phenotyping cores / centers, or any other RADIANT study unit.
6. In any way negatively influence the cooperative spirit of the collaborating investigators.
7. Require use of samples for a study of low priority as deemed by the Steering Committee.
8. Otherwise compromise the scientific integrity of the study.

1.4. Review by the Ancillary Studies Committee

All proposed ancillary studies will be submitted to the Data Coordinating Center which will coordinate its review by the RADIANT Ancillary Studies Committee. The DCC, in

consultation with the Chair of that committee, will identify at least two reviewers with such expertise as may be necessary if not already represented by the membership of the Ancillary Studies Committee. It will arrange for reviews and conference calls of committee members to discuss any proposed study. The recommendation of the Ancillary Studies Committee will be made to the Steering Committee and the Steering Committee shall vote on the proposed ancillary study. Ancillary studies that involve contact with RADIANT participants must be reviewed and approved by the OSMB. OSMB review is not required for retrospective data/tissue studies.

1.5. Funding for Ancillary Studies

The RADIANT Study cannot provide funds for ancillary studies. If funds are needed, the investigator must explore other avenues such as submission of a research grant application, or use other sources of funds, e.g., foundations or participating academic institutions. The source and amount of anticipated funds must always be identified in an application to the Ancillary Studies Committee.

1.6. Preparation of Proposals for Ancillary Studies Committee Review

The proposal submitted to the Ancillary Studies Committee should be 3 pages in length and include a description of the objectives, methods, significance and plans for analysis. Detailed descriptions must be provided regarding additional volumes of blood required (in addition that to be used in the protocol), procedures to be carried out on subjects, the length of stay in the clinic for the subject, or need for extra study clinic visits. In addition, the proposal should discuss the measure to be taken to ensure subject safety and confidentiality, and a statement by the investigator on the potential impact of the ancillary study on the RADIANT Study trial. Prior approval by the appropriate Human Subjects Committee should be demonstrated. In addition, it should clearly indicate the resources available for this study and the source of funding. If resources are being sought from granting agencies this must be indicated in the application. To facilitate the review of the proposal the investigator should specifically address each of the following points on pages, which are separate from the formal grant proposal:

1. The scientific merit of the proposal and the potential contributions that the proposal will make to the RADIANT Study.
2. That the ancillary study does not cause a deviation from the defined study protocol.
3. That the proposed study does not complicate the interpretation of the results of the RADIANT Study.
4. That it does not adversely affect subject cooperation and participation.
5. That the volume of whole blood or sera taken from subjects does not exceed safe or prudent limits.
6. That the proposed study does not create a significant diversion from the RADIANT Study.

7. That the study does not divert or expend resources from the RADIANT Study either locally or at the coordinating center.
8. That the study does not adversely influence the cooperative spirit of the collaborating investigators.
9. That the study does not compromise the scientific integrity of the RADIANT Study.
10. That adequate resources are available to complete the proposed study or are requested from granting agencies.
11. That techniques and assays essential to the study are well established in the laboratory.
12. Results of ancillary studies will not be revealed to either RADIANT Study participants or their clinical team unless as called for in the description of the proposal. All publications and presentations require approval of the RADIANT Study Publications and Presentations Committee.
13. Plan for sharing ancillary study data with the RADIANT Study Team.

Each of the points listed above are examined in detail. These points must be clearly delineated in a document separate from the proposal.

The Ancillary Study Committee must consider and make a determination for each ancillary study as to whether the ancillary study data are required to be shared with RADIANT. The Ancillary Study Committee should consider whether the ancillary study data are valuable to RADIANT's mission.

Final approval is contingent upon the Ancillary Study Committee receiving a letter signed by all investigators in which they agree to the regulations put forth by the Publications Committee of the RADIANT Study.

Finally, a yearly report summarizing study progress, results, and the impact of the ancillary study on the RADIANT Study will be submitted to the RADIANT Ancillary Studies Committee and the RADIANT Steering Committee and reviewed every 12 months for continued approval by RADIANT.

1.7. Procedures for Obtaining Approval

The investigator should send his/her ancillary study proposal to the DCC at the University of South Florida which will then distribute it to the Ancillary Studies Committee. To ensure a thorough scientific review the Chairman of the Ancillary Studies Committee may elect to seek outside expert opinion in advance to the committee meeting, as described above. Within 30 days of receipt of the proposal a conference call involving the Ancillary Studies Committee and investigator submitting the proposal will be arranged. The investigator should be available to answer questions from the committee. The committee will vote following a discussion not involving the investigator. A simple majority vote constitutes an approval by

the Ancillary Studies Committee when a quorum of at least 4 members are present. The investigator will be notified within 48 hours of the meeting of the status of his/her proposal.

The proposal and the recommendations of the Ancillary Studies Committee will be forwarded to the Steering Committee for a vote. The decision of the Steering Committee is then forwarded to the ancillary study investigator.

1.8. Publicity of Approved RADIANT Study Ancillary Studies

Publicity announcing the purposes and starting time of the study will be the responsibility of the investigator. Any publicity regarding results of the ancillary study must be approved by the Publications Committee before such announcements can be made.

1.9. Publications and Presentations of Ancillary Studies

Approved ancillary studies investigators are subjects to the rules and regulations of the RADIANT Study Publications Agreement. This agreement requires that all reports, manuscripts, or presentations of data derived from the ancillary study must be approved by the Publications Committee prior to their publication or presentation according to the procedures set forth in the Manual of Operations.