Focal Segmental Glomerulosclerosis Clinical Trial (FSGS-CT)

Ancillary Studies Policy

I. General Policy

To enhance the value of the FSGS Clinical Trial (FSGS-CT), the Steering Committee welcomes proposals from individual investigators to carry out ancillary studies. Nevertheless, to protect the integrity of the FSGS-CT, ancillary studies must be reviewed and approved by the Ancillary Studies Committee (ASC) and the Steering Committee before their inception or submission of a proposal for external funding consideration.

II. Definition of Ancillary Study

An ancillary study will be used for the collection of additional data not collected or analyzed as part of the routine FSGS-CT data set. Ancillary studies may be submitted by the investigators within the FSGS-CT or by investigators who are not a part of the FSGS-CT. Ancillary studies require external (non-FSGS-CT) funding. Examples include studies funded by investigator-initiated NIH research awards (RO1s), grants from academic institutions or private sources (e.g. private foundations, pharmaceutical companies). Any ancillary study must have sufficient funding to cover the costs incurred by the FSGS-CT Core Coordinating Centers, Participating Sites, Central Laboratory (e.g., to process shipments and ship samples), and by the DCC (for tasks such as sample selection, preparing and documenting analysis files, participating in statistical analysis, and integrating the new ancillary data back into the combined FSGS-CT database). Funds are not available for these purposes within the FSGS-CT.

III. Requirements and Procedures for Approval of an Ancillary Study

III. A. Overview

Participation in, and approval of an ancillary study is subject to review by the ASC and formal approval by the FSGS-CT Executive Committee. In unexpected select situations (e.g., an imminent funding deadline), the FSGS-CT Executive Committee may serve as the proxy for the ASC. Approval by the Executive Committee will be defined by majority vote. Concerns about a proposal will be discussed with the applicant and opportunities for clarification will be provided. If approved, all Core Coordinating Centers of the FSGS-CT agree to cooperate in the ancillary study. An ancillary study must receive approval before grant funding is submitted. Investigators are encouraged to discuss potential proposals with the Chair of the ASC prior to submitting a proposal. All ancillary study proposals must include at least one FSGS-CT investigator as a liaison.

III. B. Requests for Ancillary Studies as Part of Training or Career Awards

The FSGS-CT investigators and the NIH anticipate that the FSGS-CT will be an important resource for career development and training among members of the academic community. Special consideration, therefore, will need to be given to requests for ancillary studies to be funded through training grants or career development awards through the NIH or other funding sources. Because these funding mechanisms typically provide funding only for investigator effort, not for additional data collection, such proposals will generally propose research questions and analyses that could be considered part of the core FSGS-CT. In these cases, consideration of what analyses will be authorized could present a conflict with the interests of the FSGS investigators. Evaluation should consider the scientific gain to the FSGS-CT from the addition of the proposed ancillary analyses as well as the training and career development opportunities afforded to the applicant by the proposed ancillary study. Proposals for ancillary studies as part of training or career awards must be reviewed and approved by the ASC.

III. C. Considerations for Approval

The proposed study must meet requirements of the highest scientific merit:

1. Relevance to FSGS.

2. Opportunity for acquisition of new scientific knowledge.

3. Adequacy of experimental design, methodology and data analysis.

4. Adequacy of the investigator and research environment.

5. Participant (enrolled patients and participating site providers) burden.

6. The proposed study must be acceptable to the participants (e.g. time, discomfort, privacy).

7. The proposed study must not interfere with other parts of the main FSGS-CT.

8. The proposed study must not hamper continued participation in the main Clinical Trial.

9. The proposed study must put minimal demand on scarce FSGS-CT resources such as blood samples.

10. The proposed study must require the unique characteristics of the FSGS-CT cohort to accomplish its goals.

11. The investigators must have adequate resources to effectively complete the project, including both financial support and personnel.

12. The ancillary study investigators must agree to return the complete ancillary data set back to the DCC, if requested.

13. The proposed study must not interfere with or impede the completion of the primary or secondary objectives of FSGS-CT.

14. The proposed study must not adversely affect participant cooperation or compliance with FSGS-CT protocols.

15. The proposed study must not create a serious diversion of study resources (personnel, equipment or study samples) or investigator/staff time at the Participating Sites, Core Coordinating Centers or DCC.

III. D. Instructions for Preparation of Requests for an Ancillary Study

All proposed ancillary studies must be reviewed by the FSGS ASC and approved by the Steering Committee before submission to a funding agency. Studies should be submitted a minimum of 8 weeks before a deadline.

Ancillary Study Proposal Format

A written request for approval of an ancillary study should be submitted in two to four pages (excluding biosketches and budget) containing the following information:

1. Principal investigator and other co-investigators (include biosketch in NIH format)

2. FSGS-CT liaison investigator

3. Hypothesis to be tested

4. Background and significance (maximum of one page)

5. Design-methods-key references (maximum of two pages)

6. Description of specimen or data request (maximum of two pages)
    a. Specific type(s) of samples
    b. Volume of each sample
    c. Time of sample collection (baseline vs. post-baseline)
    d. Use of thawed vs. unthawed specimens - for blood and urine, proposals must indicate whether previously thawed specimens can be used.
    e. Number of participants
    f. Type of storage—for urine, -20 or -70^{0}F
    g. Proposed laboratory that will perform the assays

h. DNA specimens—special needs should be delineated.

7. Need for other study data (e.g., baseline and/or follow-up data) and other study resources

8. Time table with key dates (e.g., grant submission, target date for receipt of specimens, and completion of study

9. Documentation of local IRB approval [required prior to release of specimens]

10. Agreement to return any unused biological specimens and data sets

11. Budgetary issues
    a. Source(s) of funding
    b. Draft budget—see required elements in Ancillary Proposal Budget below

The investigator should send the ancillary study proposal to the chair of the ASC. To ensure thorough scientific review, the chair of the ASC may elect to seek outside expert opinion. The ASC members will have fourteen days from receipt of the proposal to provide an opinion to the DCC. No response will be considered an affirmative vote. A proposal that receives an affirmative majority from the ASC will be forwarded to the Executive Committee for authorization. Each FSGS-CT Executive Committee member should respond to the DCC within 15 days. Approval or disapproval is based on majority opinion. A failure to provide an opinion to the DCC will be considered an affirmative vote.

If a proposal is not approved, the chair of the ASC may discuss potential revisions with the ancillary studies investigator. If resubmitted, the ASC will reconsider the proposal on one additional occasion only. If an affirmative majority is obtained after re-review, the proposal will be sent to the Executive Committee for authorization. The investigator may only proceed with the ancillary study after it has been authorized by the FSGS Steering Committee.

Ancillary Proposal Budget

The investigator applying for an ancillary study must supply all additional funds needed to complete the study. Provision of funds for expenses incurred by the FSGS-CT is essential. Once a study concept is approved, ancillary studies are expected to collaborate with the DCC to develop a budget that adequately provides for expenses incurred by the FSGS-CT. Such costs include, but are not limited to, the following:

1. Statistical and data management staff for coordinating the additional data management and analyses with the DCC

2. Expenses involved in modifying identifying data to protect subject confidentiality and maintain HIPPA compliance

3. Costs for notification of alert values

4. Costs incurred by Participating Sites including space, personnel, equipment, and IRB approval

5. Costs relative to visits or examinations outside of the primary study protocol

Human Subjects/Data Confidentiality
Confidentiality of FSGS-CT enrolled patients must be guaranteed. Individually identifiable data may not be released. A signed consent must be obtained from every participant in the ancillary study, if the data collection/request is not covered in the original informed consent process for the main FSGS Clinical Trial.

Any investigator or personnel having access to FSGS Clinical Trial subject data should have received an orientation on the FSGS Clinical Trial confidentiality policy. Key personnel of the ancillary study must be certified in the NIH OHSR or equivalent training course.

A copy of the IRB letter for the ancillary study should be sent to the DCC. If a separate consent form is required for the ancillary study, a copy of the signed ancillary study consent form for each study participant must be included in the FSGS-CT record. A data file tracking all signed ancillary consent forms must be maintained by the ancillary study and an electronic copy of that file must be delivered to the FSGS-CT DCC.

The principal investigator of an ancillary study will be responsible for the following:

- Monitoring the study to assure continuing compatibility with FSGS-CT,

- Maintaining communications with the FSGS liaison investigator and

- Providing written progress report on the ancillary studies.

IV. Changes to Proposed Ancillary Study

Once an ancillary study is approved, if a change occurs in the structure or concept of the study, such changes should be disclosed to the ASC and the FSGS Executive Committee, for review and approval.

V. Analysis and Publication of Results of Ancillary Studies

Unless specifically arranged for and specifically provided for in the Ancillary Study consent form, all data analyses will take place at the DCC. Ancillary studies funded as career or training awards as well as studies taking place in a subset of clinical sites will

be situations in which data analysis requires special consideration. In such circumstances, the investigator of the ancillary study will provide interim reports on analyses to the DCC during data analysis to ensure consistency with data in the FSGS-CT database and to ensure the quality of analysis approaches.

Proposals for manuscripts resulting from all ancillary studies will be submitted for review to the Publications Committee and will require approval by the Executive Committee prior to submission for publication or presentation. The phrase "FSGS Clinical Trial" should be included in the title in all scientific presentations and manuscripts and listed as a key word whenever possible. Manuscripts should also contain an appendix listing FSGS investigators when appropriate.

VI. Feedback of Results of Ancillary Studies to Participants

Results of ancillary studies shall be reported to enrolled patients and/or their physicians if medically useful. Such reporting should follow standard FSGS-CT protocol for notification of participants.

VII. Handling of FSGS Clinical Trial Data and Specimens

At the time of distribution of FSGS-CT specimens and/or information, the FSGS-CT Liaison Investigator, in coordination with the DCC, will make explicit arrangements with the ancillary study PI for the security of these study materials and for their final disposition at the conclusion of the ancillary study. The safety and confidentiality of the FSGS-CT data at the collaborating institution is the responsibility of the ancillary study PI, as is the appropriate disposition of biological materials after the ancillary study has been completed. An archival copy of the newly collected data and/or laboratory results not already held at the DCC will be sent to the FSGS-CT DCC Coordinating Center at the conclusion of the data analysis and publication of ancillary studies. Once transferred back to the FSGS-CT, these ancillary data will become part of the aggregate FSGS-CT data. Subsequent access to these data will be governed by the FSGS-CT Study Policy on Use of Archived Study Data.