

Chapter 27

Ancillary Studies Policy

ANCILLARY STUDIES

LLFS encourages collaboration and invites investigators to propose and conduct ancillary studies. Such studies enhance the value of the LLFS and ensure the continued interest of the diverse group of investigators who are critical to the success of the study as a whole. To protect the integrity of LLFS, ancillary studies are reviewed and approved by the Steering Committee before their inception. An ancillary study is one based on information from LLFS participants in an investigation which does not coincide with a scientific aim or study question addressed by the LLFS, and requires data which are not collected as part of the established LLFS data set. In general, ancillary studies require external (non-LLFS) funding, since no costs for an ancillary study can be borne by the parent study.

Funding: Funding for an ancillary study must cover the costs incurred by an LLFS study agency, such as the Biochemistry or Molecular Biology laboratories (e.g., to process and/or ship samples), and to the Coordinating Center (for tasks such as to process and ship analysis files, provide documentation, participate in statistical analysis, and integrate the new ancillary data back into the combined LLFS database). No funds for this purpose are available within the parent study.

LLFS Co-Investigator: It is an expectation that an LLFS principal investigator or co-investigator be included as a co-investigator in every ancillary study proposal. The LLFS investigator collaborating with the ancillary study PI is expected to facilitate the preparation of the ancillary study proposal, its submission to the LLFS steering committee, and the communication between the collaborating studies throughout this process. The LLFS investigator provides copy of the LLFS ancillary study policy to the outside investigator(s), and assists in the preparation of the proposal. After favorable review by the LLFS steering committee, the LLFS makes available a copy of its publications policy to the ancillary study investigators. When applications for (non-LLFS) funding for an ancillary study to LLFS are submitted, it is requested that a courtesy copy be sent at that time to the LLFS Scientific Officer.

Role of the LLFS Coordinating Center: A co-investigator from the LLFS Coordinating Center is included as a co-investigator in every ancillary study proposal, unless the Coordinating Center deems this not to be necessary. After funding for the ancillary study has been awarded the LLFS Coordinating Center provides the ancillary study principal investigator with the data approved for use by the ancillary study. The distribution of biologic specimens to an ancillary study (if applicable) is coordinated by means of samples or lists prepared by the Coordinating Center specifically for each ancillary study. Only the LLFS Coordinating Center is authorized to provide study data to an ancillary study. Costs derived from these tasks must be covered by the ancillary study.

Role of the Central Laboratories/Specimen Repositories: To the degree that an LLFS laboratory has the capability and the interest to conduct assays for an ancillary study, it is the parent study's preference that such assays be done at the LLFS laboratory. The LLFS principal investigator responsible for a laboratory or specimen repository is responsible for the distribution of the biologic specimens approved for use by the ancillary study, based on samples/listings prepared by the coordinating Center. Costs derived from these tasks must be covered by the ancillary study.

Approval of Applications for Ancillary Studies: The LLFS Steering Committee is responsible for initial review of the ancillary study. Investigators provide a two to three page proposal following the format provided by the Ancillary Study Proposal Template. The Steering Committee considers this information to

assess the priority of the proposed study and determine its potential impact on the main study (LLFS). Highest priority is given to studies which: 1) do not interfere with main LLFS objectives; 2) have the highest scientific merit; 3) have objectives closest to those of LLFS; and 4) can draw on the unique characteristics of the LLFS cohort.

The Steering Committee reviews the proposal to determine that it does not compromise, hinder, or jeopardize the conduct of the LLFS. Burden on LLFS participants must specifically be addressed. A review of proposed ancillary studies for scientific merit is not the primary responsibility of the Steering Committee, but suggestions of a scientific nature may result from the review. Ancillary study proposals approved by the Steering Committee must be submitted to the Observational Studies Monitoring Board, who recommends approval or disapproval to NHLBI. NHLBI approval is required before grant applications or requests for funding are submitted.

IRB Approval: Studies that will collect new data from participants must obtain a separate informed consent from all ancillary study participants. This consent should clearly identify the ancillary study as one being performed in addition to the main study and inform subjects that their participation in the ancillary study is not necessary for them to continue in LLFS. IRB approval and the informed consent must be provided to the LLFS SC before implementation of the proposed study begins. If an approved proposal involves genetic studies, ethical, legal and social implications, as well as reporting of results, must be proactively addressed in the proposal.

Time Line for Submission of Applications: Because proposals for ancillary studies require review and approval by the parent study Steering Committee and then by the Observational Studies Monitoring Board advising the NHLBI, applications must be submitted to LLFS no later than 12 weeks prior to the intended date of submission to the funding agency. To facilitate planning for these reviews and to prepare for a speedy response, it is recommended that the investigators notify the parent study in advance of their plan to submit an ancillary study proposal. This letter of intent is not required but highly recommended, and should include an outline of the study aims, the proposed use of the parent study data, and the anticipated date of submission to the funding agency. Without this type of advance notification it can be difficult to convene a timely review by the steering committee.

Example: Time Line for Submitting an Ancillary Study Proposal to LLFS:

- 6/01/06: Letter of intent addressed the Chair, Steering Committee (optional, but recommended)
- 7/20/06: Deadline for submitting ancillary study proposal to the LLFS Steering Committee, for review and feed-back.
- 8/03/06: Deadline for the Steering Committee to submit the approved ancillary study proposal to the NIA, P.O. for its review and approval.
- 10/01/06: First possible NIH submission date of the proposal, if approved as above

It is requested that a copy of the proposal be sent to the LLFS Project Office at the time it is submitted to CSR.

Integrity and Disposition of the LLFS Data and Biologic Specimens: At the time of distributing LLFS specimens and/or information, the LLFS principal investigator responsible for that portion of the LLFS database (Coordinating Center, Central Laboratory) makes explicit arrangements with the ancillary study principal investigator for the security of these study materials, and for their disposition at the conclusion of the ancillary study. The safety and confidentiality of the LLFS data at the collaborating institution is the responsibility of the ancillary study PI, as is the appropriate disposition of these materials after the study has been completed. Left-over DNA and laboratory specimens are destroyed or returned, as appropriate; files of LLFS data are returned or deleted, as established at the outset of the collaboration. An archival copy of the

newly collected data and/or laboratory results is sent to the LLFS Coordinating Center at the conclusion of the data analysis and publication of the main (ancillary) study hypothesis. This transfer is the responsibility of the ancillary study principal investigator and his/her LLFS collaborator(s).

Publications: The Steering Committee monitors the development of the ancillary studies, receipt of funding, initiation dates, and progress. Publications resulting from ancillary studies follow the same policies as described in the document on LLFS Publication and Presentation policy (please see publications policy).

Progress Reports: A written progress report on ancillary studies is made periodically to the Ancillary Studies Committee. Progress Report Summaries will be made available, via a Tracking Log, on the Investigators' Only portion of the study website for review by the Steering Committee, OSMB and study investigators.

Proposal Cover Sheet: In order to expedite review of ancillary studies, LLFS has developed a proposal cover sheet that provides a synopsis of the impact of the study on LLFS. This should be followed by a brief 2-3 page proposal including aims, background and methods, including power calculations. The form can be found on the LLFS web page. The proposal cover sheet follows:

Cover Sheet LLFS Ancillary Study Information and Projected Impact on LLFS

Title of study: _____

Initiating investigator(s) name, address, phone and fax numbers, e-mail address: _____

Proposed Collaborators: _____

Proposed starting and ending dates: _____

Source of funding; date of grant submission: _____

Summary of overall impact on the main study: _____

Summary of Field Center and Coordinating Center tasks involved:

Center	Examine participants (N)	Analyze samples (N participants)	Analyze data (Yes/No)

Description of participant, specimen and staff involvement:

A. Participants

1. **Burden:** Describe number of subjects needed; special characteristics of study population; age and sex distribution. Will participants be contacted, interviewed, or examined? If so, describe participant involvement and the specific time-point of planned data collection (Note that in most cases additional data should be collected after the main study data has been collected). Estimate time/effort required of each participant.

2. **Safety monitoring:** Will the ancillary study will have its own safety monitoring or will rely on the LLFS OSMB for this? Describe the safety implications of the study and plans for reporting adverse events to LLFS.

B. Stored materials (assuming repository - if plans include separate blood draw, state plans for managing specimens):

Sample Type (Serum, EDTA, DNA, etc.)	Frozen (Yes/No)	Previously Thawed Okay (Yes/No)	Sample Volume

C. Field Centers: Describe effort (and estimated time) required of staff at each participating center.

D. Study Coordinating Center: Describe effort (and estimated time) required of Coordinating Center staff. Specifically:

1. Will the Coordinating Center be involved in data collection, tracking, or preparation of forms or software? (Note that if these tasks will be completed by the Ancillary Study, a data file must be sent to the Coordinating Center.)
2. Will data analyses be done by analysts at the Coordinating Center?

E. Assurances: Assurances that data will be provided back to the main study for use by other investigators once the ancillary study objectives have been met.

Assurance that the Ancillary Study PI will report progress of the study from status of funding through data collection and manuscript publication.

Safety Monitoring (if appropriate), and confidentiality of individually identifiable LLFS participants must be assured.

PART 2: Description of the Proposed Ancillary Study

Please provide a brief (1-3 page) description of the proposed study. Include the following:

1. Background and rationale
2. Study aims: questions or hypotheses
3. Methods, including:
 - Participant involvement (if any)
 - Safety monitoring
 - Data to be collected
 - Data needed from the main study (including outcomes/events)
 - Sample size justification
4. Literature references

Notification Letter A

Date

PI Name and Address

Re: [Ancillary Study Proposal Title]

Dear Dr. XXXXX:

The LLFS Ancillary Studies Committee reviewed the above-named ancillary study proposal and made a motion to approve the proposal, contingent upon approval by the LLFS Steering Committee and Observational Study Monitoring Board (OSMB). You will be notified in writing upon final approval, at which time you can proceed with application for external funding and/or begin the study.

The Ancillary Studies Committee will review all ancillary studies at least annually for progress and productivity and prepare a report for the Steering Committee and the OSMB. Please review your responsibilities for reporting progress and for gaining prior approval for abstracts and manuscripts that are outlined in the LLFS ancillary study policy.

Best wishes for a successful ancillary study. We look forward to working with you on the LLFS study.

Regards,

Chair, LLFS Steering Committee

Notification Letter B

Date

PI Name and Address

Re: [Ancillary Study Proposal Title]

Dear Dr. XXXXX:

The LLFS Ancillary Studies Committee reviewed the above-named ancillary study proposal and made a motion to grant provisional approval provided that you address the major comments below. Please forward your response in writing to me by [2-week deadline from date of letter]. Your response will be reviewed and we will contact you when a decision has been reached.

Once approved by our Committee, we will forward the proposal to the Steering Committee and the Observational Study Monitoring Board. You will be notified in writing upon final approval, at which time you may proceed with application for external funding and/or begin the study.

Regards,

Chair, LLFS Steering Committee

Notification Letter C

Date

PI Name and Address

Re: [Ancillary Study Proposal Title]

Dear Dr. XXXXX:

The LLFS Ancillary Studies Committee reviewed the above-named ancillary study proposal and has requested that the proposal be revised and resubmitted based on the comments listed below. Please resubmit the revised proposal by [2-week deadline from date of letter]. Upon review of the revised proposal, you will be contacted in writing regarding the Committee's decision.

Once approved by our Committee, we will forward the proposal to the Steering Committee and the Observational Study Monitoring Board. You will be notified in writing upon final approval, at which time you may proceed with application for external funding and/or begin the study.

Regards,

Chair, LLFS Steering Committee

Notification Letter D

Date

PI Name and Address

Re: [Ancillary Study Proposal Title]

Dear Dr. XXXXX:

Thank you for submitting the above-named ancillary study proposal. The LLFS Ancillary Studies Committee reviewed the proposal and regrets to inform you that it has not been accepted based upon reasons listed below.

Regards,

Chair, LLFS Steering Committee