

PFF PATIENT REGISTRY ANCILLARY STUDIES POLICY

I. General Policy and Process Overview

To enhance the value of the Patient Registry, the Pulmonary Fibrosis Foundation (PFF) welcomes proposals to carry out ancillary studies from individual investigators or study groups, including members of the Care Center Network (CCN) and persons not directly associated with this group.

To protect the integrity of the data such ancillary studies must be reviewed and approved by the Ancillary Studies Committee and the Steering Committee. The PFF Leadership Team may postpone an ancillary study if funding or staff resources are not immediately available to support it.

While we welcome all applications, we expect that proposals that are funded by governmental and philanthropic sources (that have peer review) will be most successful.

II. Definition of Ancillary Study

An ancillary study is one that utilizes data/samples from, or the unique care center network infrastructure and/or capabilities, of the PFF Patient Registry, to support an investigation or analysis that is not included in the ongoing Registry protocols.

Simple ancillary studies are those that **ONLY** utilize existing data and samples. The term “simple” has no relationship to the complexity of analyses to be performed, only that it does **NOT** require any modification to the existing structure or schedule of data or sample collection in the Registry data set.

Complex ancillary studies are those that require the acquisition of new data or samples not available as part of the current or contemplated Registry data set. In short, they require modification of the current design of the Registry or Biorepository. Some examples of complex studies would be those involving:

- collection of clinical data beyond that in the current data capture system,
- administration of a new questionnaire not currently in the PRO battery,
- additional blood collection at follow-up visits, or
- collection of additional sample types at enrollment.

III. Requirements and Procedures for Approval of an Ancillary Study

IIIa. Overview

Participation in an ancillary study is subject to review and approval by the Ancillary Studies Committee and formal approval by the Steering Committee.

Proposals for ancillary studies may be submitted by investigators within the CCN or by investigators without a prior relationship to the CCN. However, all proposals submitted by individuals outside the CCN must include at least one CCN investigator as a co-investigator.

Ancillary studies must have sufficient funding to cover the costs incurred by the PFF, including analytical work by the Registry Data Coordinating Center. Itemized costs associated with ancillary studies are provided in **Appendix A** to this document.

There are no funds available for ancillary studies within the CCN. Examples of acceptable funding sources for ancillary studies are:

- PFF Research Awards (<http://pulmonaryfibrosis.org/medical-community/pff-research-funds>),

- investigator-initiated NIH research awards (e.g. RO1s),
- grants from academic institutions, public foundations (e.g., JDRF) and private sources (e.g. private foundations, pharmaceutical companies).

The PFF will **not** conduct ancillary studies funded by:

- companies that engage in the manufacture, distribution, or sale of inhaled tobacco products, or companies engaged on their behalf

IIIb. Requests for Approval of an Ancillary Study

All ancillary study proposals must be submitted on the appropriate form and by the relevant deadline to be ensured review in the next review cycle. Submissions received after the deadline may not be reviewed until the following cycle. All applicants are strongly encouraged to contact the Ancillary Studies Committee Chair as early as possible in the process.

Review the table below to determine the proper submission processes and deadlines:

Study type	Forms to be submitted	Use instruction form:	Approximate submission deadlines
Simple	ASP-01	ASC-IF-SIMPLE	Feb 1 Jun 1 Sep 1
Complex	ASP-55 ASP-99	ASC-IF-COMPLEX	TBD

During a proposal review, the Ancillary Studies Committee discusses the protocol and provides feedback to the potential ancillary investigator regarding its suitability and its likelihood of approval by the Steering Committee, based on the criteria listed in Section IIIc. An informal vote and comments are gathered by the Ancillary Studies Committee, collated, and returned to the proposer of the ancillary study, soliciting revisions, if needed.

Proposals approved by the Ancillary Studies Committee are presented to the Steering Committee, which is responsible for formally approving or disapproving all ancillary studies.

If a proposal is disapproved by either committee, issues of concern will be provided to the applicant. Proposals revised to address such concerns may be resubmitted as early as the next submission deadline.

If a proposal is approved by the Steering Committee, the PFF leadership will review the proposal and may postpone the project if there are insufficient staff resources available to support it. After a proposal is approved, the Steering Committee Chair(s) can provide a letter of support from the PFF to the investigator for the ancillary study, if desired.

Investigators are encouraged to discuss potential proposals with the Ancillary Studies Committee and/or Steering Committee Chair(s) prior to submitting a concept proposal. As an increasing number of ancillary studies are reviewed and implemented, the need to manage potential overlap will undoubtedly occur.

The first step in the review process is identification of conflicts or overlaps with other approved or proposed ancillary studies.

In the event of potential conflict or overlap, the issue(s) will be discussed by the Ancillary Studies Committee and recommendations made to the Steering Committee for decisions and communication with the applicant(s). Within this negotiation, already approved aims or previously formally proposed studies by CCN investigators will be given priority. Investigators will be encouraged to collaborate whenever possible.

The Ancillary Studies policies and processes will be governed by the members and chairs of the Ancillary Studies Committee and Steering Committee. In the event of a potential conflict of interest, the Chair or member of either committee is expected to recuse him/her self from the approval process. Another committee member can act as a proxy throughout the remainder of the processes.

IIIc. Requirements for Approval of Ancillary Studies

A proposed study must:

- A. be consistent with the stated aims of the PFF Registry.
- B. expand the scientific breadth of activities engaged by PFF.
- C. be of high scientific merit.
- D. include at least one CCN investigator in the ancillary study's research team.
- E. have adequate resources to effectively complete the project, including:
 - a. Sufficient budget and personnel
 - b. Investigators and staff having the requisite expertise to meet the objectives of the project

A proposed study must NOT:

- A. interfere with the core activities of PFF.
- B. require excessive amounts of PFF bio-samples (as determined by the Biomarker Committee).
- C. utilize PFF resources (personnel, equipment or study samples) or investigator/staff time, either locally or centrally unless this use is agreed upon through the application process and fully funded by the ancillary investigator.
- D. jeopardize the public image of PFF.

The ancillary study investigators must agree to allow data collected as part of the ancillary study to be incorporated into the Registry datasets for use in future research, once publication of the ancillary study manuscript is complete.

The ancillary study investigators are ultimately responsible for the preparation and submission of any resulting manuscripts.

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

We anticipate that the Registry will be an important resource for research career development and training among members of the academic community. Special consideration, therefore, will be given to requests for ancillary studies to be funded through training grants or career development awards through the NIH or other funding sources.

A training proposal will only be considered if one of the mentors is also member of the CCN. A statement is required from the mentor(s) indicating his/her commitment and ability to mentor in the

proposed training area, their commitment to the individual, and their prior experience in mentoring. In addition to the Registry ancillary proposal, potential awardees of training grants should submit a brief statement detailing their mentorship plan. Further, applicants must be willing to adhere to the requirements of the RSC including, but not limited to issues surrounding authorship.

IV. Changes to a Proposed Study

Once an ancillary study is approved, if a change occurs in the structure or concept of the study (for example, as a result of the NIH review process), including any change in data elements to be collected or analyzed, or any change to study aims, such changes must be disclosed to the Ancillary Studies Committee for review and approval before the proposal is (re-) submitted to a funding agency.

Investigators must send an email to the Ancillary Studies Committee chair(s) detailing the proposed changes. If the changes are considered minor by the chair and, if necessary, the whole Ancillary Studies Committee, the proposal will be circulated directly to the Steering Committee for a re-vote. If the changes are substantial the protocol will need to be routed anew through the Ancillary Studies Committee.

V. Proposal Budget

The investigator applying for an ancillary study must supply all additional funds needed to successfully complete the study. The Ancillary Studies Committee will consider both the obvious and the hidden costs to the PFF entailed by an ancillary study. Provision of funds for these expenses is 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:

- 1) Data Coordinating Center Costs
 - a) Data management effort for coordinating the additional data management and analyses
 - b) Statistical staff and investigator effort to conduct any analyses before publication of results
 - c) Investigator and project management effort to implement the ancillary study
 - d) Expenses involved in altering key identifying data so that subjects' confidentiality will be protected
- 2) Clinical Site Costs
 - a) Personnel effort to obtain IRB approval, contact participants, obtain informed consent, schedule additional visits and ship samples
- 3) Performance Laboratory Costs
 - a) Lab supplies
 - b) Labor costs relevant to testing
 - c) Shipping costs to transfer specimens from Central Lab or lab(s) of origin
- 4) CLASS Central Laboratory costs
 - a) Lab, storage, freezer and office space
 - b) Lab supplies
 - c) Lab tech effort to receive, track, process, and either order tests or ship specimens for testing
 - d) Costs to oversee quality control of laboratory analyses conducted at labs other than the CLASS Central Lab

Once a study concept is approved by the Ancillary Studies Committee, applicants for ancillary studies must work in conjunction with the ASC to develop a budget that adequately provides for all expenses.

The proposed budget must be part of proposal that will be reviewed by the Steering Committee and the PFF Leadership.

Approval of study budget does not imply approval of the project.

VI. Human Subjects/Data Confidentiality

Confidentiality of Registry cohort participants must be guaranteed. Individually identifiable data will not be released to researchers.

A copy of the IRB letter of approval for the ancillary study is to be sent to the PFF Data Coordinating Center. Any changes in the IRB status of the study must be forwarded within one week to the ASC chair(s). It is the investigator's responsibility to ensure the ancillary study is continuously approved by their IRB including timely submission of renewals.

VII. Data Management, Analysis, and Publication of Results of Ancillary Studies

All data collected under the auspices of an ancillary study are expected to adhere to the same high standards of quality applied to data collected in the Patient Registry. All data from ancillary studies must be scrutinized for quality and consistency using the same mechanisms in place for the Registry data. All costs associated with the collection, transfer, analysis and oversight of data collected by an ancillary study will be borne by the ancillary study site. Budgets in support of ancillary studies must be sufficient to address all of these requirements regarding ancillary study data. Proposals that do not have sufficient funding to assure these data management activities will not be approved.

Proposals for manuscripts resulting from all ancillary studies shall be submitted to the Ancillary Studies Committee Chair for review by the Ancillary Studies Committee, and will require approval by the Steering Committee before submission for publication or presentation. Each manuscript and abstract is expected to include a CCN investigator. The phrase "PFF Patient Registry" should be included in the title in all scientific presentations and manuscripts and listed as a key word whenever possible. Manuscripts will also contain an appendix listing CCN investigators when deemed appropriate by the Ancillary Studies Committee.

VIII. Handling of Registry Data and Specimens

At the time of distribution of Registry specimens and/or information, the PFF, with help from 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 Registry data at the collaborating institution are the responsibility of the ancillary study PI, as is the appropriate disposition of these materials after the study has been completed. Leftover DNA and laboratory specimens are destroyed or returned, and files of Registry data are returned or deleted, as established at the outset of the collaboration. Data should be released to the Registry DCC sooner if these data are needed for scientific activities with aims separate from the ancillary studies' specific aims. This transfer is the responsibility of the ancillary study investigator. Once transferred back to the Registry, the ASC and the Steering Committee reserve the right to request preliminary data validating an investigator's laboratory method against an external standard.

IX. Timelines, Investigator Departures and Future Considerations

Approvals by the Registry Steering Committee will be active for a period of one year (unless if the investigator makes a written request to withdraw the proposal). Extensions of these approvals can be requested and may be approved by the Ancillary Studies Committee and Steering Committee.

Appendix A: Core Costs for Ancillary Studies

Simple Ancillary Studies

Effort	Cost
Development of analysis plan	\$TBD
Data de-identification and analysis	\$TBD
TOTAL Required Core Costs	\$TBD

Complex Ancillary Studies

Effort	Cost
Development of analysis plan	\$TBD
Data de-identification and analysis	\$TBD
TOTAL Required Core Costs	\$TBD

Appendix B: Template for Ancillary Study Proposal Submission

A. Research proposal

1) Identifiers:

- a) Initiating investigators, collaborators, CCN co-investigator (names and e-mail addresses) and affiliation(s)
- b) Planned start date and project timeline
- c) Funding plans and estimated cost

2) Design and Methods (limit to one page):

- a) Brief background and rationale
- b) Study questions or hypotheses
- c) Research plan

3) Specific answers to the following questions:

- a) What Registry core data and/or analyses are needed for the ancillary study?
- b) What collaboration with CCN investigators is planned? Have the collaborating investigators approved the proposal? How will the ancillary study be funded?
- c) Would any non-reimbursed work or personnel time be expected of the PFF?
- d) How will the ancillary study budget cover demands on PFF personnel time and resources?
- e) Will the ancillary study potentially impact the conduct of the Registry negatively? (Discuss, for example, risks related to additional study procedures, impact on adherence and retention).
- f) Where will the data analyses be conducted?
- g) How will the confidentiality and other aspects of protection of human subjects be maintained?
- h) When and in what form will a complete data set be returned to the Registry?

4) Data or Specimen Requirements:

- a) Data needed from Registry analysis files
- b) Specimens needed from the CLASS repository, specifying type and amount
- c) Handling of Registry Data and Repository Specimens:
- d) Disposition of stored samples from main study and those processed by ancillary study
- e) Disposition of ancillary study data at the conclusion of the ancillary study

B: Budget (to be completed for SC approval, after initial RSC informal approval):

1) Data Coordinating Center Costs

- a) Data management effort for coordinating the additional data management and analyses.
- b) Statistical staff and investigator effort to conduct any analyses before publication of results
- c) Investigator and project management effort to implement the ancillary study
- d) Expenses involved in altering key identifying data so that subjects' confidentiality will be protected.

2) Clinical Site Costs

- a) Personnel effort to obtain IRB approval, contact participants, obtain informed consent, schedule additional visits and ship samples.

3) Performance Laboratory Costs

- a) Lab supplies
- b) Labor costs relevant to testing

- c) Shipping costs to transfer specimens from Central Lab or lab(s) of origin
- 4) CLASS Central Laboratory costs
 - a) Lab, storage, freezer and office space
 - b) Lab supplies
 - c) Lab tech effort to receive, track, process, and either order tests or ship specimens for testing
 - d) Costs to oversee quality control of laboratory analyses conducted at labs other than the CLASS Central Lab

The request should begin ***at least 12 weeks before the application receipt date*** of the funding agency. All applicants are strongly encouraged to contact the Ancillary Studies Committee Chair as early as possible in the process