PHAR Ancillary Studies Policies and Procedures

PHAR Ancillary Study Review Procedures

1. Investigators wishing to propose studies that pose participant, clinic, or other burden are encouraged to discuss their studies with the PHAR Steering Committee before submitting a proposal.

2. Principal Investigator submits ancillary study proposal using the template provided on the PHAR website.

3. PHAR Steering Committee and Coordinating Center review the proposal. The Chair of the SC will decide whether to convene a conference call or handle the review by email. The review and recommendation for approval are communicated to all SC members, including the comments.

4. Proposals will be screened by the Publication and Presentation Committee to ensure there is not significant overlap with existing proposals. Proposals will be discussed by the SC, generally during their regular monthly conference calls. In some cases, the SC may also invite the PI to present the proposal and answer questions during discussion prior to voting. In the event that a member of the SC has a significant conflict of interest with regards to the ancillary study or is directly involved in the ancillary study, they will recuse themselves from voting.

5. If the proposal requires revisions, the PI must address these comments in a separate letter that accompanies the revised proposal (with changes marked).

6. The PHAR SC will evaluate proposals within 4 weeks of its submission and present a recommendation to PHCC.

7. PHCC will review the proposal for potential financial conflicts before a letter of support is offered. They will review a proposal within a 2 week time period.

8. For the successful applicant, a joint letter of approval between PHCC and the PHAR SC will be written within 8 weeks from submission of an ancillary study proposal.

PHAR Ancillary Studies Policy

Definition of an ancillary study: A PHAR ancillary study is one that uses PHAR resources and derives funding from sources other than PHAR PHA funds (or other funding sources of the parent project). Studies funded by investigator-initiated NIH research awards (R01s, etc), grants from academic institutions, or private sources (e.g., drug companies) are ancillary studies. A study that involves the collection of new data, either directly from participants or from previously collected samples, images, or other sources (e.g., medical records), is an ancillary study, regardless of the method of funding (this includes unfunded studies that collect new data). A study that provides external funding for the Coordinating Center or one or more centers is an ancillary study.

When an ancillary study proposal is not needed: If a PHAR investigator is seeking funding to support analysis of existing PHAR data, and the project does not involve new data collection, new readings of imaging data, new lab/genotyping assays, or the preparation of a complex data set by the Coordinating Center, then an Ancillary Study application is not needed. In this case, one or more Manuscript Proposals must be submitted and approved by the PHCC Publication and Presentation Committee before grant submission. The investigator may submit the Manuscript Proposal approval to the funding agency as evidence of PHAR study approval.

These distinctions can be difficult to make for some studies. If in doubt, the process will be the most streamlined if the project is discussed with the PHAR Coordinating Center (zdrager@uw.edu) first. If it is determined that there is no additional burden on the PHAR, then the proposal can be reviewed and approved by the P&P committee without submitting as an ancillary study proposal.

Philosophy: PHAR investigators are encouraged to consider ancillary studies and to involve other investigators, within and outside of PHAR, in this process.

Necessary approvals: Ancillary study proposals must first be evaluated by the PHAR Steering Committee based on the below review criteria. Potential investigators are encouraged to meet with the PHAR SC and any relevant entities (for example, the Coordinating Center) prior to submitting a proposal. The PHAR SC will evaluate the proposal and submit a recommendation in writing to the PHCC. This will be done within 4 weeks of receiving the proposal. The PHCC will then review the proposal to ensure the financial viability of the proposal within the scope of the PHCC. This review will be done within 2 weeks. Therefore, a final letter of support (from both the PHAR SC and PHCC) will be prepared for the successful applicant within 8 weeks of submitting the proposal.

Review criteria: At each level of review, highest priority will be given to studies that:

1. Do not interfere with the main PHAR objectives
2. Have the highest scientific merit
3. Produce the smallest burden on PHAR participants and the least demand on PHAR resources, including PHCC PHAR Clinic Centers, single IRB, and the Coordinating Center.
4. Require the unique characteristics of the PHAR cohort
5. Avoid overlap with previously approved research proposals

Responsibilities of Ancillary Study Investigators

1. Costs. The investigator applying for an ancillary study must supply all additional funds required to conduct the study. The Steering Committee and PHCC Inc. will be concerned with both the obvious and the hidden costs to PHAR entailed by an ancillary study (such as costs to the Coordinating Center for coordinating the additional data collection, costs to participating PHCC PHAR centers in terms of extra effort beyond that required for the PHAR, for notification of alert values, costs for obtaining and storing samples, etc.).

It is important to note that the PHAR Coordinating Center (CC) at the University of Washington nearly always incurs expenses on behalf of ancillary studies by providing support in data collection, data management, quality control, data analysis, study coordination and communications, events ascertainment, and other functions. These services can be of critical value to an ancillary study. PIs who plan to propose an ancillary study with the intention of seeking grant funding should first consult with the PHAR CC staff to determine what level of involvement will be required of the CC and the associated costs. In general, this will result in a subcontract proposal from the CC to be included in the PI's grant application. The PI will consult with PHCC Inc. staff if any subcontracts are needed to fund an ancillary study and to determine if any additional costs for the PHAR need to be considered. Additional cost for the PHAR and associated data analysis will be incorporated into the proposal budget justification.

2. Confidentiality and identification of PHAR participants. Confidentiality of individually identifiable data about PHAR participants must be assured. As a rule, no personal identification of participants will be provided to ancillary study staff. In the event that a participant consents to the release of certain personally identifiable information as part of an ancillary study, the PHAR's commitment to maintaining that participant's confidentiality is unaltered. Even if data from the PHAR will be linked with data from the ancillary study, the PHAR will ensure that personally identifiable information will be stripped from any shared datasets. There are no assurances that participants will be able to be identified and contacted in the future for the purposes of a further ancillary study.

3. Clinical implications of findings. The proposing investigator must clearly delineate any findings of clinical significance that may result from the study and propose how these will be handled, including reporting to participants and their physicians, and providing recommendations for follow up. This includes incidental findings, such as pathology identified from an imaging study that is not the focus of the study.

4. Ancillary studies to existing PHAR ancillary studies. A new ancillary study that involves participants, staff, or biological samples of an existing PHAR ancillary study but not those of the main PHAR study is considered an ancillary study only to the parent (existing) ancillary study. Such proposals are to be submitted to the parent ancillary study for review and approval, and will also be circulated to the main Steering Committee. If a new ancillary study involves participants, staff, or

biological samples of an existing PHAR ancillary study as well as those of the main PHAR study, review and approval process by both the parent ancillary study and main PHAR study will be required. Please contact the PI of the parent ancillary study for information regarding the appropriate administrative contact.

5. Inclusion of Sponsoring PHAR investigator(s). In order to request an ancillary study, a PHAR-affiliated investigator must be included as a co-investigator on the study; this individual can be anyone associated with a PHAR participating site. This individual is responsible for approving the ancillary study proposal before it is submitted to the Steering Committee, monitoring the study to assure continuing compatibility with PHAR, and serving as a liaison to the PHAR Steering Committee. In addition, each manuscript and abstract is expected to adhere to PHAR publication policies.

6. Early communication with PHAR Centers. The proposing investigator and/or their liaison should consult with PIs of pertinent centers and the Coordinating Center, depending on the anticipated involvement of center staff and oversight, study requirements, and data management and analysis. Such discussions should focus on feasibility and provision of necessary resources and do not constitute formal approval of the study.

7. Timeline. All proposed ancillary studies must be submitted to the PHAR Steering Committee for subsequent circulation and review. Studies must be submitted at least **8 weeks** prior to the grant application deadline to allow for sufficient time for review of the proposal and writing of a letter of support if deemed appropriate. Studies submitted after this deadline may not receive timely approval/necessary letter of support. In addition, studies that involve a subcontract to the Coordinating Center must have their final budget negotiated and approved for internal University of Washington review no later than **5 weeks** prior to the grant application deadline. Any financial transactions involving a PHAR ancillary study including any subcontracts will need to be reviewed by PHCC Inc. staff for PHCC Inc. Board of Directors review prior to approval.

8. Final application or proposal. The PHAR Steering Committee and PHCC Inc. may request a copy of the final proposal as submitted for funding. The PHAR Steering Committee and PHCC Inc. may request a copy of the data management and data access and sharing plans associated with the proposal.

9. Industry participation. Proposals for industry sponsorship or collaboration will be evaluated through direct communication with Pulmonary Hypertension Association. PHCC Inc. should be contacted to initiate this process. Industry led proposals should directly contact PHCC Inc. staff instead of submitting an ancillary study proposal. Any related manuscript proposals must be submitted and approved by the P&P committee before grant submission to ensure there is no overlap with existing approved proposals. If a contract with an industry sponsor could add data elements or fundamentally change elements of the PHAR, the PHAR SC should be notified prior to grant approval.

10. Status reports. The ancillary study PI must keep the Coordinating Center apprised of major developments in the life of the application or proposal, including success of funding, start date, changes in protocol, and any resulting publications or presentations. The Coordinating Center will query PIs annually or as needed for a status update on their ancillary studies, the results of which will be included in the Steering Committee reports.

11. Revising or resubmitting proposals; unfunded proposals. Once approved, ancillary studies have 3 years to become active (with or without funding), after which they will be marked as "withdrawn" and are considered inactive. After 3 years, if the original investigator wants to continue to pursue the project, a new proposal must be submitted to the Steering Committee for review, with an explanation about reactivation of the project. If the initial submission to a funding agency is unsuccessful and the PI submits the proposal as a revision application or for a subsequent funding opportunity, the PI must communicate this to the PHAR Steering Committee Chair.

Substantial changes to the science or scope of an approved ancillary study, either before or after becoming active, require re-review by the Steering Committee. The PI must submit to the PHAR SC:

1. A revised study proposal with changes from the approved version tracked, highlighted, or bolded, and with the date of the approved version and the date of the revision clearly marked;
2. A brief modification request memo summarizing the changes and stating the rationale for the changes.

Substantial changes include:

- requests for additional biospecimens
- significant additional data
- requests to add new outcomes or change the main analytical exposure
- any additional participant burden
- change of PI

Formal modification requests are NOT needed for the following:

- notification of a reduction in needed biospecimens
- requests to add co-investigators
- requests to slightly modify the analytic approach

However, all such minor changes must still be communicated to the Steering Committee

12. Review of publications and presentations. Manuscript proposals based on ancillary study data require approval of the PHAR Publications and Presentations (P&P)

committee. Publications, presentations and abstracts from an ancillary study must be reviewed and approved by the P&P Committee prior to submission or presentation, in accordance with the general rules for publications and presentations.

Incorporation of ancillary study data into PHAR database

The data collected by the ancillary study are first to be provided to the Coordinating Center to link to the main database, after which the ancillary study investigators will receive the integrated file containing necessary data from the main study. The ancillary study data may be stored separately from the PHAR parent study database. The PHAR De-Identified Data Distribution Policy describes additional requirements that must be met to receive the integrated file, including an approved manuscript proposal, a fully executed Data and Materials Distribution Agreement (DMDA), and evidence of IRB review. The ancillary study PI will be given the exclusive opportunity to analyze, present and publish data collected under the auspices of the ancillary study. After a reasonable time (in general, 12 months after data collection and cleaning are complete) the ancillary study data will be made available for additional uses by other PHAR investigators in collaboration with the ancillary study investigators. It is the responsibility of the ancillary study PI to state in writing to the Steering Committee any special circumstances that would militate against these guidelines for data sharing.

Data ownership and sharing of ancillary study data by the ancillary study PI

The ancillary study PI owns the ancillary study-derived data however *may not* directly share any PHAR data collected through support of the PHCC, including the PHAR ID or GUID, age, sex, race/ethnicity, center, or other data, without PHAR permission; PHAR data may be transferred to other investigators or centers only by the Coordinating Center.

Data sharing including the ancillary study data and other PHAR data will occur using the usual PHAR processes for P&P review and approval. Ancillary study PIs will prepare a PHAR paper proposal, obtain P&P approval, and accomplish the transfer of ancillary study data and any required PHAR contract-derived data through the CC after completing a DMDA. Ancillary study PIs are encouraged to read the DMDA to understand the important protections it provides.

Data sharing with a consortium: Ancillary study investigators who wish to share ancillary study data and some contract-derived variables (e.g., ID, age, sex, field center, other variables) with a consortium must bring a proposal describing the consortium to the Steering Committee for review. Such consortia often have their own data sharing plans and their own P&Ps, and these arrangements need to be approved by PHAR before PHAR-derived data can be contributed.