National Heart, Lung, and Blood Institute

THE CARDIOVASCULAR HEALTH STUDY

CHS Ancillary Study Policies and Procedures

Contents

Submission Deadlines

- Ancillary Study proposals must obtain CHS and NHLBI approval before submission to a funding agency.
- New proposals must be submitted to CHS a minimum of 6 weeks prior to a grant deadline, preferably earlier if the project involves a subcontract.
- Proposals received after this deadline will not receive expedited review and may require that investigators postpone their grant submission.

Definition of an Ancillary Study

An ancillary study is an investigation which is not part of the central, NHLBI-funded CHS protocol but uses CHS participants, samples, or data collected by CHS. An ancillary study can involve acquisition of additional data which are not compiled as part of the standard CHS data set, or analysis of existing CHS data only in a paper or series of papers as part of a new external funding application.

Support for ancillary studies is derived from sources other than CHS grant or contract funds. Examples include studies funded by investigator-initiated NIH research awards (R01s), grants from academic institutions, private sources (e.g. drug companies), or those performed at no cost (generally because of the special interest of a researcher).

Rationale for Ancillary Studies

Investigators are encouraged to propose and conduct ancillary studies. Such studies enhance the value of CHS and ensure the continued interest of the diverse group of investigators who are critical to the success of the study as a whole. They provide an exceptional opportunity for investigators, either within or outside of CHS, to conduct additional projects at minimal cost.

Types of Ancillary Studies

There are two types of ancillary studies in CHS:

New Data Collection studies

These generate new CHS data, either through new interaction with participants, or by using existing stored biological specimens, images, medical records, or previously collected data to create new measures.

Analysis-only studies

These analyze existing CHS data only, in a paper or series of papers as part of a new external funding application, regardless of whether significant Coordinating Center (CC) services (e.g., data set preparation or analysis by a CC Statistician) are requested.

When an Ancillary Study Proposal is Not Required

Proposals to analyze existing CHS data that are supported by external funding *already awarded* are not considered ancillary studies and may be submitted via the online manuscript proposal form. If the manuscript proposal involves billable CC services such as a dataset then these can be invoiced upon completion via the CC's fee-for-service account. If your institution requires a subcontract for such services, however, then the project must be routed as an ancillary study.

Ancillary Study Review Process

To protect the integrity of CHS, all ancillary studies must be reviewed and approved before access to CHS data or participants is permitted. The review process is as follows:

Biorepository Impact Report (1-2 weeks prior to CHS submission, if relevant):

Before submitting an ancillary study proposal for review, investigators must obtain a statement of repository impact from the CHS Laboratory. This is a brief summary of the number of samples requested and how this number will affect total samples in storage. Investigators must provide the Lab information about their needed sample type, the permissible number of freeze/thaw cycles, etc. (See the ancillary proposal form for more details).

Proposal Submission:

New proposals must be submitted to the Ancillary Study Coordinator at the CHS Coordinating Center *a minimum of 6 weeks prior* to a grant deadline, preferably earlier if the project involves a subcontract**.** Deadlines for major NIH grant cycles are posted on the CHS website.

Once the Coordinating Center ascertains that the form is completed satisfactorily, the proposal will be circulated for review. If the form is incomplete, the initiator of the proposal will be contacted and

requested to modify or add the required information. Ancillary Study forms can be obtained by downloading them from the CHS website.

Subcommittee Review (1-3 weeks):

a) If biospecimens are requested, the Laboratory Subcommittee (LC) will review the proposal via email. Investigators might be asked to respond to questions or concerns from the LC before the proposal is forwarded to the Steering Committee along with the LC's recommendation.
b) Analysis-only studies will be reviewed by the Publications & Presentations (P&P) Subcommittee at their next semimonthly conference call. Approval by the P&P is required for Steering Committee review.
c) New data collection studies that do not involve biospecimens will be routed directly to the Steering Committee.

Steering Committee Review (1-2 weeks):

Following review by the relevant Subcommittee, if required, the proposal will be sent to the Steering Committee along with any Subcommittee recommendations. If concerns are major, Steering Committee comments will be sent back to the initial investigator for response and modification of the proposal if desired.

NHLBI Project Office Review (1-2 weeks):

Once approved by the Steering Committee, the proposal will be sent to the NHLBI Project Officer for final review.

Formal Letter of Approval

Once all approvals have been granted, a formal letter documenting the approval will be sent separately by the NHLBI Project Office.

Review criteria

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

- Do not interfere with the main CHS objectives
- Have the highest scientific merit
- Produce the smallest burden on CHS participants and the least demand on CHS resources, such as blood samples
- Require the unique characteristics of the CHS cohort

Funding

No funds from the main CHS grant or contract may be used to support an ancillary study in any way. Thus, it is crucial that a subcontract to the Coordinating Center or estimate for invoicing via fee-for-

service account be included which will cover all data handling costs as well as data analyses if needed. Blood laboratory costs will be billed separately via a fee-for-service account.

It is important to note that the CHS 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 CC to determine what level of involvement will be required of the CC and the associated costs. Agreement with the Coordinating Center and, if applicable, the CHS Central Laboratory about the costs needed to perform an ancillary study is required for Steering Committee approval.

Involvement of Third Parties & Patents

Proposed research that will be supported by a third party (i.e., industry or charitable foundation) - whether the party is providing financial support, participating directly in a study, supplying study resources, or receiving special access to study results, data, findings, or intellectual property - requires a third party agreement between the sponsor and the PI's institution. Agreements should be drafted according to NHLBI Guidelines and sent to the NHLBI Project Officer for review and concurrence as a condition for NHLBI approval of the proposal prior to completion of any DMDA.

Ancillary study proposals must indicate whether a for-profit corporation is involved and whether intellectual property protection (i.e., patent or copyright, or to license any process, aspect or outcome of the study, including copyrightable software) will be sought. Local analyses performed by a for-profit corporation or an entity intending to seek intellectual property protection are required to be verified by the CHS Coordinating Center. The Coordinating Center may require that analyses also be performed centrally, depending on the extent of CHS data requested. Said corporation or entity must bear the cost of the analysis and/or verification via an agreement between the requesting organization and the University of Washington.

For-profit involvement will necessitate that the dataset exclude participants who did not consent to use of their data by private companies.

IRB Review

The use of CHS data or biological materials requires review by an Institutional Review Board (IRB) or Ethics Board. Evidence of IRB review (whether approval or exemption) must be provided to CHS as part of the data and/or specimen recipient's Data and Materials Distribution Agreement (DMDA).

Consent

Studies that will collect new data from participants must obtain a separate informed consent from all ancillary study participants.

If an approved proposal involves genetic studies, sample selection will be based on the CHS informed consent status. Ethical, legal and social implications, as well as reporting of results, must be proactively addressed in the proposal.

Inclusion of a Sponsoring CHS Investigator

A CHS investigator or other approved collaborating investigator is expected to be a co-investigator or principal investigator on an ancillary study in the role of CHS sponsor. The sponsor is responsible for presenting the study to the CHS Committees, monitoring the study to assure continuing compatibility with CHS and serving as a liaison to the CHS Steering Committee. In addition, manuscripts and abstracts are generally expected to include a CHS sponsor, except under circumstances that should be stated and justified as part of the original proposal.

The list of eligible CHS Investigators may be found in the online CHS directory.

CHS Site Involvement

All CHS sites designated for inclusion in the study must have agreement from the respective Principal Investigator.

Biospecimen Policy:

Anyone considering a CHS Ancillary Study that would use stored samples must contact the Central Laboratory as early as possible in their planning process. While there are still many CHS samples in the Repository, some sample types are limited, and any given study may not be feasible. Also, please especially note #10, below.

1) We do not set aside samples while projects are being reviewed for funding or in other ways delayed or not ready to start; we will try to work with investigators to assure availability by the time of funding.
2) We only consider projects of high scientific merit, as assessed by the Lab Committee.
3) We only consider projects that are consistent with CHS Mission and Goals; the project must add substantially to CHS.
4) We only consider projects for which CHS samples are the best resource available; in other words, why CHS samples rather than ARIC, CARDIA, MESA, etc?
5) We will approve year 9 samples first; justification is needed to obtain year 5 samples; further justification is needed to obtain year 2 samples.
6) We will approve thawed samples first; justification is needed to obtain unthawed samples.
7) We will approve the sample type (serum, EDTA, citrate) in greatest abundance first; justification is needed to obtain samples with lesser abundance.
8) We will only approve a sample volume of 250 uL or less; a Steering Committee vote is required to approve more than that.
9) We will leave one unthawed aliquot; a Steering Committee vote is required to use the last unthawed aliquot.

10) We will only consider proposals with an attached Repository Report.
11) We will only consider proposals in which the proposed assays have been validated as sensitive enough and reproducible enough for the study; if done at an outside laboratory, that laboratory must provide evidence that they understand population-based assay work, including a brief review of quality assurance/quality control.
12) We will consider the following issues as important in prioritizing proposals:
    a) Does the proposal integrate activities with other studies to limit freeze-thaw cycles?
    b) Is the proposal important to a new investigator(s)?
    c) Does the proposal help fill out the overall CHS portfolio?
13) Approved ancillary studies have 3 years to become active (with or without funding), after which they will be withdrawn and must be resubmitted for reapproval.

Data Access, Sharing and Integration

Timeline for Data Collection and Sharing

The data collected by the ancillary study and any accompanying documentation are first to be provided to the CHS Coordinating Center for integration into the main database. This must occur before the integrated file containing data from the main study will be sent to the ancillary study investigators. The ancillary study PI will be given the first and 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 investigators. Collaboration with the ancillary study investigators who collected the data is encouraged. 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. In the spirit of encouraging collaboration, reasonable and justified requests to the Steering Committee for limiting access to the data will be honored or some compromise will be worked out.

Ancillary Study Data Ownership and Sharing

The ancillary study PI owns the ancillary study-derived data and may share it with a third party without CHS permission as long as the sharing does not violate the participants' consent terms. Importantly, the ancillary study PI may not directly share any main CHS grant-derived or contract-derived data, including the CHS ID, age, sex, race/ethnicity, field center, or other data, without CHS permission; CHS contract-derived data may be transferred only by the Coordinating Center.

However, direct sharing of ancillary study data by the ancillary study PI is generally discouraged for several reasons. First, the ancillary study data alone, without any other information, are usually of very limited interest. Second, unless the ancillary study PI develops his/her own data sharing agreement, with direct data sharing there are no data protections or restrictions against further sharing. Rather than direct sharing, ancillary study PIs are strongly encouraged to collaborate with interested third parties to prepare a CHS paper proposal, obtain P&P approval, and accomplish the transfer of ancillary study data

and any required CHS derived data through the CC after completing a DMDA. Ancillary study PIs are encouraged to read the CHS 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., CHS ID, age, sex, field center, other variables) with a consortium must describe the consortium in their proposal submitted for review. Such consortia often have their own data sharing plans and their own P&Ps, and these arrangements need to be approved by CHS before CHS contract-derived data can be contributed.

Main CHS Study Data Distribution Requirements

A manuscript proposal must be reviewed and approved by CHS before data from the main study will be provided to ancillary study investigators. For information on manuscript proposals, see "Publications Resulting from Ancillary Studies" below. Studies that have a special arrangement with CHS may be exempted from this policy.

The Coordinating Center will only send CHS individual level main study data to investigators of an approved ancillary study following the steps below:

1) CC receipt of new data collected by the ancillary study & accompanying documentation (when applicable)
2) Approved manuscript proposal
3) Data and Materials Distribution Agreement (DMDA)

NIH Data Sharing and Management Policy

Effective **January 25, 2023**, all NIH grant applications that will result in the generation of new scientific data, if funded (ie, 'New Data Collection CHS ancillary studies) must

- Plan and budget for the managing and sharing of data
- Submit a DMS plan for review when applying for funding
- Comply with the approved DMS plan

Scientific Data is defined as data commonly accepted in the scientific community as of sufficient quality to validate and replicate research findings, regardless of whether the data are used to support scholarly publications.

- Scientific data includes any data needed to validate and replicate research findings.
- Scientific data does not include laboratory notebooks, preliminary analyses, completed case report forms, drafts of scientific papers, plans for future research, peer reviews, communications with colleagues, or physical objects such as laboratory specimens.

Individual NIH Institutes, Centers, or Offices may have additional policies and expectations (see NIH Institute and Center Data Sharing Policies).

Download a simplified version of the Data Management and Sharing Policy Overview Page

Publications Resulting from Ancillary Studies

All publications from an ancillary study must be preceded by a penultimate draft manuscript that is reviewed and approved by the CHS Publications Subcommittee (P&P), Steering Committee, and NHLBI prior to journal submission, in accordance with CHS publications policy. In most instances, an approved manuscript proposal must precede the penultimate draft manuscript. (See Publications & Presentations Protocol for guidelines).

Status reports

The ancillary study PI must keep the CHS 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 CHS 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 and other reports.

Modifications to Ancillary Studies

Substantial changes to the science or scope of an approved ancillary study require review by the CHS Steering Committee and, if relevant, Lab or Publications Subcommittee, followed by NHLBI. The PI must submit to the CHS Ancillary Studies Coordinator:

1) a revised study proposal with changes tracked, highlighted or bolded;
2) a brief modification request memo summarizing the changes and stating the rationale for the changes. The memo may be addressed to the CHS Steering Committee.

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 Ancillary Studies Coordinator via a memo addressed to the CHS Steering Committee.

Time Limit for Approval

All ancillary studies have 3 years to become active (with or without funding), after which their approval will expire, their status will be updated to "withdrawn" and they must be resubmitted to CHS for reapproval if subsequent grant submission is desired.

CHS Ancillary Studies Contacts

General questions:	Erika Enright, CHS Research Coordinator eenright@uw.edu, 206-897-1922
Data questions:	CHSDATA@uw.edu
Biological specimens:	Elaine Cornell, CHS Central Blood Laboratory Elaine.Cornell@uvm.edu, 802-656-8963
UW Subcontracts:	Mary Lou Biggs, CHS Project Director mlbiggs@uw.edu, 206-897-1945