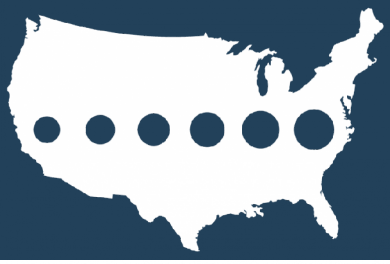

Add Health

The National Longitudinal Study of Adolescent to Adult Health

Ancillary Studies

Researcher Guidelines

Biospecimen Study

UNC | CAROLINA POPULATION CENTER

ADD HEALTH ANCILLARY STUDIES

Biospecimen Study

The development of an Add Health Ancillary Study is time-intensive and may also be costly. Please read the following guidelines carefully.

What is a Biospecimen ancillary study? An Ancillary Study is any study that adds data to Add Health that is beyond what is included in the activities of the core Add Health Study. Ancillary Study costs are supported by the investigator, and must be approved by Add Health before any grants for support are submitted for funding, and uses archived biospecimens collected by the Add Health Study to conduct new assays.

Studies Involving Archived Biospecimens

Add Health maintains a repository of biospecimens that were collected at various timepoints during the study. For more information about the use and storage of biospecimens in Add Health, please review the Biospecimen Reserve Policy.

Requests to collect new or use archived biospecimens will receive especially careful consideration in light of the ongoing need to minimize burden and ensure that adequate amounts of biospecimens are reserved for current and future Add Health objectives. Proposals to collect new or use archived Add Health biospecimens must include an explanation of the type and quantity of material needed and a justification of the amount.

All biospecimens and any data resulting from their analysis become the property of Add Health and will be made available to the research community according to the terms of the Data and Material Use Agreement. Proposals to collect new or use archived Add Health biospecimens must include an explanation of the assays to be performed and an estimate of the number of variables to be added to the Add Health data. After assays are complete, any unused biospecimen must be either returned or destroyed based on prior agreement with Add Health.

Biospecimen Ancillary Studies are conducted in 5 Phases:

- **Phase 1: Determine volume needed and sample size**
- **Phase 2: Applying for an Ancillary Study (6 months review timeline). This includes the initial proposal review and the full application review**
- **Phase 3: Obtaining funding and completing require documentation**
- **Phase 4: Conducting your study**
- **Phase 5: Receive dataset**

SECTION I

Requirements

A. Investigator Requirements

Ancillary Study investigators must meet the following criteria:

1. Have a PhD, MD, or other terminal degree.
2. Hold a faculty appointment or research position at their institution.
3. Work for an institution of higher education, a research organization, or a government agency.
4. Have an institutional review board (IRB) that complies with applicable Federal regulations governing research involving human subjects.
5. Demonstrate completion of research ethics training by all research team members who will work with the Add Health data.
6. Have a demonstrated record of using sensitive data according to commonly accepted standards of research ethics.

B. Funding Requirements

Investigators proposing to conduct an ancillary study must cover all costs incurred by the study. These costs include preparing and documenting analysis files, as well as integrating ancillary data into the Add Health Study. In most cases, investigators will need to budget for these expenses and establish a subcontract with the Add Health project to cover them. Add Health staff will work with investigators to develop a budget estimate that may include activities such as sample selection, retrieving samples from archives, processing and shipping biospecimens, and other necessary tasks. Note that some of these activities can only be performed by Add Health and must be paid for by the ancillary study. **Before submitting any proposal for funding from an external agency, investigators must contact Add Health to obtain cost estimates for budgeting purposes**.

Additionally, all ancillary data will be reviewed by Add Health staff for deductive disclosure risk, cleaned, and checked. Dataset documentation will also be reviewed, and codebooks created. Ancillary studies are required to hold a restricted-use data contract, which is a $1000 flat rate.

Please coordinate with the Add Health Studies Coordinator to create an estimate for your study.

SECTION II

Add Health Priorities and Policies

Add Health welcomes the addition of ancillary studies that have scientific merit. However, Add Health will not consider ancillary studies that:

- Duplicate or interfere with existing Add Health activities (including already approved ancillary studies).
- Adversely affect respondent cooperation in Add Health.
- Threaten the security of Add Health data and/or identities of Add Health respondents.
- Create an unacceptable diversion of Add Health study resources, including personnel or study samples.
- Jeopardize the public image of Add Health.
- Are not consistent with both Add Health scientific objectives and the priorities of our main funding agencies, the Division of Behavioral and Social Research of the National Institute on Aging and/or the Population Dynamics Branch of the Eunice Kennedy Shriver National Institute of Child Health and Human Development.

Commercial Use of Add Health

Add Health will not approve ancillary studies that are subject to consulting or licensing obligations to another institution, corporation, or business entity. Approval of an ancillary study shall not be deemed a grant under any patents (either existing or future) or any rights to use.

Released Add Health Data

It is Add Health's expectation that ancillary studies make resulting data available to the Add Health community of data users.

Biospecimen Availability

With sufficient scientific justification, Ancillary Studies are limited to the following biospecimen volumes, including any necessary “dead volume” or padding:

Wave	Serum	Plasma	DNA	Dried Blood	Urine	Saliva	Stool
Wave V	Yes - 250 uL	Yes - 250 uL	Yes - 1 ug DNA	No	No	No	No

SECTION III

Ancillary Studies Committee Review Criteria

The review of Add Health Ancillary Study proposals is both time-consuming (on the part of Add Health) and serious. We not only consider such reviews to be similar to those of an NIH Study Section (e.g., Five Dimensions of Scientific Merit), but we also give serious consideration to both Add Health priorities and policies and to the scientific priorities of our main funding agencies over the years, particularly the Division of Behavioral and Social Research of the National Institute on Aging (NIA) and the Population Dynamics Branch of the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD).

Requests to collect new biospecimens or use archived biospecimens or biological data will also be reviewed and approved by the Add Health Biology Team. All proposals will be reviewed according to the following criteria:

- Consistency with scientific objectives of Add Health.
- Consistent with the scientific priorities of our main funding agencies over the years, particularly the Division of Behavioral and Social Research of the National Institute on Aging (NIA) and/or the Population Dynamics Branch of the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD).
- Acceptable burden to Add Health respondents.
- Draws on unique characteristics of Add Health.
- No/minimal overlap with the current portfolio of studies.
- Parsimonious use of biospecimens (if applicable).
- A minimal burden to Add Health staff and biospecimen repositories (if applicable).

To allow adequate time to submit revise, re-submit, and re-review proposals and applications that are not approved, applicants are strongly encouraged to submit proposals at least six months in advance of an anticipated grant application deadline. Investigators who conduct an Ancillary Study must cover all costs incurred by the study, such as preparing and documenting analysis files and integrating ancillary data into the Add Health Study. Most funding agencies require an approval letter included with a grant submission, therefore, an ancillary study must be approved by Add Health before a grant to support it is submitted for funding.

Although Ancillary Study investigators are not required to have previous experience with the Add Health Study, demonstrated familiarity with Add Health data and its study design will significantly enhance review of Ancillary Study proposals, within both Add Health and independent funding agencies.

SECTION III (continued)

Ancillary Studies Committee Review Criteria

Scientific Merit

Significance	Does this study address an important problem? If the aims of the application are achieved, how will scientific knowledge, clinical practice, or public health policy be advanced? What will be the effect of these studies on the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?
Approach	Are the conceptual framework, design, methods, and analyses adequately developed, well-integrated, well-reasoned, and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics?
Innovation	Is the project original and innovative? For example: Does the project challenge existing paradigms, practice or policy; address an innovative hypothesis or critical barrier to progress in the field? Does the project develop or employ novel concepts, approaches, methodologies, tools, or technologies for this area?
Investigators	Are the investigators appropriately trained and well-suited to carry out this work? Is the work proposed appropriate to the experience level of the principle investigator and other researchers? Does the investigative team bring complementary and integrated expertise to the project (if applicable)?
Environment	Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed studies benefit from unique features of the scientific environment or respondent populations, or employ useful collaborative arrangements? Is there evidence of institutional support?

Section IV

Phase 1 - Before applying for a biospecimen Ancillary Study

Parsimonious use of biospecimens is an important consideration in review of the Add Health Ancillary Study proposals. Add Health maintains a repository of biospecimens that were collected at various timepoints during the study. These biospecimens are finite and have the potential for critical scientific advancement. Thus Add Health has the dual responsibility of encouraging and supporting ancillary studies that utilize stored biospecimens, while also ensuring that there is a small reserve of biospecimens set aside for research purposes that simply cannot be foreseen at the current time. For this reason, Add Health has created two types of biospecimen reserves: 1) Restricted-Use Biospecimen Reserve, and 2) Future Opportunities Protected Biospecimen Reserve. For more information about these two biospecimen reserves, please review the Biospecimen Reserve Policy.

Before applying, Ancillary Study investigators should:

- Review Researcher Guidelines.
- Review previously conducted Ancillary Studies.
- Determine whether their assay can be conducted in the Add Health laboratory or will need to be performed by another laboratory.
- Determine the smallest possible biospecimen volumes needed to complete their proposed work.
- Only request those minimum volumes.
- Only run samples in singleton, when appropriate.

When planning ancillary studies involving biospecimens, Add Health recommends and highly prefers that all testing and long-term storage of biospecimens be conducted at the Laboratory for Clinical Biochemistry Research (LCBR), our partner laboratory at the University of Vermont (UVM). Our Add Health Biology Team has a longstanding working relationship with LCBR, all of our venous blood biospecimens are archived and monitored there, and we can best implement all aspects of your biospecimen testing at this laboratory.

If your ancillary study requires a specialized laboratory outside of LCBR, please provide strong written justification for this request that includes plans for final disposition of any leftover sample. In addition, when preparing your budget please include $7.50 per biospecimen to cover the cost of pulling and shipping blood from LCBR to your approved outside laboratory.

Section V

Phase 2 - Applying for an Ancillary Study

Submitting your proposal

Step 1	Submit a brief 1-page Concept Proposal to **AddHealth_Ancillary@unc.edu** for Add Health review.

Step 2	Address feedback and resolve issues from the preliminary proposal review.

If your proposal is approved, you will be invited to submit a full application

Step 3	Submit an Ancillary Study Application Form for Add Health review, along with number of variables and a narrative description (12 pages maximum) including: Why Add Health, specific aims, brief background and significant, conceptual framework and hypothesis, data and/or biological materials requested or to be collected, sample size and justification, (i.e. formal power calculation), analysis plan for each aim, study timeline.

Step 4	Receive Add Health review. The outcome of the review may be accept, revise, or reject. • Accepted applications then move to Phase 3. • If revisions are requested, they should be made in a resubmitted application, with tracked changes and comments, along with a response to the changes in a separate document. • Rejected applications will be provided with a final determination and reason for the decision.

Step 5	Work with the Add Health Studies Coordinator to develop a cost estimate. Investigators proposing to conduct an Ancillary Study must cover all costs incurred by the study. Add Health will work with Ancillary Study investigators to develop a budget estimate, such as: sample selection; collecting or pulling samples from archive; processing and shipping biospecimens; preparing and documenting analysis files; integrating ancillary data into the Add Health Study. Some of these activities can only be performed by Add Health must be paid for by the Ancillary Study.

Section VI

Phase 3: Obtain funding and complete documentation

Accepted applications will receive a formal written notice, documenting Add Health's support for the project and guarantee for collaboration. This notice should be included in any external grant application to fund the project.

After receiving funding, the Ancillary Study Investigator will be required to complete the following distribution agreements prior to the release of any data by the Carolina Population Center (CPC)/University of North Carolina

1. Review, fill and sign the Data and Material Use Agreement.
2. Go to the CPC Data Portal and apply for a Restricted-Use Contract if one is not already in place.
3. Proof of completion of research ethics training by all research team members who will work with the Add Health data.
4. Proof of completion of HIPAA training by all research team members who will work with the Add Health data.
5. IRB approval for the ancillary study.

After an Ancillary Study is approved, changes in the scope or procedures of the study must be submitted via a modification form, reviewed, and approved by Add Health. A modification form can be found on the Ancillary Studies website or by contacting the Studies Coordinator at addhealth_ancillary@unc.edu.

Annual Status Reports

After an Ancillary Study is funded and initiated, the PI is responsible for submitting annual progress reports of the study's status to Add Health until Add Health has released final ancillary data. These progress reports must summarize the study's activities, including:

1. Progress of data collected to date
2. Analysis in progress or completed
3. Updates to scope, design, or methods
4. Updates to timeline

Annual report forms will be sent out to Ancillary Study investigators on **June 1** of every year in the study period. These forms must be completed and returned to CPC no later than **July 1** of the same year. Ancillary studies that fail to comply with the annual reporting requirement may be ineligible for renewal of their Add Health restricted-use contract and/or their Data and Material Use Agreement.

Section VII

Phase 4 - Conducting your Study

Step 1 - Develop a pull list: The Ancillary Study Investigator and Add Health work together to create a participant biospecimens pull list based upon approved selection criteria and Add Health standard biospecimen volumes. Add Health securely and solely maintains the crosswalk from the biospecimen and lab/vial ID to the participant and non-participant IDs.

Step 2 - Send the biospecimens to Ancillary Study lab: Add Health will work with the storage lab to send the biospecimens to the ancillary study lab and sends a manifest to both Add Health and the ancillary study lab.

Step 3 - Testing and quality control: The ancillary study lab performs testing. When finished, the ancillary study lab sends results to Add Health linked by a lab/vial ID as well as QC data and internal quality documentation.

Step 4 - Evaluate data quality: Add Health assesses data quality based upon the participant, non-participant, and IIV biospecimens.

Step 5 - Receive preliminary dataset: Add Health makes the participant data with masked IDs and internal quality control documentation available to ancillary study investigators to assess the data quality and look for errors.

Step 6 - Prepare documentation: The Add Health Studies Coordinator will provide a User Guide template for the dataset that the Ancillary Study Investigator will need to create.

Step 7 - Pay Invoice: The Add Health Studies Coordinator will submit an invoice annually for the work completed during the year. Payment must be received before any data can be released.

Section VII

Phase 4 - Conducting your Study (continued)

Sampling Selection

Ancillary study proposals must clearly specify the selection criteria and sample size to guide biospecimen sample selection. Once an ancillary study has been approved and funded, the Add Health Biology Team will work with ancillary study investigators and Add Health programmers to develop the ancillary study's sampling list, to develop its back-up sampling list, and to select the sample, all according to the approved study protocol. Any post hoc changes to approved ancillary study selection criteria, sample size, or protocol must be formally proposed and justified in an Add Health Ancillary Study Modification Request submitted to the Ancillary Studies group. Formal review and approval of such requests must precede sample selection.

Given the involvement of Add Health personnel in sample selection, associated costs must be fully anticipated and shouldered by the ancillary study. Costs must be negotiated with Add Health after ancillary study approval, but before submission for funding.

Masking and Quality Control

Conditional on their availability, Add Health will randomly interleave quality control (non-participant) biospecimens totaling a recommended 5% of the selected participant biospecimens into the selected sample. The quality control biospecimens will include pairs of masked duplicates, thereby totaling 2.5% of selected participant biospecimens. For example, in a study of biospecimens from n=200 participants, Add Health will randomly interleave n=10 quality control biospecimens, i.e. 2 masked duplicates from each of n=5 non-participants. Any proposed reduction in the number of quality control biospecimens designated above must be justified in detail at the time of the Ancillary Study proposal.

After including the masked duplicate pairs, Add Health will interleave n=100 Intra-Individual Variation (IIV) participant samples, depending on their availability. Costs of assaying the masked duplicate and IIV participant samples also must be fully anticipated and shouldered by the ancillary study (or selected participant sample size reduced to offset them). Add Health will replace the selected participant, non-participant masked duplicate, and IIV participant identifiers (IDs) with undifferentiated, masked ancillary study IDs before shipping samples to laboratories for assay. Add Health will control the crosswalk of participant, nonparticipant, and IIV IDs.

Add Health will not identify participant assay results to ancillary study investigators until Add Health receives the results and associated documentation of internal quality control.

Section VII

Phase 4 - Conducting your Study (continued)

Internal Quality Control

Laboratories must:

- Follow best practices for monitoring and controlling assay data quality.
- Use conventional tools (e.g., negative/positive controls, calibration standards).
- Immediately report any unanticipated changes in lab protocol, reagent shortages, substituted materials, or adverse events to the Add Health Ancillary Studies Coordinator at addhealth_ancillary@unc.edu.
- Provide documentation summarizing procedures and assay data quality (including missingness, validity, and reliability) when returning data to Add Health.
- Include conventional quality metrics in the documentation (e.g., counts of missing values, differences in/correlations between known and assayed values, and coefficients of variation within/between split samples).
- Identify masked duplicate pairs for studies requesting DNA for large-scale genotyping.

External Quality Control

- Add Health will produce an external quality control report, reviewed by the Add Health Biology Team.
- The report will include standard reliability and validity measures and summary statistics for high-dimensional data.
- Ancillary Study investigators can explore assay results but cannot publish findings until Add Health completes external quality control analyses, sends the report to investigators, and after the one-year exclusive research period, disseminates the results, documentation, and report to the Add Health user community.

Section VIII

Phase 5 - Releasing your Data

Results from the Use of Add Health Biospecimens

Upon satisfying the ancillary study protocols, Add Health exchanges the preliminary IDs for AIDs, then disseminates the AID-identified participant data to the Ancillary Study Investigator. At this time, the Ancillary Investigator is provided a one-year period of exclusive access to the data, during which they may submit manuscripts, abstracts, or presentations related to the Ancillary Study **as specified in the Add Health restricted-use data agreement.**

Following the one-year period for biospecimen ancillary studies, Add Health will release the final dataset to the user community.

Section IX

Applying for a Restricted-Use Data Contract

In order to receive preliminary ancillary data for review, the Ancillary Study investigator will need to apply for a restricted-use data contract. This contract is an agreement signed by two parties, the Ancillary Study Institution and UNC-Chapel Hill on behalf of Add Health.

To apply for restricted-use data, please download and complete the Restricted-Use Data Contract using the CPC Data Portal at https://data.cpc.unc.edu/ and select Add Health, or contact addhealth_contracts@unc.edu.

Data Security

Protecting the identity of individual Add Health respondents is a critical issue for the Add Health study. Confidentiality of individually identifiable data about Add Health respondents must be assured.
All data work will take place in the Secure Research Workspace (SRW). The SRW helps keep Add Health data more secure in our efforts to maintain the strict confidentiality of our participants. The SRW is available through remote access. All research and analysis will take place only within the SRW.

For detailed ancillary study data security obligations, see The Add Health website https://addhealth.cpc.unc.edu/.

Section X

Ancillary Study Roadmap - Biospecimens

Phase I

- Review Researcher Guidelines
- Review previously conducted Ancillary Studies
- Determine if assay can be conducted in Add Health lab or other
- Determine smallest possible biospecimen volumes needed
- Only request minimum volumes
- Only run samples in singleton

8 months prior to funding submission

Phase II

- Submit one-page concept proposal
- Respond to reviewers feedback (resubmit if applicable)
- Submit full Ancillary Study application form
- Respond to reviewers feedback
- Receive decision

8 months prior to funding submission

Phase III

- Secure external funding
- Submit additional documentation, including DMUA, ethics training, HIPPA training, and IRB approval
- Apply for restricted-use data contract (if applicable)

Dependent on funding agency's timeline

Phase IV

- Develop pull list
- Testing and quality control
- Evaluate data quality
- Receive preliminary dataset
- Prepare documentation
- Pay annual invoice

Dependent on laboratory

Phase V

- Final data review by Add Health
- Data released to Ancillary Study investigators for 1-year period
- Prepare publications, manuscripts, and presentations using the final released file

6 to 8 weeks prior to 1 year exclusive period

Add Health

The National Longitudinal Study of Adolescent to Adult Health

Please contact and submit applications to:

Email:
addhealth_ancillary@unc.edu

For more information:

Website
https://addhealth.cpc.unc.edu

X (formerly Twitter)
@Add_Health

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