HCHS/SOL Ancillary Studies Policy

VERSION CONTROL

HCHS/SOL Ancillary Studies Policy Version 4.1 (Feb. 2025) main modifications.

- Added contact information for Central Lab. [See section 5.6B]
- Updated language related to NIH data sharing. [See section 5.8B]

HCHS/SOL Ancillary Studies Policy Version 4 (Dec. 2023) main modifications.

- Parent Study co-PIs can sponsor Ancillary Studies (AS). [See section 5.0]
- Intervention trials are allowed. [See section 5.2]
- A Consortium seeking funding must submit an ancillary proposal, but first HCHS/SOL Steering Committee must approve HCHS/SOL joining the Consortium. [See sections 5.2 and 5.5]
- Career Development grants and Secondary Analyses grants must have an associated manuscript proposal approved before submitting to the Ancillary Studies Committee. These types of AS do not need to submit a concept proposal followed by a full proposal; these have an expedited review. [See sections 5.2 and 5.5]
- Diversity Supplements for doctoral students, post-doctoral fellows and Early-Stage Investigators are considered an AS. [Section 5.2]
- Grant renewals are not amendments to a previous Ancillary Study. A new concept and full proposal must be submitted. [See sections 5.2 and 5.5]

5.0 Ancillary Studies Policy

To enrich the scientific value of HCHS/SOL, the Steering Committee (SC) invites proposals from individual researchers interested in conducting ancillary studies (AS) to advance scientific knowledge. To protect the integrity of HCHS/SOL, AS must be reviewed and approved by the Ancillary Studies Committee (ASC), the HCHS/SOL SC, and the HCHS/SOL Observational Study Monitoring Board (OSMB), if there is participant burden; and the NHLBI prior to submission for funding.

All AS proposals must be sponsored by a Principal Investigator (PI) or Co-Principal Investigator (co-PI) from the Field Centers or Coordinating Center. Proposed AS that leverage data or resources from another ancillary study must also receive approval from that ancillary study's PI/MPI team.

5.1 Definition of an Ancillary Study (AS)

An ancillary study uses data from HCHS/SOL in an investigation that is not described in the HCHS/SOL protocol; requests biospecimens; and conducts data collection or data analyses with additional funding that is not included as part of the HCHS/SOL parent study. Funding must cover the costs incurred by the Field Centers, the HCHS/SOL Central Laboratory (e.g., to process or ship samples), and the Coordinating Center (for tasks such as sample selection, preparing and documenting analysis files, participating in statistical analysis, and integrating the new ancillary study data back into the centralized HCHS/SOL database). Career development grants (e.g., K, AHA fellowship), diversity supplements generating new data, and administrative supplements are also considered ancillary studies. A request for DNA samples from HCHS/SOL to replicate a non-HCHS/SOL study's results is also considered to be an ancillary study.

5.2 Types of Ancillary Studies (AS)

There are several types of AS, but these can be classified into seven general categories:

(1) Career Development or Diversity Supplement conducting data analysis only;
(2) Data analysis only;
(3) Consortia seeking funding (including those only doing secondary data analyses);
(4) Stored biospecimens and data use only;
(5) Participant burden only;
(6) Participant burden *and* stored biospecimens
(7) Other including Administrative, renewal grants, and expired AS extension.

5.3 Local (Single-Center) vs. Multi-Center Studies

AS proposals that would collect new data on participants may involve one or more or all HCHS/SOL Field Centers. However, proposers of AS are encouraged to take advantage of the unique characteristics of HCHS/SOL inherent to the multi-site sample and design. In general, AS should be proposed as a single-center study only if involving all centers is not feasible or appropriate to the scientific question of interest.

5.4 Access – Who Can Apply

A. Any HCHS/SOL PI or co-I of an HCHS/SOL contract or subcontract may submit an AS proposal. The Center's PI or Co-I sponsor is required.

B. Non-HCHS/SOL investigators may submit AS proposals with required sponsorship of an

HCHS/SOL PI or Co-PI. Non-HCHS/SOL investigators do not need to be at an HCHS/SOL institution.

C. HCHS/SOL PI and Co-PI serving as sponsors for non-HCHS/SOL AS PIs are responsible for the following:

1. Ensuring that the HCHS/SOL AS policies and Publications policies are followed;
2. Serving as a liaison between the AS and the parent study;
3. Ensuring appropriate communication between the AS PI and the HCHS/SOL PIs, the CC PI, and Reading Centers PIs (as appropriate) during the AS proposal planning phase; and
4. Providing guidance on data collection, analysis, interpretation, and publication of AS results.

5.5 AS Proposal Process

The proposal process and submission template (Administrative, Concept, Full, Secondary Data Analyses, or Amendment/Extension) depends on the type of AS (as defined in section 5.2). Templates can be found on the AS page of the HCHS/SOL website. Proposals must be submitted via the HCHS/SOL web portal and follow the file naming convention.

AS Proposal Forms and Additional Documentation Required for Each Type of AS.

AS Type	Concept	Full	Other Form and Additional Documentation
(1) Career Development or Diversity Supplement (only doctoral, postdoctoral, ESI/ECI)			Secondary Analyses Form and one manuscript approved
(2) Secondary data analyses only			Secondary Analyses Form and one manuscript approved
(3) Consortium (including those only doing secondary data analyses)	Y	Y	Consortia must be approved by HCHS/SOL SC first and will have an assigned tracking #.
(4) Stored biospecimens** or Material and data only	Y	Y	Biorepository Impact Statement for stored biospecimens
(5) Participant burden only	Y	Y	
(6) Participant burden and stored biospecimens**	Y	Y	Biorepository Impact Statement
(7) Administrative Supplement	Y	Y	Biorepository Impact Statement if needed
(7) Renewal grant proposal to continue an already funded AS	Y	Y	Biorepository Impact Statement if needed
(7) Amendment			Amendment Form
(7) AS time extension			Amendment Form

Abbreviations: AS, Ancillary Study; ESI/ECI, Early-Stage Investigator / Early Career Investigator; Y, Yes.

**A request for specimens from the "Restricted Biorepository Reserve" (urine, RNA, citrated plasma specimens) will need to have a scientific review by the Lab Committee.

A. Administrative Section

All forms include general administrative, demographic, and key AS type characteristics. For example, it includes fields for PI and co-I name, degree, institution, Hispanic/Latino heritage, and career stage. AS characteristics include type, sponsoring PI(s), funding mechanism, submission deadline, etc. It also requires ID numbers to allow linking, when needed/required, to approved manuscripts, ancillary studies, or consortium numbers.

B. AS Secondary Data Analyses Form (NOT DONE AS PART OF A CONSORTIA)

AS only involving secondary data analysis ONLY must submit the AS Secondary Data Analyses Proposal Form which requests:

- NIH Aims page.
- At least one related manuscript proposal approved by HCHS/SOL Publications Committee. This serves as a placeholder for those specific aims and analyses. The manuscript tracking number must be provided.

AS deriving complex variables must send the variables and their documentation to the Coordinating Center after the primary manuscript is published. These will become part of HCHS/SOL database. Examples of these variables include those derived from census data, new readings of previously collected images, or genetic risk scores.

C. AS Concept Proposal Form

The development of an AS proposal involves planning and consultation with HCHS/SOL Field Centers, the CC, the Central Lab, and Reading Centers as appropriate. This involves a good deal of work on the part of the proposing investigator. Thus, to ensure initial support of the AS concept, the proposer must first submit a Concept Proposal via the HCHS/SOL web portal. AS only conducting secondary data analyses which are NOT part of a Consortia do not need to submit a Concept Proposal, as stated above. Under exceptional circumstances, and with the approval of the ASC chair and co-chair, a Full Proposal can be submitted directly. The review process for Concept Proposals is described in Section 5.6 below.

Priority is assigned to an AS Concept Proposal according to:

1. The potential for contributing to the health of Hispanic/Latino persons.
2. The ability to draw on unique characteristics of HCHS/SOL.
3. The degree to which it complements the current portfolio of studies.
4. The value of the scientific resource to be contributed to HCHS/SOL.

D. AS Full Proposal Form

1. **Form:** If, based on the concept proposal review, the HCHS/SOL SC invites the AS proposing investigator to submit an AS Full Proposal, the investigator must use the Full Ancillary Study Proposal Form template found in the AS page in the HCHS/SOL website. Consultation with the sponsoring HCHS/SOL Principal Investigator is necessary. AS requesting stored biospecimens must contact the Central Lab and request a Biorepository Impact Statement which must be included when submitting the Full Proposal.
2. **Contacting and Obtaining Consent from HCHS/SOL Participants:** Note that HCHS/SOL participants have consented only to be in HCHS/SOL, and many of them have

agreed to be invited by HCHS/SOL staff to participate in approved AS. They cannot be contacted directly by an AS investigator before giving consent to participate in the AS. They can only be contacted for recruitment into the AS by HCHS/SOL staff and HCHS/SOL investigators under the parent study contract. Once a participant has given consent to the approved AS, the AS staff can contact the participant. Thus, communications informing participants of an opportunity to join an AS must come under the signature of the HCHS/SOL Principal Investigative team.

3. **Requesting Biospecimens:** The HCHS/SOL is supportive of AS and strives for a balance between providing specimen volumes sufficient to test the AS hypotheses and preserving HCHS/SOL biospecimens for future studies. The amounts of specimen approved for an AS should be considered a maximum amount. Investigators with an approved AS can request that HCHS/SOL make up for dead volume in an aliquot and can request an increase of up to 10% in the approved specimen volume, for example responding to recommendations from funding agencies' reviewers. A request for an increase in specimen volume or in the number of aliquots of more than 10% of the approved amounts requires full review of a revised AS proposal. A request for specimens from the "Restricted Biorepository Reserve" (urine, RNA, citrated plasma specimens) will need to have a scientific review by the Lab Committee.
    a. Types of specimens and amounts available to AS:
        i. Serum, EDTA plasma, citrated plasma: 250 µL total serum plus plasma per AS
        ii. DNA/RNA (solution): 0.5 µg
        iii. Urine: 0.5 mL
    b. Larger amounts of specimens may be requested if HCHS/SOL determines that a scientifically compelling justification exists.
    c. Once an AS is approved and funded and an executed Data and Materials Distribution Agreement (DMDA) is received at the Coordinating Center, the HCHS/SOL Central Laboratory retrieves the specimen aliquots approved for the study based on a list of IDs prepared by the HCHS/SOL Coordinating Center. AS investigators are responsible for the CC and Central Lab associated costs and must contact them before submitting the grant for funding.
    d. HCHS/SOL stores its biospecimens in aliquots larger than the amounts released to AS. Since it may be required to thaw (and re-aliquot) a larger volume of biospecimen to release specimen to an AS, the HCHS/SOL SC reserves the right to negotiate an optimal timing for the release.

4. **Costs to be considered in the planning of an AS:** AS Investigators are responsible for expenses directly related to the performance of their specific project, as well as expenses related to bridging activities between the parent contract and the AS. It is the responsibility of each Center PI to review each AS proposal involving his or her Center and to determine that the Center efforts are adequately supported.

Examples of specific costs for which the AS is responsible include, but are not limited to:

a. Field Centers
    i. Contacting and recruiting participants
    ii. Obtaining appropriate IRB or other approvals
    iii. Coordination of additional data collection, data transfer, and archiving
    iv. Participant incentives, transportation, and meals
    v. Explaining test results and alerts to participants, then providing appropriate medical referrals.
    vi. Direct and indirect costs for lease of clinic space when appropriate
    vii. Direct and indirect costs center infrastructure as required by each field center

b. Coordinating Center
    i. Creating recruitment or sample lists
    ii. Creating data management system
    iii. Coordinating Field Centers, Central Lab, and Reading Centers
    iv. Data and QC reports
    v. Assistance with the development of the statistical plan (prior to submission for peer review), data management and other Coordinating Center related activities as appropriate
    vi. Creating datasets for AS conducting only secondary data analyses
    vii. Managing access to the Secure Research Workspace to use confidential data (e.g., geocodes, immigration status)

c. Central Lab
    i. Pulling samples
    ii. Shipping samples
    iii. Performing lab tests if requested

d. Single IRB
    HCHS/SOL is being conducted under a single IRB (sIRB) managed by the UNC Office of Human Research Ethics. However, UNC IRB will not serve as the sIRB of record for AS for which UNC is not the primary awardee.

E. Amendment & Expired AS Extension Form

Approved AS must submit an amendment for any change in the approved ancillary such as adding new procedures or questionnaires, requesting additional stored biospecimens, increasing the sample size, among other changes. The amendment template can be found on the AS page of the HCHS/SOL website.

The approval of an AS proposal remains effective for 24 months from the date of approval by the Steering Committee, during which time the AS proposal may be submitted and re-submitted as an application for funding. If the application is not selected for funding within this 24-month time frame, HCHS/SOL AS approval lapses unless a formal extension request, using the corresponding form template, is approved by the ASC and the SC.

Renewal grant proposals to continue an already funded AS cannot use the amendment form. Instead, a new AS Proposal must be submitted.

5.6 AS Review Process for Concept Proposals and Full Proposals

A. AS proposals must be submitted via the HCHS/SOL web portal AS Proposal Submission page for distribution to the ASC for review. The ASC may recommend approval, revision, or rejection of the proposal based on majority opinion. The ASC will make its recommendations based on the priorities listed in Section 5.5.C and other rationale garnered during the review. In the course of its review of Full Proposals, the CC ASC Coordinator will also verify that all participant burden and other information requested in the Full Ancillary Study Proposal Form template is addressed in the proposal. The ASC may refer the proposal to another committee or body for expert advice (e.g., Publications Committee; Operations Committee; Genetics Committee).

B. AS proposals requesting biospecimens must contact HCHS/SOL Central Laboratory and request a Biorepository Impact Statement to submit with the Full proposal. Please contact Sharon Minnerath (minne002@umn.edu) and Bharat Thyagarajan (thya0003@umn.edu)

C. Criteria for Approval by ASC and the SC

1. An AS proposal must be designed to answer important scientific questions or lead to innovation in research. The scientific merit of an AS proposal is assessed by the ASC and the SC according to the NIH study section review criteria modified for use by HCHS/SOL. HCHS/SOL criteria for evaluating AS Concept Proposals, listed in Section 5.5C above, are also used to evaluate Full AS Proposals.
2. Use of the HCHS/SOL data and resources for pilot studies is discouraged, except under exceptional circumstances justified by the AS investigator(s).
3. Career development awards and training programs are favorably considered, provided their aims have scientific merit.
4. The AS must not place undue burden on HCHS/SOL participants.
5. The AS must not place undue burden on HCHS/SOL Centers (Lab, Coordinating Center or Field Centers).
6. The AS must be culturally sensitive to the Hispanic/Latino community and not jeopardize the relations between a HCHS/SOL study site and its participants and community.

D. The ASC will review AS proposals and submit their recommendation (approval, rejection, or revise/resubmit) to the SC for final determination.

E. Following HCHS/SOL SC review, the SC Chair will notify the AS proposing investigator and the HCHS/SOL AS sponsor in writing of its determination.

If the SC approves a Concept Proposal, the SC Chair notifies the proposing investigator within two weeks as to whether he or she may proceed with developing the Full Proposal.

If the SC approves a Full AS Proposal, the SC Chair's communication will include:

1. A clear statement that a final step in the review process (review by NHLBI and HCHS/SOL OSMB) remains before the AS proposal can be considered to have final approval.

2. A request that the AS proposing investigator incorporates all required revisions recommended during the review process into a final, clean version of the AS proposal for the HCHS/SOL Coordinating Center ASC Coordinator. This final and clean version is necessary prior to proceeding with the OSMB review.

F. The ASC Coordinator will submit the Full AS Proposal, updated with any agreed-upon revisions incorporated as requested by the SC Chair, and the signed approval letter from the SC Chair to the NHLBI for review by the HCHS/SOL OSMB and the NHLBI.

G. The Steering Committee Chair will notify the AS proposing investigator of the NHLBI's decision, with a copy to the HCHS/SOL AS Coordinator and the HCHS/SOL Project Officer. Only after the AS proposing investigator is notified of approval by the NHLBI can the AS be submitted as an application for funding or, if funding is available, commence as an active AS.

5.7 Timeline for Review

A. Investigators who submit AS proposals should allow for the following turn-around times:

1. Concept Proposal approval by ASC: up to 4 weeks after receipt of the proposal by the ASC Chair.
2. Concept Proposal approval by SC: up to 4 weeks after approval by ASC.
3. Full Proposal review by the ASC: 4 weeks after receipt of the proposal by the ASC Chair.
4. Full Proposal review by the SC: up to 4 weeks following ASC review.
5. Full Proposal review by the NHLBI, including HCHS/SOL OSMB review: up to 8 weeks following SC review.

B. Some variability in these turn-around times can be expected reflecting the complexity of the proposed AS; the levels of review needed; and the potential need for additional information and/or a final, revised Full Proposal from the AS proposer.

C. Principal Investigators of AS proposals to be submitted as grant applications to NIH that require a budget >$500K in direct costs in any given year of funding should be aware of the NIH requirement for prior budget approval of such applications (see NIH Grants Policy Statement). Each NIH Institute or Center has its own timeline and procedures for implementation of this policy, which are described on its public website.

1. For a description of NHLBI's implementation, see the NHLBI web page, Applications with Direct Costs of $500,000 or more in any one year. Investigators whose AS grant applications that may fall into this category are encouraged to initiate communications with the NIH concurrently with notification of approval of the HCHS/SOL Concept Proposal to assure that the required timelines for both the HCHS/SOL Full Proposal review process and the NIH ">$500K" review process are met by the grant application submission due date.

2. AS proposals that will be submitted to the NIH for funding, and that require a budget between $500K and $1.515M in any given year, need to be submitted to the NIH for budget approval at least 10 weeks prior to the aimed submission deadline (February 5, June 5 or October 5). Thus, the simultaneous submission of a Full AS Proposal in this category to the ASC and NIH would be appropriate for time-saving purposes. However, AS PIs need to be aware that these simultaneous reviews could result in revisions of scientific goals and budget that may extend beyond the desired submission cycle.

3. AS proposals that would be submitted to NIH for funding, and that require a budget greater than $1.515M in any given year, need to be submitted to NIH for budget approval. These proposals are reviewed at the NHLBI only twice a year (refer to the weblink).
4. AS proposers and their sponsoring PI are responsible for familiarizing with and following the review guidelines and requirements from other Institutes at the NIH or other funding agencies.

D. The approval of an AS proposal remains effective for **24 months from the date of approval by the HCHS/SOL Steering Committee**, during which time the AS proposal may be submitted and re-submitted as an application for funding. If the application is not funded within this 24-month time frame, HCHS/SOL AS approval lapses unless a formal extension request, using the corresponding form template, is approved by the ASC and the SC.

5.8 AS Data

A. When funded, AS investigators who are not HCHS/SOL investigators or who are not affiliated with the HCHS/SOL Institutions must sign an HCHS/SOL Data and Materials Distribution Agreement (DMDA) in order to receive study samples or data. The DMDA template is available on the AS page on the HCHS/SOL website. Upon signing the DMDA, AS PIs must indicate that they are cognizant of the requirement to send the AS data to the HCHS/SOL Coordinating Center for inclusion into the HCHS/SOL database, and that the AS data are will be part of the NHLBI Data Repository HCHS/SOL dataset available to outside investigators.

B. NIH has issued the Data Management and Sharing (DMS) policy NOT-OD-21-013, effective January 25, 2023, to promote the sharing of scientific data. The NHLBI Policy for Data Sharing from Clinical Trials and Epidemiological Studies requires including a data sharing plan at the time of NIH submission, which will be reviewed and approved by the relevant NHLBI PO. Any changes to the data sharing plan must be discussed in advance with the relevant program official. Repositories where scientific data and metadata can be archived include NHLBI BioData Catalyst, BioLINCC, dbGaP and other NIH repositories in accordance with the Limited Access Data Policy and Health Insurance Portability and Accountability Act (HIPAA) privacy standards. The HCHS/SOL Coordinating Center will incorporate data collected in the AS into the de-identified HCHS/SOL Data Set submitted to the NHLBI Data Repository. As **per NHLBI policy, the incorporation of AS data into the HCHS/SOL database will be made yearly, and will include data used in any AS publications published within the prior 12 months; and a final incorporation of all AS data into the HCHS/SOL database will be made at the end of the AS study.** The AS must provide appropriate documentation to the Coordinating Center for the data to make them useful to outside investigators. The data and accompanying documentation will be made available to the public in accordance with the NHLBI data sharing policy.

C. Genome-wide association study (GWAS) data collected in HCHS/SOL AS are required to comply with the NIH Policy for sharing of Data Obtained in NIH Supported or Conducted GWAS. AS investigators involving GWAS are encouraged to familiarize themselves with this policy's requirements and timeline.

5.9 HCHS/SOL Data and/or Materials to be provided to the Active AS

A. The HCHS/SOL Coordinating Center will provide the partial data set needed by the AS, as requested in a manuscript proposal once approved by the Publications Committee and the SC.

B. Partial data sets comprise study data, with certain deletions and recoding, which are released to requesting institutions and investigators for specific purposes and with certain restrictions and conditions. The partial data set is provided to the AS Principal Investigator by the Coordinating Center.

C. Receipt by the HCHS/SOL Coordinating Center of a DMDA signed by the AS Principal Investigator and institution specifying that the AS investigators follow NIH and HCHS/SOL policies enables the Coordinating Center to provide data to the AS with an approved manuscript proposal. For receipt of study materials by the AS, the DMDA must also be signed by the NHLBI's HCHS/SOL Project Officer.

5.10 Notification of Clinically Significant Findings to HCHS/SOL Participants

A. The HCHS/SOL Steering Committee has agreed to inform participants of clinically significant findings derived from the study procedures. Some of these findings require urgent intervention, whereas others may require further confirmatory or screening tests, counseling (including genetic counseling), or medical follow-up.

B. AS investigators shall communicate these findings to the Field Centers and the Coordinating Center. HCHS/SOL staff will notify participants of these findings. AS investigators will not directly inform participants about the results.

C. AS proposals need to include provisions for the following:

a. Project the number of participants with clinically significant findings.
b. Include recommendations according to the finding, including but not limited to:
    i. Referral to urgent/emergent care
    ii. Need for further clinical correlation and/or confirmatory tests
    iii. Need for treatment and clinical follow-up
    iv. Genetic counseling
c. Include percent effort salary support for HCHS/SOL staff that will contact participants and inform the AS findings, and administrative costs (e.g. mail, phone service) for this activity.
d. Include percent effort salary support or consultant fee for genetic counseling, if necessary.

5.11 Papers Arising from the AS

A. Papers arising from the AS must be submitted to the HCHS/SOL Publications Committee for review and approval before submission for publication in journals. Similarly abstracts and presentations for national or international conferences must be submitted to the HCHS/SOL Publications Committee.

B. HCHS/SOL Publications Committee procedures apply.

5.12 Responsibilities of PIs of Active AS

A. The AS PI must notify the HCHS/SOL Coordinating Center when funding for the AS has been obtained.

B. The AS PI must send a progress report on the status of the AS to the HCHS/SOL Coordinating Center each year before November 1 so that the SC and the NHLBI OSMB can receive an update on its progress. This succinct report should be written using the HCHS/SOL Ancillary Study Yearly Report Form template.

C. The AS PI is expected to inform the HCHS/SOL SC of any substantial changes in the research plan that may impact the parent HCHS/SOL study.