

5.0 Ancillary Studies Policy

5.1 Definition of an Ancillary Study (AS)

An ancillary study typically requires the collection of additional data, either from participants enrolled in HCHS-SOL or from stored biospecimens or other study resources collected by HCHS-SOL. In order to protect the integrity of the HCHS-SOL, ancillary studies must be reviewed and approved by the Ancillary Studies Committee (ASC), the HCHS-SOL Steering Committee (SC), the HCHS-SOL Observational Study Monitoring Board (OSMB), and the NHLBI prior to submission for funding.

5.2 Types of Ancillary Studies (AS)

There are several types of AS:

- A. Studies requiring collection of data through additional questionnaires not originally used in the baseline or follow-up collections of HCHS-SOL.
- B. Studies requiring additional exam procedures in HCHS-SOL participants. Depending on their duration and complexity, such procedures may require that participants pay a separate visit to the clinic site or to another testing location.
- C. Studies using stored biospecimens or other previously collected materials.
- D. Questions that expand HCHS-SOL scientific aims.
- E. Questions that are not part of the HCHS-SOL scientific aims.
- F. Pooling projects or consortia that wish to use HCHS-SOL data and/or samples.

Proposals for clinical trials using HCHS-SOL participants will not be approved at this time. Proposals in which use of technical support (e.g. analytical and/or management support from the Coordinating Center) is sought and which do not intend to propose use of sample, data or additional measurements on the HCHS-SOL cohort will not be considered AS. In addition, proposals seeking to compare other cohorts with the HCHS-SOL cohort, without incorporating use of HCHS-SOL samples or data or additional measurements on the HCHS-SOL cohort will not be considered AS.

5.3 Local (one-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; therefore, an AS should be proposed as a single-center study only if involving all centers is not feasible or appropriate.

5.4 Access – Who Can Apply

- A. Any HCHS-SOL Principal Investigator or co-Investigator of an HCHS-SOL contract or subcontract may submit an AS proposal. The Center's Principal Investigator's signature is required.
- B. Non-HCHS-SOL investigators may submit AS proposals with sponsorship of an HCHS-SOL Investigator as an AS Co-Investigator. The signature of a PI at the HCHS-SOL Co-Investigator's Institution is required. Non-HCHS-SOL investigators do not need to be at a HCHS-SOL institution.
- C. HCHS-SOL Investigators serving as Sponsors for non-HCHS-SOL AS PIs are responsible for the following:
 1. Ensuring that the HCHS-SOL AS 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. Participating as a Co-Investigator on collection, analysis, interpretation and publication of AS results.

5.5 AS Proposal Process

A. AS Concept Proposal

The development of an AS proposal involves planning and consultation with HCHS-SOL centers and reading centers as appropriate. Since this involves a good deal of work on the part of the proposing investigator, the proposer must send a one-page **Concept Proposal** via the HCHS/SOL web portal Ancillary Studies Proposal Submission page using the Proposal Submission Memo of Intent/Concept template found in the AS page of the HCHS-SOL website.

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 the 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 the HCHS-SOL.

The review process for Concept Proposals is described in Section 5.6 below.

B. AS Full Proposal

1. **Format:** If the HCHS-SOL invites the AS proposing investigator to submit an AS Full Proposal, the investigator will use the Full Ancillary Study Proposal Form template found in the AS page in the HCHS-SOL website.
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 by an AS investigator before giving consent to participate in the AS; they can only be contacted by the HCHS-SOL staff, including HCHS-SOL investigators under the parent study contract. Once a participant has given consent, the AS staff can contact the participant. Thus, communications informing participants of an opportunity to join an ancillary study must come under the signature of the HCHS-SOL Principal Investigator.
3. **Requesting Biospecimens:** The HCHS-SOL is supportive of AS and strives for a balance between providing specimen volumes sufficient to test the AS investigators' hypotheses and preserving HCHS-SOL biospecimens for future studies. The amounts of specimen approved for an ancillary study should be considered a maximum amount. Investigators with an approved AS can ask HCHS-SOL to make up for dead volume in an aliquot, and can request an increase of up to 10 percent in the approved specimen volume if this responds to recommendations from study section reviewers. A request for an increase in specimen volume or in the number of aliquots of more than 10 percent of the approved amounts requires full review of a revised AS proposal.
 - a. Types of specimen and amounts available to AS:
 - i. Serum, EDTA plasma, citrated plasma: 250 μ L total serum plus plasma per AS
 - ii. DNA (solution): 0.5 μ g
 - iii. Urine: 5 mL
 - b. Larger amounts of specimen may be requested if the 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. Ancillary study investigators are responsible for the associated costs.

- d. HCHS-SOL stores its biospecimen 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.

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

- a. Field Center Costs
 - 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. Direct and indirect costs for lease of clinic space when appropriate.
- b. Coordinating Center Costs
 - i. Costs to the Coordinating Center for assistance with the development of the statistical plan (prior to submission for peer review), data management and other Coordinating Center related activities as appropriate.
- c. All Centers
 - i. Mailing, photocopies, fax, etc.
 - ii. Telephone service
 - iii. Other hidden costs

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.

5.6 AS Review Process for Concept Proposals and Full Proposals

- A. AS proposals must be submitted via the HCHS/SOL web portal Ancillary Studies 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 on Section 5.5.A 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.
- B. The CC ASC Coordinator will if appropriate refer the proposal for HCHS/SOL Laboratory Committee Review (Form: Request for Use of HCHS/SOL Stored Materials) and for HCHS/SOL Coordinating Center Review (Form). The ASC may refer the proposal to another committee or body for expert advice (e.g., Socio-Cultural Committee; Community Committee; Genetics Committee).
- 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 the HCHS-SOL.

2. HCHS-SOL criteria for evaluating AS Concept Proposals, listed in Section 5.5.A above, are also used to evaluate Full AS Proposals.
 3. Use of the HCHS-SOL data and resources for pilot studies is discouraged, except under exceptional circumstances justified by the AS investigator(s).
 4. K awards and training programs are favorably considered, provided their aims have scientific merit.
 5. The AS must not place undue burden on HCHS-SOL participants.
 6. The AS must not place undue burden on an HCHS-SOL Center (Laboratory, Coordinating Center or Field Centers).
 7. The AS must be culturally sensitive to the Hispanic/Latino community and not jeopardize the relations between a HCHS-SOL study site and its community.
- D. If the ASC requests revisions to the AS proposal, the ASC Chair will communicate this determination to the AS proposing investigator. If the ASC recommends approval or rejection, the ASC Chair submits this recommendation along with the Concept or Full Proposal to the SC for its review. If the ASC recommends rejecting the AS proposal, the ASC Chair will also forward to the SC a statement of the rationale for the ASC's 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 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 the NHLBI and the HCHS-SOL OSMB) remains before the AS proposal can be considered to have final approval.
 2. A request that the AS proposing investigator incorporates any revisions agreed to 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 NHLBI OSMB and the NHLBI.
- G. The NHLBI 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 Steering Committee: 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: 3 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. Authors 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 [Section 2.3.7.2](#) of the [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 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 NHLBI for funding, and that require a budget between \$500K and \$1.515M in any given year, need to be submitted to the NHLBI 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 NHLBI 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 the NHLBI for funding, and that require a budget greater than \$1.515M in any given year, need to be submitted to the NHLBI for budget approval. These proposals are reviewed at the NHLBI only twice a year (refer to the weblink).
 4. AS proposers and their sponsors 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 the notification of approval by the NHLBI to the AS proposing investigator, 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 request for cause is approved by the ASC and the SC. The AS proposing investigator and/or the HCHS-SOL AS sponsor must notify the HCHS-SOL Coordinating Center ASC Coordinator if and when the AS proposing investigator is notified that the application has been selected for funding.

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 in 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 eventually made a part of the NHLBI Data Repository HCHS-SOL dataset available to outside investigators.
- B. AS investigators have exclusive rights to use the data generated by the AS for **one year** after the data set is finalized for analysis. However, access to HCHS-SOL data will only be granted once the AS data has been received by the HCHS-SOL Coordinating Center. After the one year of exclusive use by the AS investigators is up, the Coordinating Center will incorporate the AS data into the main HCHS-SOL data base for use by other HCHS-SOL investigators and collaborators.
- C. The [NHLBI Policy for Data Sharing from Clinical Trials and Epidemiological Studies](#) requires the HCHS-SOL Coordinating

Center to incorporate data collected in the AS into the de-identified HCHS-SOL Data Set submitted to the NHLBI Data Repository **two years** after the AS data set is finalized for analysis by the AS investigators. The AS must provide appropriate documentation to the Coordinating Center for the data to make them useful to outside investigators. The NHLBI Data Repository data and accompanying documentation will be made available to the public in accordance with the NHLBI data sharing policy.

- D. 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 Genome-Wide Association Studies \(GWAS\)](#). 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. (See [HCHS-SOL Publications Policy](#)).
- 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 notify these findings to the Field Centers and the Coordinating Center. HCHS-SOL staff will not 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 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.
- B. HCHS-SOL Publications Committee procedures apply (please refer to the [HCHS-SOL Publications Policy](#)).

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.