



# **Manual 1**

## **Visit 2 Study Protocol, General Description and Study Management**

**October 15, 2013 - Version 1.01**

**Study website - <http://www.csc.unc.edu/hchs>**

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## **1.0 Objectives and Background**

### **1.1 Objectives**

The scientific aims of Visit 2 phase of the HCHS/SOL are to: (1) identify putative causes for diseases and conditions highly prevalent in Hispanics/Latinos [e.g. diabetes, left ventricular hypertrophy, and gestational diabetes mellitus]; (2) describe the transformation of health-related risk and protective factors related to migration, acculturation, and length of time living in the U.S.; and (3) assess the impact of changes in socioeconomic factors, cultural values, risk behaviors, and medical care access on health in Hispanics/Latinos.

The aims stated above will be accomplished through contracts by the National Heart, Lung, and Blood Institute (NHLBI) with four Field Centers, the Coordinating Center and an Echocardiography Reading Center. The Coordinating Center will provide the services for a Central Laboratory as needed. Study protocols will be directed by a Steering Committee consisting of the Principal Investigators of the Field Centers, the Coordinating Center, the Echocardiogram Reading Center and the NHLBI Contracting Officer's Representative (COR).

### **1.2 Background**

The Hispanic Community Health Study / Study of Latinos (HCHS/SOL) began in 2006, and a baseline examination was conducted between 2008 and 2011 among over 16,000 Hispanics/Latinos, ages 18-74 years, living in four U.S. communities: San Diego, CA; Chicago, IL; Miami, FL; and the Bronx, NY. The cohort includes Hispanics/Latinos who self-identified their origin or heritage as Mexican (41%), Puerto Rican (17%), Cuban (15%), Dominican (9%), and Central or South American (18%). The baseline examination aimed to estimate the prevalence of major cardiovascular and pulmonary diseases (CVPD) and their risk (or protective) factors, and the prevalence of other chronic conditions including hypertension, diabetes, obesity, hearing impairment, neurocognitive disorders, dental and periodontal disease, and sleep disorders, among others. Since 2009, the cohort has been contacted annually (retention rate = 85%) to ascertain clinical CVPD events. The cohort has been prospectively followed to assess changes in health status (new diagnoses and CVPD risk factors), and visits to the emergency room, hospitalizations and deaths due to CVPD, and all-cause mortality. Preliminary baseline cross-sectional analyses (based on 2/3 of the cohort) have been presented in several scientific meetings. Publications of final cross-sectional analyses are underway. Study protocols and manuals of operations implemented during the last contract period can be found in the study website [www.csc.unc.edu/hchs](http://www.csc.unc.edu/hchs), under "About the Study/Public Manuals and Docs". The study design and sampling design publications can also be found in the study website under "About the Study/Published Manuscripts".

Preliminary analyses from the baseline examination disclosed: (1) less than 40% of Hispanics with hypertension have it well controlled; (2) a higher overall prevalence of diabetes mellitus than previously reported among Hispanics in the U.S.; (3) within the cohort, a higher prevalence of diabetes among Puerto Ricans, and a lower prevalence among Cubans; (4) greater than 30% prevalence of pre-diabetes across groups; (5) 50% prevalence of cigarette smoking among Puerto Rican men and women, the highest across groups; (6) higher prevalence of asthma and COPD among Puerto Ricans; and (7) no relationship between years living in the U.S. (whether a lifetime or first generation immigrant) and prevalence of diabetes. In addition, sleep apnea across groups is associated with obesity, diabetes mellitus, hypertension and chronic lung diseases.

Given the high prevalence of specific cardiovascular and pulmonary risk factors and disease, and the differences across groups, further study of the relationships between risk (or protective) factors and

disease onset, morbidity, and mortality among Hispanics is needed. A larger number of CVPD events that will result from a longer period of follow-up will increase the statistical power for analyses in age- and gender-specific subgroups. Additional data collection will explore how acculturation changes overtime (in this primarily first generation immigrant cohort) and how this change interacts with health status in Hispanic groups with such distinct migratory histories. Finally, further study of this cohort will increase understanding of the impact of socioeconomic factors, including access to and utilization of health care services in the U.S. and outside of the U.S., on changes in CVPD risk and incidence.

## 2.0 Study Design

### 2.1 Study Methodology

**2.1.1** The 4 field centers each recruited over 4,000 persons of Hispanic/Latino origin to participate in the study. The age range is 18-74 with 9,714 persons age 45-74, and 6,701 persons age 18-44. Recruitment was designed to occur in stable communities so that persons can be contacted over time, and possibly examined more than once. Each community has a community social infrastructure and organization that enables community support and feedback.

**2.1.2** At Visit 2 the originally recruited individuals are invited to attend a re-examination. The risk factors of particular interest are described in section 2.1.3 on examination questionnaires and procedures. The study strives to make the percent of re-examination high, to reduce bias from non-response. There is no exclusion of persons based on existing health status. Those who have developed health problems, disabilities, or mental problems so severe as to prohibit informed consent and actual clinic attendance may be excluded from Visit 2.

**2.1.3 Examination Components.** The components of the examination are listed below:

**Table 1. Components of the Participant Initial Interviews and Informed Consent**

Procedure	Description
Contact Information	Update participants' personal and contacts' information, including physical and mailing addresses, telephone numbers (including mobile phones), and email addresses.
Informed Consent	Obtain signed informed consent that complies with all required standards.
Medical Release Form	Renew signed medical release allowing the study to obtain access to participants' medical records for adjudication of events at follow-up.

**Table 2. Components of HCHS/SOL Visit 2 Participant Questionnaires**

Questionnaire	Description
Medical History	Update personal medical history of conditions under study such as cardiovascular disease, stroke, diabetes, liver and kidney disease, dementia and other memory disorders.
Pregnancy Related Outcomes	Identify GDM, pre-eclampsia and eclampsia diagnoses on women of childbearing age at baseline. The following topics will be administered to this group of women: history of hormonal birth control method(s) use; age at first pregnancy; number of pregnancies, including dates of delivery and outcomes (live births, stillbirths, miscarriages, premature births, fetal demise), method of delivery (vaginal delivery, cesarean section), and babies' weights; history of GDM, de novo hypertension during pregnancy, and/or pre-eclampsia/ eclampsia or other cardiometabolic complications during pregnancy prior to Visit 1; history of GDM, hypertension and/or pre-eclampsia/ eclampsia or other cardiometabolic complications during pregnancies between Visit 1 and Visit 2. Additional relevant questions may be included.
Social and Acculturation	Expand and reassess the cultural measures included in Visit 1 including assessment of ethnic identity, health practices and beliefs, cultural values including role of the family members, family structure, gender roles, social networks, faith, resilience, positive and negative emotions, years lived in the U.S., lifestyle and mainstream culture.
Socioeconomic	Assess changes in socioeconomic factors including SES, annual household income, educational level and home ownership.
Health Care Access	Access to and utilization of health care services to be assessed through a questionnaire to address: updated insurance coverage from baseline/ reasons for not having coverage,; barriers to access to healthcare; awareness and utilization of preventive services , utilization and type of health services, use of alternative or complementary medicine in the U.S. and outside of the U.S. mainland and frequency of their use.
Smoking	Past and current cigarette use, ever use of cigars and pipes, cessation attempts including use of medications to assist without quitting, and use of modified harm-reduction tobacco products.
Alcohol Consumption	Usual intake and drinking patterns.
Medication	Reported use of medication for specified conditions, including alternative or complementary medicine
Exit Interview	

**Table 3. Components of Medical Examinations**

Exam	Descriptions
Anthropometry	Measurement of weight, standing height, abdominal hip circumferences, and percent body fat.
Blood pressure	Standard epidemiologic procedures (5 minute rest, 3 measures), and using an automated blood pressure device.
Echocardiography	Assessment of cardiac structure and function using echocardiography (cardiac ultrasound).

**Table 4. Components of the Blood, Urine, and Laboratory Measurements**

Measure	Description
Biospecimen Collection	Fasting blood and spot urine samples are obtained for laboratory assays and long term storage. Whole blood, serum, plasma, and leukocytes are divided into aliquots and stored for future analyses.
Glucose Tolerance	A two-hour oral glucose tolerance test is performed (preceded by a glucose meter reading).
Additional Blood	Additional tubes of blood to use for 5% blind replicate samples are collected and repeatability studies are conducted.
Lab Measurements	From blood: Total cholesterol, HDL cholesterol, triglycerides, glucose (pre- and post-OGTT), insulin, glycosylated hemoglobin, iron, creatinine, ALT, AST, UIBC, CBC with differential, platelets. From urine: albumin, creatinine

**2.1.4 Visit 2 Study Startup.** Study startup is preceded by central training and certification of staff, pretest of forms, and conduct of a pilot run-through of all study components. Questionnaires and procedures are implemented using state-of-the-art quality control procedures including repeat measurements, quantitative evaluation of performance, and retraining and recertification as needed. Site visits by the coordinating center are conducted in the first year to assure compliance with study standards.

**2.1.5 Data Collection.** Data collection for the HCHS/SOL study requires questionnaires in each domain of measurement to be available in both English and Spanish versions. New questionnaires for which no existing Spanish translations are available are translated by a subcontracting firm with expertise in multilingual instrument development for large-scale surveys. Both new and existing translations are then reviewed by members of the Translation and Validation Subcommittee. This committee includes members from the four field centers and the coordinating center who are bilingual and represent all four countries of origin for the study (Mexican, Cuban, Puerto-Rican, and Central/South American).

**2.1.6 Medical Information.** Appropriate medical information from the examination is provided to the participant and/or doctor. This includes alerts which require prompt attention by the participant, as well as standard reports of measurements of value to each person.

**2.1.7 Annual Follow Up.** Participants are contacted annually, either by telephone or in person, and administered a brief questionnaire. The questionnaire obtains information on any doctor or hospital visits in the interim, questions on health during the interim, and an update of contact information.

**2.1.8** The Study identifies, abstracts, reviews, and validates pregnancy-related, cardiovascular and lung events (requiring emergency room visit or hospitalization, or based on death information) which occur in the interim between the baseline exam and each subsequent annual follow-up. Pregnancy related events include gestational diabetes mellitus, pre-eclampsia, and eclampsia. Cardiovascular events include myocardial infarction, stroke and heart failure. Lung events include chronic obstructive lung disease and asthma. In more detail, we do the following:

- A. Identify possible events from the annual follow-up questionnaire which provide a self-report that a hospitalization or ER visit took place and the self-reported reason for the visit.
- B. Abstract information from these records and enter into the study data base.
- C. Validate the diagnosis by review of the abstracted information either by computer or a review committee.
- D. Identify deaths from information obtained at the annual follow-up and from a review of the vital statistics lists and obituaries from the state in which the community is located. The Coordinating Center (or Field Center if required for confidentiality) is responsible for conducting a match to the National Death Index periodically.
- E. Establish cause of death by obtaining, abstracting, and reviewing all relevant information from next-of-kin, coroner, physician, and hospital.
- F. Review the abstracted information and validate the diagnoses using trained and certified clinicians designated from each Field Center (a morbidity and mortality classification committee).
- G. Ascertain, review, and validate events.

**2.1.9 Data Collection.** Data collected at the Field Center is transmitted to the Coordinating Center daily for editing and processing. Most data are entered directly over the internet on the secure server in the Coordinating Center.

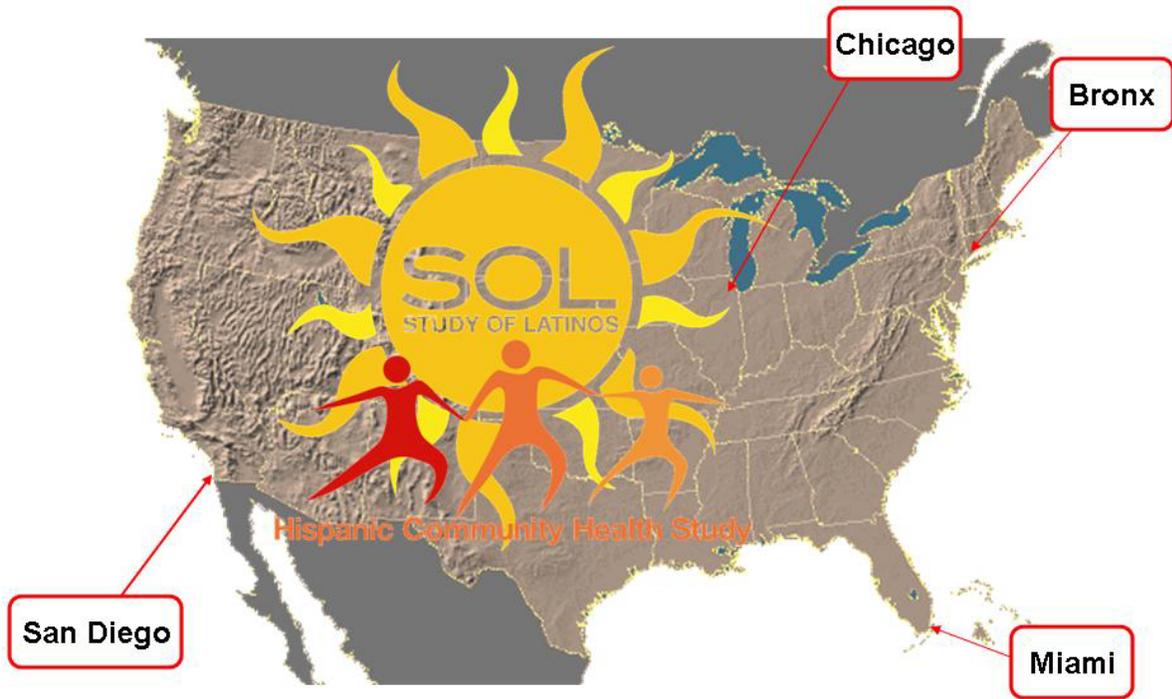
**2.1.10 Community Input.** The field centers maintain close connection and cooperation with the community by providing for community consultation, focus groups, and community interaction in relation to the goals and performance of the study, and for any unusual or sensitive issues such as genetic testing for identification of ancestry. Health education is provided to the community. An assessment of the impact of this education and feedback on study data is provided. Cooperation, feedback, and education are essential for successful retention in the study.

**2.1.11 Data for Other Researchers.** The Coordinating Center is responsible for preparing a limited access data set (LADS) of data from this study. Limited access data refers to study data, with certain deletions and recoding, that are released to requesting institutions and investigators for specific purposes and with certain restrictions and conditions. Limited access data are made available to the public in accordance with the draft NHLBI Policy for Distribution of Data. (<http://www.nhlbi.nih.gov/funding/inits/ladspolicy.doc>.)

**2.1.12 Ancillary Study Opportunities.** Investigators with the study promote the development and implementation of ancillary studies through Federal and non-Federal grant mechanisms. An ancillary study is one which is not required in the statement of work, and not funded under the negotiated contract.

## **2.2 Field Centers**

Study participants will be re-examined in the original four field centers located in Bronx, New York; Chicago, Illinois; Miami, Florida; and San Diego, California.



## **2.2.1 Center Description**

### **Bronx, New York**

Albert Einstein College of Medicine/Montefiore Medical Center (AECOM) is the major provider of primary, secondary, and tertiary health care services in Bronx, NY. The primary research clinic for the Bronx Field Center is located at 1 Fordham Plaza. This facility, located in an area convenient to multiple bus lines, subway and Metro-North railway, is in a large building which houses Montefiore administrative offices, as well as other tenants unrelated to AECOM or Montefiore. The site was selected with the advice of Community Board members. The clinical site is dedicated to the HCHS/SOL and is constructed specifically for this study. It includes a waiting area, a play area for children, a reception area, six staff/interview offices, work area for phone interviewers, four examining rooms, a conference room, a laboratory, a locker room, and a changing area.

### **Chicago, Illinois**

The Hispanic Community Health Study/ Study of Latinos Chicago Field Center (CFC) is housed at the Institute of Minority Health Research (IMHR) at the University of Illinois at Chicago (UIC) under the continued leadership of Dr. Martha L. Daviglus, MD, PhD (the HCHS/SOL CFC PI), and in collaboration with other investigators at UIC, and from Northwestern University. The UIC IMHR --a distinct research facility within the Department of Medicine at the UIC College of Medicine-- was founded by Dr. Daviglus in June 2012. The Visit 2 examinations will be conducted in the Institute's 5,160 square-foot research clinic that is fully staffed, equipped, and operational. Dr. Daviglus is responsible for overseeing daily operations, monitoring the progress of retention and follow-up efforts, preparing and reviewing local presentations and publications, and mentoring junior investigators. She is assisted by Dr. James Lash, the HCHS/SOL CFC Co-PI.

### **Miami, Florida**

The Miami Field Center represents a university-wide collaboration involving the College of Arts and Sciences and the Miller School of Medicine of the University of Miami, which engages multiple community partners including community-based primary care practices affiliated with Jackson Memorial Hospital/University of Miami, volunteer medical organizations, community-services agencies, the Miami-Dade County Health Department, and a Community Advisory Board. Within this context, the University of Miami Field Center provides expertise for the administration of all required questionnaires as well as components of medical examinations, recruitment, and follow-up activities. The Miami HCHS/SOL Community Advisory Board, consisting of individuals, community leaders and businesses, supports the recruitment, retention, and health education efforts of the Miami Field Center and provides advice and guidance regarding potentially relevant relationships among the community, study participants, and the HCHS/SOL. Research education and career development for investigators, staff, pre- and post-

doctoral fellows associated with the HCHS/SOL are facilitated by the University of Miami Clinical and Translational Science Institute (CTSI).

Administration of questionnaires, interviews, and most examination procedures are conducted in the Clinical Research Building (CRB) of the University of Miami/Jackson Memorial Medical Center in the city of Miami. Adequate parking is available on site and the CRB is in close proximity to public transportation including an elevated train, buses, and taxis. The Miami Field Center also has a dedicated 12-passenger Ford Econoline van for transporting HCHS/SOL participants. The fifteen story building is dedicated to research 7 days a week with 24-hour security. During regular working hours the service/reception area is staffed by the University to greet, orient, and direct participants within the strict guidelines of privacy prescribed for clinical research protocols. At other times, as necessary, the service/reception area for the HCHS/SOL is staffed by the Miami Field Center.

The CRB provides research office space as well as clinical examination and laboratory space. All investigators and staff for the Miami Field Center have assigned office space in the CRB. The clinical space for the HCHS/SOL is located on the 7<sup>th</sup> floor of the CRB, within the Behavioral Medicine Research Center. This includes 12 dedicated rooms specifically designed for HCHS/SOL interactions with participants as well as dining, conference and waiting room space. Facilities are appropriate for blood draws, sample preparation, oral glucose tolerance tests (OGTT), echocardiography, etc. and allows approximately 10 participants to be seen at the same time. Storage facilities for refrigeration, ultra-low temperature (-70°C) freezers, and centrifugation are all conveniently available within the Behavioral Medicine Research Center as are facilities for data management, equipment maintenance, etc.

## **San Diego, California**

San Diego State University is the primary institution from which the San Diego Field Center (SD FC) is funded. The SD FC works collaboratively with investigators at the University of California, San Diego and other local specialists. The SD FC is housed within the Institute for Behavioral and Community Health (**IBACH**) and more specifically its South Bay Latino Research Center of Excellence (**COE**) located in the most southern city of San Diego and is located next to the northern border of Mexico. The SD FC continues to be housed at the COE, the site from where the SD FC visit 1 was performed and where ongoing ancillary studies are currently conducted, as well as other epidemiological studies and community-based research studies.

The SD FC's primary functions will include scheduling the examination for visit 2, long-term retention of the study cohort, contributing to the development of psychosocial and behavioral instrumentation, conducting clinical measurements, mentoring and training for core activities, and community relations. UCSD investigators contribute their expertise to CVD epidemiology, subclinical disease and CVD events ascertainment and medical records adjudication.

The San Diego Field Center is located in the heart of the target area in the city of Chula Vista between Interstate 5 and 805 and includes de communities of Chula Vista, Bonita, National City Imperial Beach and San Ysidro. The field center is accessible by bus, a light rail system and

there is ample parking for those that drive. The clinical space occupies 10,600 square feet in commercial medical office space on the campus of the Scripps Chula Vista Hospital. The suite has about 20 rooms to comfortably accommodate participants during the screening process including staff offices with views of San Diego Bay.

### **2.3 Project Office/Contract Office**

The Project Office (also known as Contract Officer Representative, COR) for this study is located in the Epidemiology Branch, Division of Cardiovascular Sciences at the National Heart, Lung, and Blood Institute (NHLBI). The Project Officer and the Deputy are responsible for ensuring that the conduct of the study proceeds at the highest scientific and administrative level, that the Statement of Work is followed, that timelines and recruitment goals are met, and that scientific productivity is maximized to improve the health for not only Hispanics/Latinos but for the U.S. population as a whole. The Project Officer is a member of the Steering Committee.

The Contract Office for this study is located in the Office of Acquisitions, Division of Extramural Research Activities at the NHLBI. The Contract Officer and the Contract Specialist (or Contract Officers) are legally responsible for the administration of all of the contracts for this project and ensures that the expenditure of funds is appropriate and consistent with the agreed upon statement of work.

National Institutes of Health Sponsors:

During the first phase of the HCHS/SOL, NHLBI provided the majority of the funding, along with the co-funding and collaboration from five other Institutes and one Office. During this second phase of the HCHS/SOL, NHLBI continues providing the majority of the funding, along with co-funding and collaboration from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). In addition, the National Institute of Dental and Craniofacial Research (NIDCR) is co-funding the genetic analysis component of the Omics in Latinos (OLa) initiative.

### **2.4 Coordinating Center**

The Coordinating Center (CC) for the HCHS/SOL Study is part of the Collaborative Studies Coordinating Center (CSCC), a division within the Department of Biostatistics of the Gillings' School of Global Public Health at the University of North Carolina at Chapel Hill. The mission of the CSCC is to improve public health by coordinating important health research, developing innovative research methodology, and providing practical training in the application of research methods. As the coordinating center for a number of multi-center public health and medical studies, it provides statistical, data management, quality assurance, and study management services.

The Coordinating Center works cooperatively and coordinates study activities among the Field Centers, the Central Laboratory, the Echocardiography Reading Center, and the NHLBI Project Office. The Coordinating Center also implements, distributes, and maintains HCHS/SOL data collection and management system. This system is designed to optimize the accuracy and completeness of collected data and maintain its security.

In providing protocol development and training, the Coordinating Center participates fully as a member of the Steering Committee and its subcommittees. The Coordinating Center also coordinates the quality control activities, data processing, analyses, and support for all Field Centers. Also, the Coordinating Center provides both scientific and methodological expertise for analyzing and publishing important findings related to study objectives.

Finally, the Coordinating Center maintains a website with downloadable files (i.e. study manuals, protocols, publications lists and manuscript proposals), to permit investigators outside the study following appropriate procedures, to participate in data analysis. In the course of study implementation and data analysis, the external website will include lay summaries of publications for general reading and other information to provide the community with information about HCHS/SOL progress and findings.

## **2.5 Central Laboratory and Echocardiography Reading Center**

### **2.5.1 Central Laboratory**

The Advanced Research and Diagnostics Laboratory (ARDL) at the University of Minnesota serves as the central laboratory for the study. The Clinical Laboratory performs analytical tests at high levels of quality control on cholesterol, HDL cholesterol, triglycerides, glucose, insulin, HbA1c, urinary albumin/creatinine, serum alanine and aspartate aminotransferase, gamma glutamyl transpeptidase, serum creatinine, cystatin C, CBC, serology for hepatitis HCV RNA (on the subset of hepatitis C positive). The Central Laboratory also aliquots and stores samples including serum, plasma, whole blood and urine for future use. The Department of Laboratory Medicine and Pathology oversees the performance and monitors the quality control for the analytical tests and DNA isolation. The Central Laboratory also provides the Steering Committee guidance with respect to laboratory tests, quality control, and specimen collection procedures

### **2.5.2 Echocardiography Reading Center**

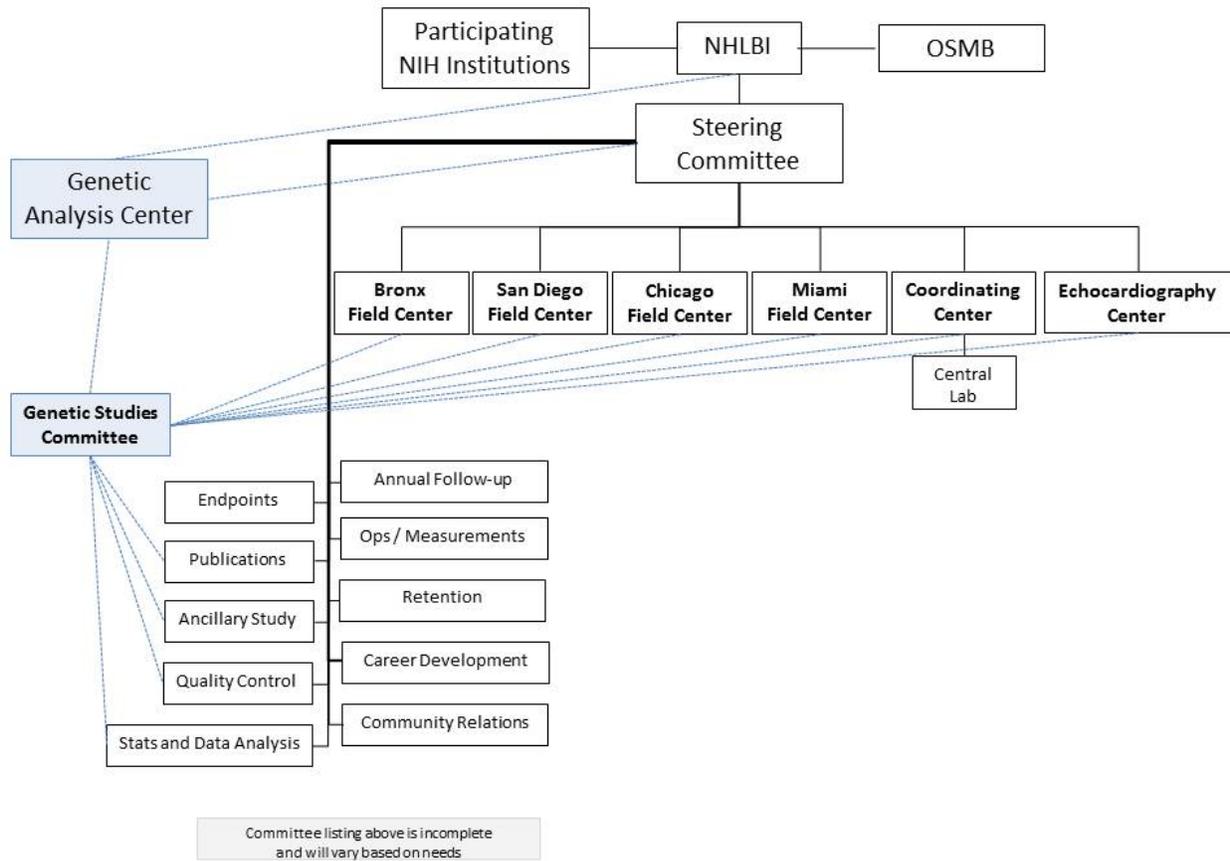
The Brigham and Women's Hospital (BWH) Cardiovascular Imaging Core Laboratory (CICL) serves as the Echocardiography Reading Center for HCHL/SOL. The CICL is centrally located within BWH in a recently renovated, dedicated 2600 square foot research space designed to enhance the cohesion and communication among project team members as well as smooth and efficient operations. Members of the CICL staff include a team of BWH faculty cardiologists, expert sonographers, highly trained analysis technicians, and experienced project management professionals. All staff members have successfully met the Institutional and IRB requirements for conducting human-subject research. The CICL maintains a well-documented training program for all staff that is both role- and study-specific. The CICL conducts all operations in compliance with Institutional guidelines concerning human-subject research, ICH E6 Good Clinical Practice Guidelines, and applicable regulations under FDA-regulated guidances for safe and ethical conduct of human subject research. All technical staff members have undergone extensive on-site training in cardiac image digitization and analysis. Staff members performing echo analysis have completed rigorous training and their work is focused solely on echocardiographic measurements. From a day-to-day trial management perspective, the CICL works closely with field centers, research sites, and coordinating centers to ensure high quality

images are received and to ensure that high-quality feedback and final data are provided in a clear, consistent, and timely manner.

The Echocardiography Reading Center will receive, store, process, and interpret the cardiac ultrasound images obtained from the participants at the HCHS/SOL field centers. Periodic transfers of the image data interpreted by specially trained and board certified cardiologists that summarizes cardiac structure and function will occur to the collaborative study database at the Coordinating Center.

Review of cardiac ultrasound images do not occur in real time at the Echo RC, therefore the responsibility to identify and manage critical findings lies with the Field Center. Critical abnormalities detected by the sonographer will be communicated locally to the site investigator, and then the site will use the mechanism of an eCRF to notify the RC. The RC will read these flagged studies within 24 hours and send a notification back to the CC so that the FC can be notified on a timely basis. Anticipate a normal 4 to 6 week lag for the usual interpretation of a study which implies feedback letters would take a several months to reach the participant. Non-critical abnormalities identified at the RC would be handled routinely.

### 3.0 Study Management



Study Organizational Chart

### 3.1 Introduction

HCHS/SOL is funded by the National Heart, Lung, and Blood Institute, with support from other Institutes as described in Section 2.3. The Study is directed by the Epidemiology and Biometry Program of the Division of Epidemiology and Clinical Applications. Principal Investigators and their affiliations are listed in Appendix I. The operations of the study are directed by the HCHS/SOL Steering Committee whose members are the Principal Investigators of the field centers, Coordinating Center, Echocardiography Reading Center, and the NHLBI Project Officer, as shown in the list of committees and membership maintained on the study website <http://www.csc.unc.edu/hchs>. The Principal Investigators of the laboratory and the Project Officers of the other participating NIH Institutes are ex-officio members of the Steering Committee.

The Steering Committee has subcommittees responsible for various functions. These committees report and make recommendations to the Steering Committee. The subcommittees and their charges are listed in the next section. An Observational Study Monitoring Board (OSMB) provides an annual evaluation of the study with recommendations to the NHLBI. It is further described in Section 3.4 and the membership listed in Appendix II.

### **3.2 Committees and Charges**

Members of the committee/subcommittees are principal investigators, co-investigators, representatives designated by the principal investigators, representatives of the Project Office and other Institutes. Committee conference calls as well as other activities (including study-related training activities) and assignments will be held among members of the different subcommittees and led by their respective Chair/Co-Chair. Conference calls and other activities are not open to the public. Advisors, experts and consultants who are not study personnel can temporarily participate in committee meetings/conference calls and other activities to review topics of mutual interest, at the invitation of the Chair of a subcommittee and not as standing members of the committees. Voting will be exercised by the members of the Steering Committee and other subcommittees. The different subcommittees will submit recommendations to the Steering Committee. The final voting and approval will be exercised by the members of the Steering Committee. The list of committees below is subject to change with the addition of special topic committees as the Steering Committee deems necessary.

**3.2.1** The **Statistics and Data Analysis** committee establishes study appropriate analysis methods and recommendations for using the study data. The committee has representation that includes faculty level biostatisticians and epidemiologists from the participating institutions and also includes statistical analysts at all levels.

**3.2.2** The **Translation & Validation** committee contracts for translation of questionnaires and for overseeing assessment of appropriateness of the translation for the various communities to be included in the study.

**3.2.3** The **Operations and Measurements** committee oversees development of protocols for clinic operations and measurements: blood pressure, anthropometry, questionnaires, and interviews. In matters pertaining to the examination, the committee is also responsible for oversight of equipment selection, design of exam flow, and for design of the pilot study. The committee works together with appropriate sub-committees to develop sections of the field center Manual of Operations and forms.

**3.2.4** The **Endpoints** committee, comprised of physicians and epidemiologists from the Coordinating Center and each field center, is responsible for the process of assigning all medical events of interest in the HCHS/SOL into diagnostic classes defined by the study. Hospitalized events may be classified into disease categories by computer algorithm. The committee reviews this process by independent diagnoses. For fatal events, computer assignment is more limited. The committee classifies the cause of death wherever classification cannot be done by computer and independently reviews the computer classification for most cohort events. The committee operates by assessing medical information received from each field center. In most cases, this involves independent assessment by two committee members with differences adjudicated by the full committee. Problems in classification may result from lack of clarity in the study diagnostic criteria. Under these circumstances the committee recommends specific case law procedure for dealing with the ambiguity, or providing alternate diagnostic algorithms for classification. The Endpoints committee decides on the definition of events to be ascertained in the follow-up cohort and what specific information is to be collected for each type of diagnosis. It establishes criteria for diagnosing these events as well as the procedures by which the sub-group of classification experts make the diagnoses. The adjunction subcommittee(s) develops the protocol for the areas

of hospitalization and death investigations, and for selection/design of instruments on medical care in hospital. The subcommittee is responsible for working with the Coordinating Center to training interviewers, adjunction members, and abstractors.

**3.2.5** The **Retention** committee monitors completeness of annual telephone contact and also proposes methods to improve retention of participants.

**3.2.6** The **Annual Follow-up** subcommittee coordinates the development of the AFU interview instruments and trains field center staff in the scheduling and collection of data from these annual telephone calls. Assessments are coordinated with endpoints committee to ensure that the data can be used reliably for outcomes analysis.

**3.2.7** The **Community Relations** subcommittee works with community organizations and leaders to encourage participation in the study and to learn from these community contacts how best to maintain community interest and support.

**3.2.8** The **Publications** committee reviews manuscript proposals, abstracts, and manuscripts and makes recommendations to the Steering Committee with regards to approval. The committee, with the Coordinating Center, also tracks all proposals, from submission of proposal to publication of manuscript, and works to assure that there is no overlap in approved proposals.

**3.2.9** The **Ancillary Study** committee reviews concept and final ancillary study proposals and makes recommendations to the Steering Committee with regards to approval. The committee, with the Coordinating Center, also tracks all ancillary studies with respect to data transfer and, with assistance from the Publications Committee, publications resulting from the ancillary studies.

**3.2.10** The **Quality Control** committee develops and monitors procedures to ensure high quality of data collected and to review regular data quality reports produced by the Coordinating Center. The committee provides feedback to field centers, echocardiography reading center and the central laboratory on quality issues and reports to the Steering Committee on these issues and resolutions to quality problems

**3.2.11** The **Career Development** committee recognizes and provides encouragement for the site specific efforts to encourage Hispanic/Latino and other underrepresented groups to pursue careers in research, as well as junior faculty in the early phases of their careers. Its purpose is to provide career development information and to foster training opportunities for the next generation of investigators within the Hispanic Community Health Study/Study of Latinos. The committee develops and monitors overall efforts for career development.

**3.2.12** The **Laboratory & Sample Processing** committee is responsible for developing the procedures for blood collection, field center processing, shipping, and laboratory measurements and developing associated quality control procedures.

### **3.3 Communications**

#### **3.3.1 Periodic Reports**

The field centers and central agencies prepare routine periodic reports to the HCHS/SOL Project Office which document the progress to date in each major activity, administrative matters, staffing changes, and current or anticipated problems. The Coordinating Center also provides reports on the data collection at the field and laboratory centers, quality control findings on examinations, re-abstracted records, re-certification of staff, laboratory result determinations, and protocol adherence. Status reports on recruitment and data collection prepared for the Project Officer and Steering Committee are also sent to the field centers. Quality control reports are likewise sent to the central laboratory and the echocardiography reading center.

#### **3.3.2 Study and Public Websites**

The Coordinating Center maintains a HCHS/SOL website to facilitate communication among HCHS/SOL investigators and staff. In general, the site includes (1) reports from the Project Office, the Coordinating Center, the central laboratory and the Echocardiography reading center, and the Steering Committee, (2) a description of the facilities and staff of the field centers and other central agencies, (3) general information on data management, and (4) a calendar of events. The website also provides applications for generating reports on issues such as participant follow-up rates and serves as an archival repository for all study documents. The portal to HCHS/SOL websites is found at <http://www.csc.unc.edu/hchs/>. A public website is available (<http://www.saludsol.net>) to foster communication with the local Hispanic/Latino communities, community leaders, and to provide general information for study participants (in Spanish as well as English).

#### **3.3.3 Electronic Mail**

All field centers, central agencies, the Coordinating Center, and the Project Office are linked by electronic mail using microcomputers at each center. The electronic mail network is used to facilitate rapid and efficient official communications among centers and agencies for messages such as announcements, meeting agendas, abstracts and manuscripts for review, and acknowledgements of receipt of data.

#### **3.3.4 Field Center Visits**

Project Office and Coordinating Center staff conduct periodic monitoring visits to field centers as needed in the first year of the contract to (1) maintain channels of communication with field center investigators and staff, (2) solve participant follow-up problems, (3) monitor adherence to the study interview and examination protocol, and (4) provide technical support for activities such as data management and quality control.

#### **3.3.5 Periodic Conference Calls**

The Coordinating Center facilitates conference calls among the members of the study committees by acting as a distribution hub for call content (agendas, materials, etc.) and arranging the scheduling and logistics of the teleconferences. Regularly scheduled calls for standing committees such as the Steering Committee, Quality Assurance committee, or special purpose working groups such as the project coordinators, occur on at least a monthly basis during the active conduct of the study. A member of the Coordinating Center works with each committee as a liaison to facilitate interaction between the committees and provides support for

implementation of the study protocol. Conference calls occur weekly or semi-monthly, or monthly as needed during the initial year.

### **3.3.6 Publications Tracking System**

A publications and presentations database and tracking system are provided for the study as communication support for study committees so that information about manuscripts can be followed from initial proposal stage through the process to the stage of a completed paper, or presentation. The system provides the publications committee with a tool that generates reports useful for managing the review and approval process.

### **3.4 Observational Study Monitoring Board (OSMB)**

An OSMB is constituted to provide an annual evaluation of the study with recommendations to the NHLBI regarding:

- A. Participant safety, burden, confidentiality and any other matter pertaining to protection of the study participants;
- B. Study performance in terms of retention, implementation of procedures and questionnaires, follow-up for events, and all aspects of quality control; and
- C. Study productivity in terms of significant research results to improve the health of Hispanics/Latinos and non-Hispanic/Latino alike.

The Board meets in person on an annual basis with members of the study Steering Committee (others investigators if needed). The Coordinating Center provides materials to inform the Board of HCHS/SOL progress, and the investigators provide presentations and respond to any concerns addressed by the Board. The Board has the responsibility of reviewing all Ancillary Study proposals to determine whether the Ancillary Study could provide harm to the conduct of the main study. The Ancillary Study review by the Board can be done during the annual Board meeting, or by email review. An Executive Secretary for the Board is an NHLBI staff member not associated with the HCHS/SOL who provides for all interaction between the Study and the Board.

The following NHLBI website describes the responsibilities of OSMBs:

[http://www.nhlbi.nih.gov/funding/policies/osmb\\_inst.htm](http://www.nhlbi.nih.gov/funding/policies/osmb_inst.htm)

### **3.5 Data Management**

#### **3.5.1 Approach**

HCHS/SOL involves intensive data collection, closely coordinated to permit re-examination and interview of 5-6 fasting study participants per day. The Data Management System (DMS) for this study provides maximum flexibility to field centers to meet their constraints on scheduling, the availability of equipment and trained technicians. The web-based Data Management system allows immediate update of the central database (located at the Coordinating Center) upon data entry; “transparent” and immediate installation of DMS updates once implemented by the Coordinating Center; and ease of integration of laboratory and reading center data with field center data for generating results reports, alert reports to participants and their providers of medical care.

Features of the DMS include a menu-driven graphical user interface, data validation upon entry, transaction auditing, database updating, database closure, reports, data archiving, and data retrieval. Reading center and laboratory data are uploaded to the Coordinating Center server over the web and automatically loaded into the centralized data management system files. Participant result reports are assembled within 24 hours of file creation at the Coordinating Center and are available to be periodically downloaded by field centers.

### **3.5.2 Data Entry**

The Coordinating Center Carolina Data Acquisition and Reporting Tool (CDART) software has the capability of being used either for direct electronic data entry & capture, (data recorded directly on-screen and validated during collection) or for distributed data management (data recorded first on paper forms and then keyed and validated at the field centers). Field centers have the flexibility to select the data collection method for each data collection instrument, and the location of administration depending upon the facilities at that location. Current versions of each data collection instrument in English and Spanish are available for situations in which the computer systems are not appropriate or inaccessible for any reason.

### **3.5.3 Consolidated Database**

Computers at the Coordinating Center are connected via a Local Area Network. Clustered servers running the Microsoft network operating system and Linux provide web services for the data management system. The web servers are isolated by a router from the servers holding study data. The consolidated database is stored in a SQL-server database. Standard transaction validity checks are applied to all updates to the database (e.g., to prevent the addition of records with duplicate keys, etc.). Audit logs from the DMS provide complete documentation for changes to the consolidated database. Backups of the consolidated database as well as processing reports are made daily. Once a month, the current backup tape is permanently archived at an off-site data storage facility.

### **3.5.4 Reading Center and Central Laboratory Data Transfer and Tracking**

An integral component of HCHS/SOL is the incorporation of central reading center data (Echocardiography) and laboratory results into the study database. Laboratories and reading centers with established data management systems in place may prefer to use those systems for transfer data into our CDART system, in addition to using for data collection and local data management. Managing central agency data could alternatively involve direct use of customized CDART screens developed by the Coordinating Center. The Coordinating Center tracks the shipment of samples from the field centers to the central laboratory and provides feedback to the centers on whether all expected samples have been received.

### **3.5.5 Reporting**

The CDART provides each field center with the ability to generate a variety of reports. These include participants contacted and examined, indicators of data quality, completion status of participant result reports and specimen tracking reports, among others. The reports for study participants and their dentists or physicians are described in Section 3.6, Reporting of Study Results. The field center data quality reports are complementary to the Steering Committee reports, which are produced monthly.

### **3.5.6 Data Security and Confidentiality**

Data confidentiality and security are applied at all levels of data acquisition, transfer and storage, for all study agencies, from field centers to coordinating center. The password controlled access to the study equipment and the DMS is the initial level of security. All data collected at the field centers and in hospital record rooms are encrypted by the system and can only be decrypted for display on-screen by authorized study personnel. Personal identifiers are collected on separate forms (and transferred as separate, encrypted records). Should paper data collection forms be used they will be retained at secure locations at the field centers until the Steering Committee acts on recommendations from the Coordinating Center to dispose of such records (e.g., incremental data closure). The secure storage and disposition of hard copy records at field centers will follow institutional procedures at each site.

The CDART server is housed at the UNC Office of Information Technology in a physically secure controlled access server room, and exclusively managed by Coordinating Center IT personnel. Measures to ensure the security of the data include: restricting access to users with valid IDs and passwords; using a firewall to restrict access to the web server and to shield the UNC Coordinating Center LAN from web users; using the secure sockets layer standard to provide encryption and user authentication. System scans for viruses and malware are run weekly with the resulting reports reviewed by network administrators for violations and the need to implement corrective action.

All data transferred to the Coordinating Center is stored, processed, and analyzed within the Coordinating Center office suite, with access to office space containing data controlled through locked doors. Access to computer data files is controlled by passwords released only to the Coordinating Center personnel who use such files. In addition, data files with personal identifiers (and sensitive information per designation by a study's Steering Committee) are encrypted. As standard practice, output transferred to a field center identifies participants only by ID number. No individually identifiable information is distributed by the Coordinating Center to any study agency other than the originating field center. Printed material containing confidential information is discarded through supervised loading, transportation, and storage using a chain of custody control process, until the material can be recycled into paper pulp.

All Coordinating Center staff are required to complete a confidentiality certification procedure upon employment.

### **3.5.7 Data Retrieval and Statistical Computing**

Data is retrieved from the study database and converted into SAS files on a regular schedule (e.g., monthly). Most statistical computing is done using SAS software. Statistical computing is performed by a dedicated statistical programming staff, using a well-established statistical computing request system that has proven itself through use with many long-term, multi-center research projects managed by the Coordinating Center. This system includes thorough documentation of requested computing, programming standards, naming conventions for datasets, programs and program results, inventorying and tracking of computing requests, procedures for program review, and permanent archival of completed programs, results, and datasets.

### **3.5.8 Database Closure**

Data queries are generated on a monthly basis, immediately following data retrieval. Typical data checks include classifying the universe of enrolled IDs, assuring all expected forms were received, performing consistency checks between related data fields, assuring all queries generated are resolved, etc. If there are unexpectedly high error rates for a site or a user, we explore the causes of the error and take corrective action, such as retraining personnel or making changes to the data management system.

Periodically the study's consolidated database is subjected to closure checks for completeness and accuracy of data collection and processing. These checks are performed on a "frozen" version of the database defined by a specific time cut point, and precede the use of data for publication. Typical closure checks include classifying the universe of IDs, assuring that all expected forms were received and all queries were resolved, examining the consistency of items across forms and visits, and checking distributions of key variables for possible errors.

### **3.6 Reporting of Study Results**

The Coordinating Center is responsible for reporting of study results at two levels: we support the assembly and distribution of study results to participants and their providers of medical care and also prepare statistical data reports for various study committees, as needed and on an established schedule. Both types of reporting are outlined below.

#### **3.6.1 Participant Results Reporting**

Although the majority of tests and examinations performed by the HCHS/SOL are of research value and not intended for medical diagnosis or treatment, a number of test results/examination findings are of value to the examinees. Investigators thus have the opportunity to "give back" to the study participants and to their communities, particularly information that improves the individual's ability to make health choices as well as test results that are pertinent to the guidelines widely used by health practitioners and the public. In some instances test results carry an ethical responsibility to communicate the result (and its meaning) to the participants, and with his/her authorization also to the designated provider of care. Assay values and measurement results that exceed the thresholds underwritten by diagnostic and treatment guidelines are clearly identified to the participant in the reports, with a recommendation for review or confirmation in consultation with their provider of medical care and clarification that these results originate from a research program and do not substitute for a visit to a physician.

Based on input from the pertinent experts among the HCHS/SOL investigators, the Coordinating Center drafts the contents and format of the participant results report and prepares automated templates that are assembled from the central database at UNC, for field center staff to edit and/or print. In this process the Coordinating Center also identifies clinically relevant threshold values for the pertinent study data to be considered an "alert value" that warrants follow-up and/or an expedited notification of the participant/provider of care. For this purpose, a secure web-based Report and Alert Notification feature is maintained and updated daily by the Coordinating Center that can conveniently be interrogated by the field centers to prepare their "routine" reports of results as well as expedited notifications.

### **3.6.2 Reports to Study Investigators and Agencies**

The Coordinating Center prepares detailed data reports at regular intervals for the Steering Committee, and on an *ad hoc* basis as determined by the Steering Committee.

*Steering Committee Reports:* The routine reports to the Steering Committee focus on study progress, including status of annual follow-up and re-examination, quality control issues, and data collection quality and timeliness. Objective, field center-specific, analyses of performance are presented.

*Observational Study Monitoring Board (OSMB) Reports:* Among the essential tasks of the Coordinating Center is the preparation of the statistical and management reports for the OSMB. While the content of these reports are ultimately responsive to OSMB requests, the reports initially consist of three major sections: publication, re-examination status, and data quality. The publication section provides the status of manuscripts and publications. The re-examination status section is summarized by field center, including graphs comparing performance to goals. It also details reasons for refusal and rates of response, and data acquisition.

## **4.0 Publication Policy**

### **4.1 Policy Objectives**

The objectives of the publications policy of the HCHS/SOL Study are to assure:

- A. Expeditious and timely dissemination of major HCHS/SOL findings to the scientific community;
- B. Accurate and scientifically sound publications from HCHS/SOL;
- C. Encouragement of high-quality manuscripts among the HCHS/SOL investigators;
- D. A system for fair determination of collaborative authorship on HCHS/SOL collaborative publications;
- E. Opportunities for investigators from participating HCHS/SOL centers, NIH, and other outside investigators with appropriate expertise to participate and be recognized in study-wide publications and presentations.

### **4.2 Definitions of HCHS/SOL and non-HCHS/SOL Investigators**

HCHS/SOL investigators are paid investigators with funded effort on any current Institute contracts or subcontracts for the study. HCHS/SOL affiliated investigators are investigators not currently on any HCHS/SOL contract or subcontract, that are investigators in a funded ancillary study, an invited or approved consultant in specific study-related topics. In the fulfillment of any of these roles, affiliated investigators may also participate in committees or working groups and data analyses for publications pursuant to study policy.

HCHS/SOL authors/co-authors/collaborators are persons at any level of training or career stage, not funded by any of the HCHS/SOL contracts, whose only role is that of lead author or co-author in a HCHS/SOL related manuscript, or solely participating in a writing/working group. Those receiving funding through Diversity Supplements for the exclusive purpose of working on sub-analyses of the HCHS/SOL dataset or any of its ancillary studies' datasets fall in this category.

### **4.3 Priority / Primary Papers**

**4.3.1 Priority Papers** The Publications Committee (PC) and Steering Committee (SC) can if deemed necessary; periodically develop a list of **priority papers**. Process for authorship of these papers will be established by PC for approval by SC. One method may be to rotate first authorship among the centers, and PO (Project Office).

### **4.3.2 Group-Authored and “Unauthored” Publications and Presentations**

The HCHS/SOL PC may recommend to the SC, and the SC may decide that one or more publications be written on behalf of the HCHS/SOL group. For example, a design paper might be unauthored or group authored. An appropriate list of participating investigators will be identified in an appendix to such publications, and members of the actual writing group will either remain anonymous or, as appropriate per journal policy, be acknowledged in the publication.

### **4.3.3 Manuscript Progress Tracking**

The PC will produce an updated progress report, with assistance from the CC, of all approved HCHS/SOL publications (e.g., approved, in preparation, submitted, in press, published) which the CC will post on the website, along with approved manuscript proposals.

## **4.4 Proposals for Other Papers**

### **4.4.1 First Author**

The first author of a paper will generally be the proposer unless that proposer indicates in writing that he or she nominates another member of the writing committee to be lead author. Approval of the PC is required.

### **4.4.2 Proposal Submissions**

Paper proposals may be submitted by:

Any HCHS/SOL investigator, HCHS/SOL connected investigator in a Field Center, Reading Center or Coordinating Center, with the local PI approval, for local tracking and priority setting.

- A. PO staff, upon invitation by the PC. PO staff may not be first, last, or corresponding authors on primary papers.
- B. Non- HCHS/SOL investigators: These require approval by any one of the HCHS/SOL PIs, in a Field Center, Reading Center, Coordinating Center or Project Office.
- C. Ancillary Study Investigators (See Section 11 for manuscripts from ancillary studies.)

**4.4.3** In general, first authors should lead no more than 3 study-wide papers at any one time, unless there are special considerations. This policy is to ensure timely progress on the papers and to afford the opportunity for others to propose papers. The Publications Committee will determine at its discretion exceptions to this 3 paper limit.

**4.4.4** Publication Committee Policy with Regard to Genetics Papers. Paper proposals and manuscripts that involve analyses of genetic data will be submitted to the PC in the usual way: proposals should be uploaded onto the website; manuscripts are sent to HCHS Administration with copy to the Chair of the PC. These proposals will then be referred to the Genetics Analysis Committee (GAC) which will provide its recommendations to the PC. The GAC has at least one

member who is also a member of the PC. At the PC meeting (by phone or in person) when the genetics proposal or manuscript is being considered, the PC member who is representing the GAC will be the primary discussant of the proposal or paper.

In most cases, the PC will accept the recommendations of the GAC. There may be some instances when the GAC recommends approval but the PC votes for disapproval or approval with required changes due to policy or other issues. In such cases, the PC decision holds, or if there is a dispute, the matter may be brought for formal consideration by the Steering Committee. In cases where the GAC finds problems with the analyses but the PC wishes the paper to proceed, the proposers are encouraged to consult with the GAC in order to resolve design and analysis issues.

## **4.5 Authorship and Writing Groups**

**4.5.1** Each study-wide paper should give each of the field centers, PO, and CC and the relevant reading center, depending on topic of paper, opportunity for representation on the writing group. PO staff may be co-authors on primary and secondary papers if requested by the PC. Others may be nominated for special expertise.

**4.5.2** The lead author (writing group chair) determines the order of authorship. A major criterion for the order of authorship is the level of effort and contribution made by the members of the writing group.

**4.5.3** When the writing group chair is identified, it is his/her responsibility to communicate with other writing group members to identify data needed from the CC, and to establish a plan for writing the manuscript.

**4.5.4** All members of the writing group should review the final manuscript proposal and the final manuscript draft before its submission to the PC.

**4.5.5** By the determination of the writing group chair, if some members of a writing group have shown little or no interest in participating in the work of the group or have failed to contribute to the task of preparing the manuscript, their names may be left off the list of authors, pending review by the PC. If a problem emerges, the PC will resolve it.

**4.5.6** The Chair of each writing group is to update the PC on manuscript progress every six months after the writing group is formed. If the PC has not received a report from a lead author within 12 months, or if satisfactory progress has not been made:

- A. The PC may replace the lead author with another member of the writing group.
- B. If no writing group members are interested in assuming the lead position, other HCHS/SOL investigators outside of the writing group may be solicited to be lead author.

**4.5.7** The writing group should see the manuscript after revisions suggested by the journal are made.

**4.5.8** The writing group must prepare a lay summary that will be used by the PO for publicity and also be available to participants on the HCHS/SOL website.

## **4.6 Data to be obtained from HCHS/SOL**

**4.6.1** Some papers will have data analyses done by the CC. Other papers will have analyses done locally under the supervision of the lead author.

**4.6.2** For those analyses done by the writing group, the following rules apply:

- A. HCHS/SOL data required for analyses for the paper will be provided by the HCHS/SOL CC, after approval of manuscript proposals that specify the dataset required. The data may also be available from complete files distributed to HCHS/SOL PIs.
- B. NHLBI rules for data distribution will apply, implemented through signed data distribution agreements.

## **4.7 Local Papers**

Most papers will be study-wide, i.e. will use data from all the field centers, to preserve and make maximum use of the full, unique cohort. A proposal for using only local data may be considered if appropriate. Authorship for local papers will be considered on a case-by-case basis.

## **4.8 Abstracts**

**4.8.1** Abstracts should be derived from approved paper proposals.

**4.8.2** Abstracts must be submitted to the committee for review at least two weeks before the due date unless special circumstances prevail. The process for submission is available on the HCHS/SOL investigator's website.

**4.8.3** Abstracts will be expeditiously reviewed by two PC members with simultaneous review by the Project Office (PO). PC reviewers will be asked to respond expeditiously and to recommend approval, modifications, or disapproval of the abstract.

**4.8.4** All abstracts accepted for presentation or publication should be submitted to the CC for archival purposes.

**4.8.5** It is permissible to submit previously cleared abstracts to other meetings; copies should be sent to the CC for inclusion in the listings of HCHS/SOL Publications and Presentations.

## **4.9 Invited talks**

**4.9.1** An investigator receiving an invitation for a national talk on behalf of HCHS/SOL should send an abstract of the talk to PC and must obtain PC and PO approval. No approval is necessary for local talks or grand rounds.

**4.9.2** When an invitation is directed to the Chair of the Steering Committee or the Chair of the PC, the respective chairs will decide who is to represent HCHS/SOL. Invitations directed to the NHLBI will be reviewed and approved by the NHLBI Project Office.

**4.9.3** When a HCHS/SOL investigator or PO scientist receives a personal invitation to make a presentation, they should notify the Chair of the PC to ensure listing of the presentation on behalf of the HCHS/SOL Research Group.

**4.9.4** All presentations in response to such invitations should be based on published HCHS/SOL reports unless prior approval is granted by the PC and the Project Office.

**4.9.5** Requests received by PIs or their staff to present or discuss at investigator's institution meetings any previously published HCHS/SOL data need no prior clearance by the PC and acceptance of such invitations is encouraged.

#### **4.10 Ancillary Studies**

Ancillary studies follow the same publications process as main HCHS/SOL papers. The AS must submit proposal to PC, but ancillary study may select its own author group. In most instances, this should include representation from Field Centers (if data from the larger study are included in analyses), the Coordinating Center, Project Office and relevant Reading Centers. Ancillary studies will get only partial datasets relevant to their analyses (see AS policy statement).

All ancillary study proposals that involve analyses of genetic data will be submitted to the ASC in the usual way: i.e., they will be submitted to HCHS Administration and to Neil Schneiderman as Concept or Full Proposals as appropriate. The proposals will then be referred to the Genetics Analysis Committee (GAC), which will provide written reviews and recommendations to the ASC. The GAC will have at least one member who is also a member of the ASC participate in the ASC meeting (by phone or in person) when a genetics proposal is being considered. The ASC member who is representing the GAC will be the primary discussant. Because genetic analyses may involve issues in which the ASC and its members do not have specialized expertise, the ASC invites the GAC to have additional representatives participate in any planned genetic discussions and also to serve as permanent members of the ASC.

#### **4.11 Ancillary Study Paper Proposal Process**

**4.11.1** Requests for proposed publications should include a 4-6 page document, to be submitted to the PC Chair that includes:

- A. tentative title;
- B. name of proposer;
- C. name of up to 3 suggested co-authors;
- D. rationale;
- E. keywords;
- F. main hypothesis or study questions/objectives;
- G. analysis plan (pertinent variables, analysis definitions, characteristics of population to be analyzed, table shells limited to a reasonable number);
- H. pertinent references;
- I. shell or "dummy" tables.

**4.11.2** The request should be in the format provided in the current Manuscript Proposal Form found on the HCHS/SOL website.

**4.11.3** Proposals will be expeditiously reviewed by the PC. Reviewers will be asked to respond expeditiously and to recommend approval, modifications, or disapproval of the proposal.

**4.11.4** The PC will consider the issue of overlap with other proposals and publications, and if a problem emerges, the PC will confer with the involved writing group chairs to resolve the situation. The CC will provide a search engine to all investigators to enable an easy search of the set of approved proposals of related proposals. Proposals will be reviewed by the PC and PO, with a decision to request modifications of the proposal or with recommendation to approve or reject, and if approved a priority will be recommended.

**4.11.5** After PC conference calls, requests for modifications to the proposals will be sent directly to the proposer, whereas the PC recommendations for approvals or rejections for manuscript proposals will be first circulated electronically to the Steering Committee. Steering Committee members are invited to comment by email within one week on the recommendations. After consideration of SC recommendations the PC will notify submitters of proposals of the decision.

## **4.12 Review of HCHS/SOL Publications and Presentations**

**4.12.1** The Chair will assign the final manuscripts to 2-3 reviewers for review for scientific merit, analytic issues, interpretation and discussion issues, and policy issues, and reviewers will be asked to agree to a specific deadline date for submission of reviews to the PC.

**4.12.2** The materials will simultaneously be submitted to the Coordinating Center for data verification. The Coordinating Center will randomly select manuscripts for data verification.

**4.12.3** The materials will simultaneously be submitted to the Steering Committee for optional review due by the same date asked for required reviews.

**4.12.4** Reviews will be discussed by the full PC at monthly calls, and proposals, papers and presentations will be approved by full committee.

**4.12.5** When the final manuscript has been approved by the PC it will be sent for review by the NHLBI Project Office.

**4.12.6** Review and approval by the PC and review by the NHLBI Project Office are required for all HCHS/SOL publications prior to their submission for publication. When the final manuscript has been approved by the PC and reviewed by the NHLBI Project Office, it may be submitted for publication.

**4.12.7** All review and approval functions of the PC and review by the NHLBI are to be done judiciously and expeditiously.

**4.12.8** The writing group chair will provide a copy of the published paper to the CC and to the NHLBI Project Office for archiving.

**4.12.9** Once published, the PC will send notification of publication to the HCHS/SOL Investigators.

**4.12.10** Publications and presentations shall be in compliance with the rules and procedures of disclosure set forth in the Privacy Act. Confidential or proprietary information shall not be disclosed without the prior written consent of the individual or institution. Privacy Act compliance and documentation of written disclosure consents are the responsibility of each institution involved in the paper/presentation.

**4.12.11** An acknowledgment of all HCHS/SOL Centers with their PIs and a reasonable number of key personnel are to appear in each publication, printed in an appendix per journal guidelines. There may be a short list and a long list developed.

**4.12.12** The NHLBI support statement is to be on the front page of the manuscript. The acknowledgement should include all Institutes and Centers directly relevant to the specific paper.

Baseline:

The currently required text for Baseline examination publications is available on the study website: *“The baseline examination was initiated and funded by the National Heart, Lung, and Blood Institute, in conjunction with the National Institute of Diabetes and Digestive and Kidney Diseases, the National Institute of Neurological Disorders and Stroke, the National Institute on Deafness and Other Communication Disorders, the National Institute of Dental and Craniofacial Research, the Office of Dietary Supplements, and the National Center on Minority Health and Health Disparities; National Institutes of Health, Department of Health and Human Services. The study is supported by contracts (number/institutions to be inserted).*

Visit 2:

The required most up to date text for Visit 2 examination publications will be available on the study website: *“The HCHS/SOL second examination was initiated and funded by the National Heart, Lung, and Blood Institute, in conjunction with the National Institute of Diabetes and Digestive and Kidney Diseases, and the National Institute of Dental and Craniofacial Research, Department of Health and Human Services. The study is supported by contracts (number/institutions to be inserted).*

**4.12.13** All requests for reprints are to be directed to lead authors.

**4.13 Authorship for Ancillary Studies**

**4.13.1** Proposals for publications and presentations based on special data sets collected on HCHS/SOL participants in ancillary studies are also to be submitted to the PC. The writing group preparing such a report will consist of individuals designated by the participating Ancillary Study investigators. This should include representation from Field Centers (if data from the larger study are included in analyses), the Coordinating Center, Project Office and relevant Reading Centers.

**4.13.2** All HCHS/SOL PIs and investigators will be informed of such ancillary proposals through periodic circulation

**4.13.3** In addition to a statement of authorship, an ancillary study paper is to have a clear statement that this work was a substudy or ancillary study of HCHS/SOL and the support from NHLBI is to be acknowledged.

#### **4.14 Use of Data for Theses or Similar Academic Projects by Graduate Students**

**4.14.1** All requests for use of HCHS/SOL data by graduate students, medical students, residents and other trainees for theses or similar academic projects are to be reviewed by the PC and the Project Office.

**4.14.2** It is required that the student requesting use for HCHS/SOL data is associated with the study through one of the HCHS/SOL investigators who is acting as the student's "sponsor" with regard to the data.

**4.14.3** HCHS/SOL data may not be used by students if the data relate to major HCHS/SOL papers in progress or if the PC deems that data to be necessary for a future major paper.

**4.14.4** If the PC recommends approval for the use of the requested data, a writing group is to be established and is to include the student as convener of the group.

**4.14.5** The writing group is to take no action regarding the paper until the student has completed and defended the thesis provided this occurs in a reasonable length of time, to be determined on a case-by-case basis. The student's sponsor is to report the student's progress to the PC at least annually.

**4.14.6** The student must include in the completed thesis:

- A. a statement acknowledging HCHS/SOL for use of the data, and
- B. a statement indicating that opinions, ideas, and interpretations included in the thesis are those of the student alone and not those of the HCHS/SOL investigators.

**4.14.7** When the thesis has been completed, as determined by the sponsor, the entire writing group is to proceed to prepare the paper(s) for publication. It is the responsibility of the HCHS/SOL PI "sponsor" to ensure that the thesis accurately reflects the conduct and data from the HCHS/SOL, as dissertations are technically available to the public without going through the PC review process.

**4.14.8** The standard HCHS/SOL publication policy applies to any material published from the thesis.

**4.14.9** HCHS/SOL reserves the right to proceed with preparing a paper for publication on the thesis topic through the activation of a writing group if, in the view of the PC and the student's sponsor, the student has not made reasonable progress in completing the thesis.

#### **4.15 Use of Data for Grant Application or Contract Proposal**

HCHS/SOL data which have not been previously published but which are needed for grant applications or contract proposals must have prior approval for use by the HCHS/SOL Steering Committee and Project Office.

## **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 are AS. 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. Pooling projects or consortia that wish to use HCHS/SOL samples.
- E. K-award and Other Data Analysis Grant Proposals  
All proposals that seek external funding need to go to the ASC for review. If the proposal solely involves only the writing of manuscripts using HCHS/SOL data it needs approval of the Publications Committee and an abbreviated review (in lieu of a concept proposal) by the ASC.

#### **5.2.1 Types of Studies Not Considered as Ancillary Studies**

There are studies that the HCHS/SOL will not consider as Ancillary Studies:

- A. Intervention studies using HCHS/SOL participants may be considered by the Ancillary Studies Committee providing that each participant to be enrolled has already completed the HCHS/SOL Visit 2 Examination.
- B. Proposals in which use of technical support (e.g. analytical and/or management support from the Coordinating Center) is sought may need a subcontract with the CC but if there are no additional measurements on the HCHS/SOL cohort, they will not be considered AS.
- C. Proposals seeking to compare other cohorts with the HCHS/SOL cohort, without incorporating use of HCHS/SOL biospecimens/samples 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, Co-Investigator or Director of a Reading or Laboratory Center may apply. 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 Application Process**

#### **A. AS Concept Proposal**

The development of an AS proposal involves planning and consultation with HCHS/SOL 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 to the ASC Chair (with copy to the HCHS/SOL Coordinating Center ASC Coordinator) 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: 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 (from visit 2):

- i. Serum, EDTA plasma, citrated plasma: 250  $\mu$ L total serum plus plasma per AS
- ii. Urine: 1 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 to the ASC Chair and the AS Coordinator 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 AS 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 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.
- D. Requesting Biospecimens  
The HCHS/SOL is supportive of ancillary studies and strives for a balance between providing specimen volumes sufficient to test the ancillary 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 ancillary study can ask HCHS/SOL to make up for dead volume in an

aliquot, and can request for an increase of up to 10 percent in the approved specimen 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 ancillary study application.

Types of specimen and amounts available to ancillary studies (from visit 2):

Type of Specimen	Volumes per Study Generally Allowable §
Serum	250 µL (total of serum and plasma per study)
EDTA plasma	250 µL (total of serum and plasma per study)
Citrate plasma	250 µL (total of serum and plasma per study)
Urine	1 mL

§ Larger amounts of specimen may be approved if a scientifically compelling justification is submitted.

Once an ancillary study is approved and funded, 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.

HCHS/SOL stores its biospecimen in aliquots larger than the amounts released to ancillary studies. Since it may be required to thaw (and re-aliquot) a larger volume of biospecimen to release specimen to an ancillary study the HCHS/SOL Steering Committee reserves the right to negotiate an optimal timing for the release.

## **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 (detailed on investigator website).

### **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 October 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.

## **Appendices**

## Appendix I Principal Investigators and Affiliation

### STEERING COMMITTEE PRINCIPAL INVESTIGATORS & Co-PI List

Bronx Field Center

**Robert Kaplan, Ph.D.**

Co-PI: Sylvia Wassertheil-Smoller, PhD, FACE, FAHA

Project Office – National Heart, Lung and Blood Institute

**Larissa Avilés-Santa, MD, MPH** (Project Officer)

Deputy Proj Officer: Paul Sorlie, PhD

Chicago Field Center

**Martha Daviglius, MD, PhD**

Co-PI: James P. Lash, MD

Coordinating Center

**Jianwen Cai, PhD**

Co-PI: Gerardo Heiss, MD, PhD

Miami Field Center

**Neil Schneiderman, PhD**

Co-PI: David J. Lee, PhD

Co-PI: Leopoldo Raij, MD

Echocardiography Reading Center

**Scott Solomon, MD**

Brigham and Women's Hospital

San Diego Field Center

**Greg Talavera, MD, MPH** ( Steering Chair )

Co-PI: John Elder, PhD, MPH

--- Listed above in large print are the Investigators who are voting members of the Steering Committee

--- Listed below are Investigators who are Ex-Officio Members of the Steering Committee

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### READING CENTERS PRINCIPAL INVESTIGATORS

Central Lab

**Bharat Thyagarajan, PhD**

Medical Center, Fairview

University of Minnesota

## Appendix II Membership of the OSMB



### NHLBI Observational Study Monitoring Board Listing of Members (August, 2013)

#### Chair

**George Howard, Dr.P.H.**  
Professor of Biostatistics  
University of Alabama at Birmingham

**Odilia I. Bermudez, PhD, MPH**  
Associate Professor of Public Health and Community Medicine  
Tufts University School of Medicine

**Hannia Campos, PhD**  
Senior Lecturer on Nutrition  
Harvard University School of Public Health  
School of Nutrition

**Judy Dubno, PhD**  
Professor  
Medical University of South Carolina  
Department of Otolaryngology/ENT

**Anne B. Newman, MD, MPH**  
Professor of Epidemiology and Medicine  
University of Pittsburgh  
Graduate School of Public Health

**Roberto P. Treviño, MD**  
Director of Social & Health Research Center

**Jean L. Olson, MD, MPH**  
(Executive Secretary, HCHS/SOL OSMB)  
Affiliation: NHLBI