Response to OMB Questions
Hispanic Community Health Study

1. Why did NIH decide to conclude the study within 3 years? Is 3 years enough time to get the type of longitudinal data NIH wants? What type of changes (e.g. health behaviors, health outcomes, etc.) are likely to be observed within 3 years?
It will take three years to recruit and examine 4,000 persons in each of 4 Field Centers. Each Field Center has the capacity to handle 6 or 7 participants each day. Thus, the three year time period is only to collect baseline data on the full cohort of individuals. This data collection will provide extensive data on the health status of these Hispanic/Latino populations, but will also provide a basis for future data collection after the three year period. A future examination is not included in the current contract period, but is anticipated with future funding by the NHLBI.

To better justify the extent of the initial data collection, please modify the supporting statement to discuss the plans for long-term follow up (how long you intend to follow the cohort, the types of follow up data collection activities anticipated, and how often you will conduct the cohort to conduct these follow up activities). Please link these follow up activities into specific hypotheses and time lines needed to test these hypotheses.

Response
(Added to Supporting Statement A8.1)
We are indeed pleased to describe in more detail the scientific aims of this study, regarding both the cross-sectional and longitudinal components. As noted in an attachment to our original application, the scientific merit of this study was reviewed at many steps including the final review by the Advisory Council of the NHLBI. The minutes of that Council meeting were attached in the original OMB request, but we have now added the roster of members. Please note that the Council review of this study, which includes attention to both the scientific merit and the total cost, was conducted by scientists at the highest level, including among others, a professor of epidemiology, a chief of a division of cardiology, the editor-in-chief of the New England Journal of Medicine, a dean of a nursing school, a professor in a department of medicine, a professor of internal medicine, and a professor of preventive medicine.

(Added to Supporting Statement A.14)
The second item is to clarify the contracting process of the NHLBI. As you requested, attached in the appendix is the annual budget for each year currently approved for funding by the NHLBI. This funding is committed by the budget office of the NHLBI, and extends for a six and one-half year period. This funding provides for the recruitment process, the baseline examination and all of its components, and ascertainment of hospitalized disease events for cardiovascular and lung diseases for an average of 3 ½ years. As described below, this will provide sufficient number of major cardiovascular disease events for global estimates of incidence and relationships with common risk factors. To provide appropriate stewardship of the government's funds, however, the NHLBI establishes a review process before future funds are awarded for continuation of projects. A renewal of the funding of this project, i.e. funding beyond the 6 ½ years, will again require presentation of progress to various review committees, including the Advisory Council of the NHLBI described above. Thus, while the NHLBI has committed 6 and ½ years of funding to the study, to provide appropriate oversight of federal funds, future funding is not committed until appropriate review and approval is complete.

The following information is provided both here and in the body of the supporting statement:
(Added Supporting Statement A. 1)

The Hispanic Community Health Study/Study of Latinos, is an extremely comprehensive research study, utilizing questionnaires, measurements of risk factors, identification of disease, and measurement of components of the blood. These measurements will provide the capability to investigate a multitude of hypotheses on the nature, emergence, and risk factors for and causes of various diseases in the Hispanic/Latino population of the United States. The study sample size is large because it is necessary to include each of the major groups of Hispanics/Latinos that reside in the U.S. While most prior research on Hispanics in the U.S. has concentrated on those of Mexican origin, each group has differing cultural and behavioral traditions, differing food, differing reasons for immigration and, from the little information currently available, differing levels of health and risk. Research on one group will not provide answers related to one of the other groups.

(Added to Supporting Statement A.2.a)
BASELINE DATA COLLECTION AND CROSS-SECTIONAL ANALYSIS

The cross-sectional hypotheses can be grouped into broader research areas. These objectives can be accomplished within the funded contract period of 6 ½ years. Below is a small selection of the many research questions related to cross-sectional data only:

Obesity and physical activity:

- ✓ *Measurements/questionnaires*: height, weight, waist girth, daily activity by accelerometer, a questionnaire on physical activity and weight loss, type of occupation.
- ✓ *Research questions:* How is obesity related to country of origin, length of stay in the U.S., degree of acculturation, type of dietary intake, work on the job, leisure activity, intensity of activity, age and sex? Answers to these questions can help understand the causes of weight gain, and to target weight programs for the various Hispanic groups.

Diabetes

- ✓ *Measurements/questionnaires*: reported diagnosis of diabetes, fasting and sugar challenged blood glucose and insulin, hemoglobin A1C.
- ✓ *Research questions*: How does the prevalence of diabetes vary by country of origin, acculturation, and obesity? Is diabetes prevalence higher in those with greater acculturation and length of stay in the U.S., and if so, why? What is the degree of association of diabetes with obesity, physical activity, and a glycemic diet? Have participants sought and obtained appropriate health care for diabetes? Is diabetes associated with diseases of the kidney and liver? Since diabetes is a major health problem in Hispanics, answers to these questions can help in identifying causes, define prevention strategies, and improve medical care.

Hypertension and high cholesterol

- ✓ *Measurements/questionnaires*: sitting blood pressure, plasma total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides.
- ✓ *Research questions*: How does the prevalence of hypertension vary by country of origin, acculturation, obesity, physical exercise, stress? What is the

association between hypertension and life style behaviors including diet, smoking, and access to health care? How does the prevalence of high cholesterol (or other adverse lipids) vary by country of origin, length of time in the U.S., medication use? What are other correlates of an adverse lipid and blood pressure risk profile? Answers to these questions can assist in understanding the etiology of adverse blood pressure and lipid levels in Hispanics, and can provide guidelines for treatment.

Acculturation and health

- ✓ *Measurements/questionnaires*: Questionnaires on length of stay in the U.S., retention of Spanish language and customs/behaviors/attitudes from country of origin, retention of food preferences and eating behaviors from country of origin, identification of values with country of origin.
- ✓ *Research questions*: How is acculturation related to specific health conditions (cardiovascular, diabetes, kidney, liver, dental, hearing, cognition)? What are the components of the acculturation relationships and how do they help understand the etiology of these diseases? How does acculturation affect health seeking behaviors and access? Answers to these questions can provide understanding on the general observation that acculturation to the U.S. generally worsens aspects of cardiovascular health and diabetes. The consequence of acculturation to other health conditions is mostly unknown and will be explored in this study.

Dental and hearing conditions

- ✓ *Measurements/questionnaires*: A dental exam will identify tooth loss, tooth caries and periodontal disease. A hearing exam will identify components of hearing loss.
- ✓ *Research questions*: What is the prevalence of dental and hearing conditions by country of origin, length of stay in the U.S. and acculturation? What are the significant correlates of higher prevalence of these conditions? Answers to these questions will provide totally new information on the severity of diseases and conditions and will inform regarding the burden of the conditions, the causes of the conditions, and ways to prevent the conditions from occurring.

Peripheral vascular disease

- ✓ *Measurements/questionnaires*: The ankle/brachial blood pressure index will be measured and calculated. This simple non-invasive test measures early atherosclerosis in the peripheral arteries.
- ✓ *Research questions*: Are there differences in the prevalence of early atherosclerosis by country of origin, acculturation or length of time in the U.S.? Is atherosclerosis associated with diabetes, obesity, cigarette smoking in this population? Answers to these questions will provide evidence regarding the differential development of disease in Hispanic subgroups and with acculturation, providing information to understand the impact of the U.S. life style on immigrant groups.

Cognitive impairment

- ✓ *Measurements/questionnaires*: There will be performance measures of cognitive impairment involving memory and decision making.
- ✓ *Research questions*: How is the degree of cognitive impairment related to age, sex, county of origin, length of stay in the U.S.? How is the degree of cognitive

impairment related to vascular parameters such as blood pressure, ankle-brachial index, lipid levels, kidney impairment or other factors? Cognitive impairment is a significant component of disability in advanced age and current research supports a vascular component of etiology.

Liver and kidney diseases

- ✓ *Measurements/questionnaires*: Blood measures for the various hepatitis types, creatinine, liver enzymes, iron, and urine values of albumin and creatinine.
- ✓ *Research questions*: How does the prevalence of hepatitis types vary by country of origin, length of stay in the U.S. and acculturation? What is the prevalence of kidney impairment and how does this vary by country of origin and other cofactors of cardiovascular disease. Information on the degree of kidney and liver diseases will provide estimates of the burden of disease, and strategies for preventing and treating these conditions.

LONGITUDINAL DATA COLLECTION AND ANALYSIS

The longitudinal portion of this study has two components. The first component, which is funded in the current 6 and ½ year period, is to contact individuals annually by telephone (or in person if unable to contact by phone), to ascertain current household location and contact information, to conduct a brief health history, and to identify any hospitalizations that may have taken place in the previous year. When these hospitalizations are identified, the study (with signed permission from the participant) will obtain the medical record from the hospital, will abstract relevant information and will provide a validated diagnosis for the disease and this will become part of the study data base. This process will provide identification of incident occurrences of coronary heart disease, stroke, heart failure, and exacerbations of chronic obstructive lung disease and asthma. In the time frame of this funded portion (6 ½ years) the expected average follow-up for incident disease will be 3 ½ years. The number of validated cases of myocardial infarction or coronary heart disease death in this follow-up time period is estimated to be around 100. This is a small number, but will provide initial estimates of incidence and of relative risk for major risk factors in the total population. The statistical strength of a longitudinal study is in future long term follow-up. An additional follow-up period, adding at least 5 additional years of follow-up will provide extensive endpoint events to be able to analyze baseline characteristics in their association to future disease. As described earlier, this will require future funding.

The second component, not funded in the current cycle of funding, is a re-examination of the entire cohort. The scientific objective is to re-examine the population approximately six years after their first baseline examination. This will provide additional data on change in the characteristics under consideration, and will allow analysis of factors relating to either beneficial or adverse changes in the factors identified at baseline. For all of the research groups listed above, there are questions related to the etiology of change in these risk factors and their consequences to disease. This second component will be proposed, reviewed, and subject to the same scientific review process as occurred during the initial review and approval.

a) In an appendix please provide evidence that this study has funding support in the out years (how long funding is anticipated to be provided. It does not make sense for us to

approve such an expensive start up without a fairly strong commitment on the part of the administration to funding the out years.

Response:
(Supporting Statement 14 and 14.1)
The annual budget for each year currently approved for funding by NHLBI is attached <budget.response 1-31-08> Because of interest in the cost over the contract period, average annual costs in Table 14.1 have been revised to reflect average annual cost over the duration of the 6 ½ year contract period rather than the time period covered by the OMB submission. This funding is committed by the budget office of the NHLBI and extends for a 6 ½ year period. This funding provides for the recruitment process, the baseline examination and all of its components, and ascertainment of hospitalized disease events for cardiovascular and lung diseases for an average of 3 ½ years. A renewal of the funding of this project, i.e. funding beyond the 6 ½ years, will again require presentation of progress to various review committees, including the Advisory Council of the NHLBI described above. Thus, while the NHLBI has committed 6 and ½ years of funding to the study, to provide appropriate oversight of federal funds, future funding is not committed until appropriate review and approval is complete.

2. What kinds of policy recommendations does NIH expect to be able to make with 3 years worth of data?
The data collected during the recruitment and baseline examination will provide information regarding the prevalence of risk factors for cardiovascular and pulmonary diseases across Hispanic nationalities (place of birth), ethnicities, geographic locations gender, and age-groups.

For the first time, across several groups of Hispanic origin, we will have prevalence information such as smoking, hypertension, diabetes, dyslipdemia, family and personal history of cardiovascular and pulmonary disease, hearing loss, sleep problems (which are a risk factor for CVD), lifestyle, nutritional habits and physical activity among other information.

Therefore, this study will permit comparisons across a variety of Hispanic groups from different regions of origin and will be used for policy recommendations that will impact the health of the current participants, the communities to which they belong , the U.S. Hispanic/Latino community at large and the U.S. general population. These data could inform policy recommendations related to:

- New screening guidelines for the prevention, diagnosis and treatment of hypertension, diabetes and dyslipidemia especially design to implement prevention and diagnosis early in life (young adults)
- A task force to improve health literacy level among Hispanics/Latinos, especially the elderly.
- A national task force to prevent obesity using culturally-proficient educational methods
- Improving the quality of food available at local markets and grocery stores, and increase the availability and affordability of foods with high nutritional value.
- A task force to increase the knowledge and awareness of the nutritional value of foods (for example, interpreting labels, glycemic index, contents of polyunsaturated and saturated fats).

It seems like NIH could embark on all of these missions in the absence of the data being collected in this study. Why do you feel that such an intensive field investigation is necessary to

justify funding THESE missions? Please clarify in the supporting statement whether you are truly justifying this study on its merits after three years or on a long term basis. If on its merits after three years, please include a more detailed justification for why the current cross-sectional data available from NHANES is not adequate for the purposes outlined in the bulleted list above.

Response:
(Added to Supporting Statement A.4)
As described above, this study is planned to provide data from two components of the study. Both the cross-sectional and the longitudinal components will provide critical information and are necessary for the aims of this study. The cross-sectional component will provide information to gauge prevalence and cross-sectional associations. The longitudinal component will provide information on causes of change in risk factors and the consequences in relation to incident disease. While the cross-sectional component is similar to NHANES, there are important differences. NHANES is not collecting data with this sample size for the various Hispanic subgroups. NHANES is not collecting the intensive information on Hispanic acculturation and all of its components. NHANES is not collecting information on sleep, physical activity, peripheral vascular disease, and other parameters important for this study. The NHANES is not designed to do follow-up of participants for a clinical re-examination or for incidence of disease.

3. Rather than a stand-alone study, could this study be done as an "add-on" to NHANES (e.g. as a supplement)? Please provide a cross-walk of the questions asked in NHANES that are also being asked in this study.
There are distinct and important differences between NHANES and the Hispanic Community Health Study (HCHS). The HCHS is a cohort study, meaning that the goal is to measure the participants at baseline and at subsequent clinic visits. A cohort study also collects extensive information about the occurrence of disease that happens in the participants over time. The HCHS is community based, meaning that it is a sample from a defined community, that the medical care occurs in hospitals and doctor's offices in proximity to that community, and that the study exists with the full support, encouragement, and cooperation of the community. This community support is required for successful functioning of a cohort study. The NHANES is a cross-sectional study of a national sample, without community involvement, without repeat examinations, without further follow-up for medical care, and without the research goals inherent in at cohort study. Since the research goals of each study design are different, the HCHS could not be an "add-on" to the NHANES.

See our note re: items one and two – if this is truly being justified as a baseline for a long-term follow up, please recast the supporting statement to emphasize the nature of the goals of this study – currently it reads like a three year cross-sectional study rather than a long term follow up study.

Response:
As noted above, there are two major components of this study, cross-sectional and follow-up. Both are essential and both will provide critical information. For the time period requested in the OMB submission, we only concentrated on the 3 year period covered by the OMB. Also, as described above, currently approved funding will mostly cover the cross-sectional data collection and analysis, though the study will begin the follow-up process. While the long term goal is to continue follow-up and re-examination, the study also stands scientifically on the value of the cross-sectional data.

A “cross-walk” of the questions asked in NHANES is attached (file: Xwalk. Rev.12-20-07.doc) The NHANES-HCHS/SOL comparison is found in the first three columns.

4. How often will all the testing be done? Is this only once at baseline or at each annual follow-up?
Testing is done one time at baseline. Annual telephone follow-up will be used to 1) maintain contact and address information on cohort participants, 2) update information on contact persons, 3) ascertain participant’s vital status, and 4) obtain information about medical events/hospitalizations and life events since the baseline examination.

See our note re: item one – many more details are needed. We are concerned that no additional testing is anticipated. If that is the case, we need a much stronger justification for many of the clinical and laboratory tests being conducted. The additional justification needs to clearly spell out how each of the test results being collected will be used in the long term analysis. Some of the tests that you are collecting are best used for observing trends. Please justify the expense of collecting this information without future follow up.

Response:
(Supporting Statement A.2)
Examples of the clinical and laboratory measurements were provided in response to question 1. These measurements have value both for cross-sectional and longitudinal analysis. A one-time, extensive examination of this population sample of Hispanic residents of the HCHS study communities is scientifically important and has public health and policy implications, even in the absence of repeat examinations. The characterization of this minority population (and its subpopulations by country of origin) is uniquely informative to fill the gaps in current knowledge of the health related beliefs, behaviors, socioeconomic context, risk factor profile, metabolic phenotypes, self-reported and objectively quantified illnesses. Since information on these attributes is fragmentary or non-existent for this minority group, the one-time testing designed for this study represents a significant and fully informative contribution.

(Supporting Statement A2.b)
An additional justification for the testing described above is that it serves as a baseline description that enables the ascertainment of the study outcomes as newly developed, incident events. In turn, the various baseline measurements incorporated into the examination permit the estimation of the antecedent factors that influence the population’s susceptibility to these health outcomes. Risk factors as well as protective factors can thus be identified for this population, over a range of modifiable beliefs, behaviors, and phenotypes.

What is outlined above represents the measurements and scientific inquiries that led to effective risk estimation, to health policies and clinical guidelines for priority health issues in other population groups. Such information is not available at this point for Hispanics/Latinos resident in the United States.

As noted in response to Question 1.a. the current project period is funded for 6 ½ years. As this time period draws to a close, a renewal will be requested for long-term follow-up.

5. On page 14 of the supporting statement part A, it says that identifiable data will not be provided to outside consultants or investigators. Does that mean that in other circumstances, identifiable data will be disclosed? To whom will identifiable data be disclosed and under what circumstances?

Data that is collected from participants in this study will be stored in encrypted form in the database and maintained in a way that separates personal names and address from the clinical information and questionnaires. Participant data will be de-identifed in a manner that complies with NIH guidelines for security and confidentiality. Only the originating field center investigator and the coordinating center have access to personal information in order to provide individual reporting of results and referrals back to the participant. Data stored at the coordinating center is maintained in accordance with an NIH approved information technology system security plan. The coordinating center on behalf of the study investigators in this multi-site study will apply for a Certificate of Confidentiality from DHHS so that the information is further protected under those statutes. Only information mandated by law (e.g. instances of child abuse or neglect, communicable diseases, etc.) would be reported to outside public health agencies or other explicitly authorized authorities. The study will, with permission of the participants, use identifying data to link to the National Death Index and possibly other medical databases. In this process, the data will be provided and linked using the data security provisions provided by these systems.

Please clarify this section of the supporting statement.

Response:
(Added to Supporting Statement 10.5)

6. What are the "NIH limited access data use policies?" (page 14 of part A)
The Limited Access Data Set (LADS) policies are described in detail on the following website: http://www.nhlbi.nih.gov/resources/deca/default.htm

Data sets distributed under this policy include only "limited access data", i.e., records with personal identifiers and other variables that might enable individual participants to be identified, such as outliers, dates, and study sites, removed or otherwise modified. Data sets are only distributed to qualified researchers who agree in advance to adhere to established policies for confidentiality and distribution. Identifiable information is never released under the limited access data set policy.

Please clarify this section of the supporting statement.

Response:
(Added to Supporting Statement A10.7)

7. Have the IRBs approved this study?
Three of the 4 participating field centers (Northwestern University, Albert Einstein Medical Center, University of Miami) and the Coordinating Center at the University of North Carolina, Chapel Hill have received full IRB approval for the study (approvals attached). The IRB for San Diego State has provided provisional approval and full approval is imminent. No recruitment or research related activity will take place in San Diego until final approval is documented. Documentation will be forwarded to OMB as soon as it is received. Provisional IRB approval for the San Diego field site is attached.

What was the San Diego approval provisional on? Also, some of the IRB approvals appear to be expiring soon.

Response:
(Added to Supporting Statement A.10)

The San Diego State University principal investigator received provisional approval and a number of detailed questions from the IRB because an early version of the protocol and of the study forms was submitted for IRB review in July of 2007. The P.I. has addressed the questions and re-submitted his application to the board with updated versions of the supporting materials. Approval is pending as was noted.

IRB review generally takes place on an annual basis. As individual field centers and the coordinating center approach their respective IRB approval expiration dates, well established mechanisms at each institution are set in motion for timely renewal submissions to occur. Updated IRB approvals are filed with the coordinating center for review by the NIH and the Study.

8. Please explain further what has already been done with regard to focus groups, and what will be done in the future with focus groups (see response #2 in part B of the supporting statement). If the focus groups have not been conducted yet, what is the timeline for implementation of the focus groups? What is the burden involved and where is the burden accounted for?

Prior to study formation, informal discussions were undertaken with staff and community representatives regarding issues related to study design, content, Spanish translation, and cultural issues related to this study. Each community sampled in this study has completely unique Hispanic origin composition, community interaction and resources, cultural influences, Spanish word usage, and cultural history. Thus, these small informal discussions were undertaken separately in each community and constituted a unique set of interactions with communities of Cuban, Mexican, Puerto Rican, Dominican, and Central/South American influences. Focus groups of more common goals will be undertaken to perfect the questionnaires, and Spanish translation.

Focus groups are planned to occur upon OMB approval and continue for approximately 6 months. We regret that we overlooked incorporating that overall burden in the Supporting Statement and appreciate that you pointed that out. The focus groups provide feedback on questionnaire items in order to verify appropriate translation of Spanish idioms and to discuss alternatives should problems be detected in the first several months of use. The total activity would include eleven groups consisting of approximately 7-10 individuals at each field center (4 field centers), lasting approximately 1.5 hours each and discussing approximately 12-15 items in each group. Any modifications made to the Spanish translation of the questionnaires will be forwarded to OMB. Estimated burden is:

81 individuals x 1.5 hrs. (90 minutes) for each group or 121.5 hours total.

Please allow us to clarify that this should be incorporated in the overall study burden. The I-83 (attached) has been revised to incorporate these hours.

OK: Please revise the burden estimates in ROCIS as well. ROCIS has been opened for amendment for you.

Response:

(Added to Supporting Statement Tables 12.1 and 12.2)

The burden tables in the Supporting Statement have been modified to include focus group hours. ROIC system has been revised.

9. The supporting statement says that participants will not receive compensation. The consent form, however, indicates that compensation will be provided. Please clarify.
Participants will not be paid to participate in the study. As indicated in the consent form, they may receive compensation to offset costs associated with child care, transportation, gas, tolls, and parking.

Please revise the supporting statement to clarify that participants will receive an incentive, and that the amount of that incentive is $X (e.g., $25), designed to cover transportation and child-care related expenses. OMB strongly prefers this uniform, lump sum approach rather than direct reimbursement for differential, itemized reimbursements.

Response:
(Added to Supporting Statement A.9)
This was intended to be a lump sum rather than reimbursement for itemized expenses. It is clarified in the Supporting Statement as follows:
Participants will receive a lump sum incentive in the amount of $75 to cover expenses associated with participating in the clinic examination including child care and transportation (gas, tolls, parking, public transit).

10. Please explain explicitly what steps from previous studies like Jackson Heart Study and ARIC will be adopted for use in this study (page 13 of part B).

Answer: The following procedures are being conducted in the Hispanic Community Health Study. Previous use of these procedures is listed in the table.

Procedure	Source of Same or Similar Protocols
Sitting Blood Pressure	ARIC, MESA, CHS
Ankle-Arm Blood Pressure	Framingham, MESA
Pulmonary Function	MESA, Framingham, CARDIA, NHANES
Electrocardiogram	ARIC, MESA
Anthropometry	Framingham, ARIC
Physical Activity Monitors	CARDIA, NHANES
Dental Examination	This procedure was used in the NHANES, and was slightly modified from a procedure previously used in the ARIC study.
Audiometry	This procedure was used in the NHANES.
Sleep Monitors	This device has been tested and validated. Results are published in *Chest* 2005:128, “A Novel Method to Diagnose Sleep Apnea-Hypopnea in the Home. Westbrook, et.al.

Venipuncture ARIC, Framingham, MESA, CARDIA, CHS,

ARIC – Atherosclerosis Risk in Communities (NHLBI, NIH)
CHS – Cardiovascular Health Study (NHLBI, NIH)
CARDIA – Coronary Artery Risk Development in Young Adults (NHLBI, NIH)
Framingham – Framingham Heart Study (NHLBI, NIH)
MESA – Mult-Ethnic Study of Atherosclerosis (NHLBI, NIH)
NHANES – National Health and Nutrition Examination Survey (NHLBI, NIH)

The attachment <X.walk.doc> provides the source studies for the questionnaires used in HCHS.

Please add the discussion re: the source of the methods used as well as the importance of using the same (or different) methods to the supporting statement.

Response:
(Added to Supporting Statement B.4)

11. The race/ethnicity question on the personal information questionnaire does not comply with OMB standards. Please revise.

The personal information questionnaire has been revised. The modification is highlighted. Please see the attached file: <personal information 12-20-07.doc>

The study participants will be composed of individuals who only self-identify themselves as Hispanic/Latino by the time the personal information questionnaire is administered. There will be no non-Hispanic participants in this study by design.

While a respondent may not know their race/ethnicity or may decline to state it, these options (e.g. "don't know" or "refused to report") should not be offered to the respondent as response categories. Please revise or let us know how you will train your interviewers to comply with OMB standards.

Response:
Staff are instructed in the question by question instructions for the Personal Information form (see attachment <Personal Information QxQ 1-29-08> where self-identification of race is recorded to not volunteer the don't know or "refusal" options so that one of the standard categories for race can be recorded. At this stage of the interview it is already known that the individual has self identified as Hispanic/Latino.

Question by Question Instructions for Item 6 of Personal Information Form "Q6. Assess the self-described race of the participant. In order to distinguish from the previous question you should emphasize the word "addition" at the beginning of this sentence when asking this question ("In addition to…."). Read the response options 1 through 5 in the order presented, omitting the "Unknown or Not Reported" category. You may need to repeat the response options. If unknown, not reported or refused check box number 6. OMB reporting guidelines for observational studies and clinical trials mandate that study recruitment be reported annually by race/ethnicity, so it is important this information should never be missing.

12. Many of the questions seem to require a fairly high literacy level (e.g. the SSN disclosure statement on the Personal Identifiers instrument). NIH states in the supporting

statement that literacy may be an issue with this population. Please revise the instruments so that everything is in "plain English."

The SSN Disclosure Statement has been modified and is highlighted. The revised Personal Identifier form is attached. File: < personal identifiers.12-20-07.doc>

Educational level and literacy were factors seriously considered during the development of all the instruments to be used in the study. **It is important to emphasize that all of the questionnaires will be administered verbally by trained interviewers in either English or Spanish.** Because a wide range of literacy levels are expected among the participants, they will not be asked to read or answer any questionnaires on their own. The interviewer will be able to repeat questions, and in the cases that merit it, participants will receive a card with the scales or alternative answers printed on them, to facilitate their understanding and get more accurate responses.

With permission of the participant, the interviews will be monitored for quality control purposes. Modifications will be made to questionnaires as needed based on experience with the interviews and these quality control checks. Any modifications to the questionnaires will be forwarded to OMB.

Most of the instruments to be used in the study have been used or adapted from other epidemiological studies and, therefore, have been previously validated in their current version. Therefore, for comparability, the language needs to remain consistent. One questionnaire is under copyright. Some of these instruments had been translated and validated in Spanish. For others, a translation was necessary. For this purpose, the Coordinating Center established a contract with an outside company to perform the translations.

The Translation and Validation committee reviewed all the instruments and evaluated the reading level, the quality of the translations (grammatical quality and use of terms that are understood by Hispanics/Latinos of a diversity of origins), and the cultural relevance and appropriateness of the questions. This process of evaluation was not limited to existent versions in Spanish or translations done for the study. The English versions were evaluated as well. During this process, the committee identified some phrases or words that could have different interpretations or that needed some modification of their reading level. Finally, an outside Spanish scholar and translator, evaluated the final product before its certification.

Due to the occasional medical vocabulary used in the questionnaires, and the variety of idioms in both English and Spanish, the Translation and Validation Committee created a series of definitions for those specific terms. These are the **Question By Question instructions** or "**QxQs**." If a participant does not understand the meaning of a term, the interviewer will be able to download a menu with the definitions or alternative term (for example, idioms dependent on birth place or community). In consultation with our medical investigators, medical terms need to remain in the questionnaires with appropriate explanations to the interviewers and participants.

Please add this discussion to the supporting statement.
(Added to Supporting Statement B.3)

Examples of QXQs – Instructions to the interviewer to explain questions to the participant

Hearing Exam Questionnaire

Question 13. ***What type of surgery was done?***

1 Tympanoplasty
2 Mastoidectomy
3 Stapedectomy
4 Cochlear implant
5 Other

QXQ Explanation: Tympanoplasty is surgical correction of damage to the middle ear. Mastoidectomy involves the removal of the mastoid bone (behind the ear) and the opening of diseased mastoid air cells. A stapedectomy involves removal of a portion of the stapes bone (a small bone in the inner ear) and replacing it with a prosthesis to restore the ear's ability to transmit sound. A cochlear implant is an electronic prosthesis, surgically implanted in the ear, that can restore a sense of sound to people with hearing impairment. Some participants may not be familiar with the medical term for their procedure. If the description the participant provides matches any of the descriptions for choices 1 – 4, code as such. If uncertain, or if the participant is unable to describe the procedure, record as 5.

Question 16. ***Have you ever had an acoustic neuroma?***

No Yes Don't know/refused

QXQ Explanation: An acoustic neuroma is a tumor on the auditory nerve. The participant may not be aware of the medical term. If he or she reports that they have had a tumor and that the tumor was on a nerve affecting their ear, code as yes. Tumors that are not on a nerve should be coded as no.

Question 17. ***Have you ever had a cholesteatoma?***

No Yes Don't know/refused

QXQ Explanation: A cholesteatoma is a mass or growth in the middle ear.

Question 18. ***Has a doctor ever told you that you have Meniere's Disease?***

No Yes Don't know/refused

QXQ Explanation: Meniere's Disease is a syndrome characterized by nausea, vomiting, tinnitus (ringing in the ears) and progressive hearing loss.

Question 19. ***Has a doctor ever told you that you have otosclerosis?***

No Yes Don't know/refused

QXQ Explanation: Otosclerosis is a disorder of the bones of the middle ear.

Medical History Questionnaire

Question 3. ***Has a doctor ever said that you have angina?***

No 0 □ **GO TO QUESTION 3b**
Yes 1

3a. *At what age were you first told this?*

_____ Age in years

Has a doctor ever said that these relatives had angina?

3b. Mother No or Don't know 0 Yes 1
3c. Father No or Don't know 0 Yes 1
3d. Brother(s) or sister(s) No or Don't know 0 Yes 1

QXQ Explanation: Assess personal and family history of angina as well as respondent age at diagnosis for this condition. Chest pain is a hallmark symptom of persons with angina. However,

not all persons who experience chest pain have this condition. Therefore, it is important to check the yes box on this set of questions only if they can state that a doctor told them they had angina.

Question 4. ***Has a doctor ever said that you had a heart attack?***
No 0 □ **GO TO QUESTION 4b**
Yes 1
QXQ Explanation: Assess personal and family history of heart attack. The clinical name for heart attack is myocardial infarction. Age when the heart attack occurred is obtained for both the respondent and for blood relatives. This latter information is important to ascertain because some studies suggest that history of heart attacks in family members that occur at relatively young ages is a risk factor for heart disease in other family members. Q4b-c assess history of doctor-diagnosed heart attack in biological parents, followed by the age at which first such occurred. Q4d assesses family history of heart attack in brother(s) or sister(s). In rare cases there may be more than one sibling with a history of heart attack. In this case record the younger age at which there was a heart attack. For example, if the respondent reported that a brother had a heart attack at age 50 and a sister had a heart attack at age 40, then you would record 40 as the age for item 4d.

Question 5. ***Has a doctor ever said that you had heart failure?***
No 0
Yes 1
QXQ Explanation: Assess personal and family history of doctor diagnosed heart failure. Another clinical name for this condition is congestive heart failure or congestive cardiac failure. This diagnosis covers a variety of conditions in which the heart is unable to pump a sufficient amount of blood through the body. Heart failure should not be confused with heart attack or myocardial infarction.

Question 6. ***Has a doctor ever said that you had rheumatic heart disease?***
No 0
Yes 1
QXQ Explanation: Assess personal and family history of doctor diagnosed rheumatic heart disease. Persons with this condition have damaged heart valves, which can be a consequence of untreated streptococcus infection that typically occurred in childhood.

Occupational Questionnaire

Question 23. ***At the job you currently work the majority of your work hours per week, how often are you exposed to any type of organic solvents, for example styrene, trichloroethylene, toluene, or xylene?***

None of the time 1
25% of the time 2
50% 3
75% 4
100% 5
Occasionally 6
Don't know 9

QXQ Explanation: Read as given, but if the participant is not familiar with what a given term means, (e.g., manganese) take this as a NO. Do not explain. People exposed will typically know. Those needing an explanation are much less likely to actually come in

contact with these substances.

13. At what frequency will each of the instruments be used? For example, will the SF-12 questions be asked at follow-up or only at baseline?

Each instrument will be administered one time. Within the 3-year OMB period of approval for the collection, annual telephone follow-up will take place to maintain contact with the participants, verify addresses, ascertain vital status and to obtain information on medical events or hospitalizations and other life events since the baseline examination.

14. Will recruitment take place in person? (the recruitment script seems to imply an in-person screening visit).

The recruitment plan consists of three basic steps:

- Initial mailings to sampled households describing the study and inviting the household to be screened
- Optional telephone contacts to households with telephone numbers available from the sampling frame
- In person contacts for households without telephone numbers, households unable to be reached through telephone contacts, and households in Field Centers not conducting any telephone screening.

If contact is established with a household through a telephone call, then household screening is conducted via telephone. If a household visit is required to establish contact, then household screening is conducted in person. Three Field Centers plan to use a combination of telephone and in-person screening, while one Field Center (Miami) plans to conduct all screening visits in person. Once eligibility of a household is established, and individual household members who are present are screened for eligibility, clinic visits are scheduled. If not present, individual household members are contacted at a later date by phone or in-person for screening and scheduling of clinic visits.

What about the call is “optional”? Who determines? Please add to the supporting statement.

Response:

(Added to Supporting Statement B.1.c)

The field centers have the option in the recruitment procedures to either make the first contact with a prospective household via a phone call, or an in-person visit. So, the qualifier 'optional' used in the 2nd step in the recruitment protocol to reflects the fact that at least one site, Miami, plans to use a lead letter followed by home screening visit, thereby skipping the telephone screening step (Step 2). The Miami target area is geographically small and dense, so this plan represents an efficient approach. The other three sites plan to use all three steps at this point, but may drop the telephone screening if response is not high and move directly to in-home screening after the lead letter.

15. This study requires a HIPAA form. Please submit it.

HIPAA forms for all of the four field centers are attached.

Thank you for including the forms. We are a little confused about what participants are giving permission for, and thus worry that participants may be equally confused.

The following statement suggests that the focus is on giving the folks collecting the information for this study to pass it on to UNC : "By signing this document, you give your permission to HCHS/SOL employees, physicians and staff to disclose information about you to the University of North Carolina at Chapel Hill, including the Principal Investigators, co-investigators, study coordinators, and other members of their research team."

But, this later statement seems to refer to medical information in prior and future provider records (rather than specific study information) "All health information pertaining to my medical history, mental or physical condition and treatment received as well as dental records.

If you are hospitalized or treated in an emergency department or urgent care center, we will use this signed medical release to obtain and review a copy of the hospital or outpatient records, emergency department/urgent care, cancer registry, and your physician's medical records."

Please clarify the language to specify whether this letter means that the study staff can take the form to any medical provider the participant has ever had, past, present, or future. If this is the case, where does the participant provide a list of the medical providers to whom he/she is specifically giving permission to release medical records to the local data collection team (as opposed to providing permission for the local data collection team to disclose to UNC)? Are there any limits on what information may be requested (is this a blanket request for access to any information ever collected or specific information related to the hypotheses being studied?

With regard to the Northwestern University consent/HIPAA form, the wording is much clearer. However, on page 2-3, the form says "However, Northwestern University may not re-use or re-disclose your personal health information collection in this Study for another purpose other than the research Study described in this document unless it obtains permission to do so from the Northwestern University IRB." Is there some reason why the patients themselves aren't offered the chance to provide permission?

Response:

HIPAA template for the Study is attached.

We agree that the language in the Northwestern University consent/HIPAA form is much clearer and have adopted this version as the Study's HIPAA form. We appreciate your pointing out the inconsistent statement on page 2-3 of the form initially submitted ("However, Northwestern University may not re-use or re-disclose your personal health information collection in this Study for another purpose other than the research Study described in this document unless it obtains permission to do so from the Northwestern University IRB.") We have modified this statement to read: "However, _____ University may not reuse or re-disclose your personal health information collected in this Study for another purpose other than the research described in the informed consent document you have signed for this Study, unless it obtains permission to do so from you and the _____ University Institutional Review Board." This revision now frames the reuse or re-disclosure of the personal health information in the terms specified by the participant in his/her informed consent, as well as any updates to this informed consent which the study will track over the duration of an individual's participation in the study.

We have also modified the following statement in the original Northwestern University consent/HIPAA: "The Principal Investigator may also use the results of these tests and procedures to treat you." It now reads: "The Principal Investigator may also use the results of these tests and procedures to refer you to a medical provider to verify your study results or to treat you." A revised version of the HCHS HIPAA form is attached.