Supporting Statement for
Cardiovascular Health Study (CHS)
OMB 0925-0334, Exp. 09/30/07

Submitted by:

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Cardiovascular Health Study
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OMB Submission: Request for Revision of OMB Clearance

Summary and Supporting Statement

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ATTACHMENTS

Summary of the Cardiovascular Health Study

The Cardiovascular Health Study (CHS), OMB No. 0925-0334, expiration 09/30/2007, is an NHLBI contract-funded longitudinal observational study of the development and progression of heart disease and stroke in the elderly initiated in 1988. A random sample of 5,201 men and women aged 65 years and older was recruited from four communities between June 1989 and May 1990. An additional 687 African-Americans were recruited to the study between August 1992 and May 1993. This cohort was followed prospectively on a semi-annual schedule with alternating clinic examinations and telephone calls for development of new cardiovascular risk factors, subclinical disease, and overt cardiovascular disease through May 1999. Contract renewals on June 1, 1999 enabled semi-annual phone calls after the last exam in 1999-2000 to continue identification of clinical cardiovascular and cerebrovascular disease events through May 2005. Cohort follow-up continues via investigator-initiated grant support to three of the CHS field centers and a no-cost extension of NHLBI's contract to the Pittsburgh field site. The entire examination schedule for CHS may be found as Attachment 7. CHS was originally approved by OMB for a 3-year period ending May, 1992. Approval was extended five times with the most recent revision approval ending September 30, 2007. On June 1, 2005, NHLBI awarded a new 3-year contract to the study's coordinating center (CHS - Transition Phase) to support CHS study operations but no new data collection, and a 3-year renewal of this contract is planned. The University of Pittsburgh is the only CHS field site still sponsored by CHS contract funds to conduct new events ascertainment efforts. This OMB submission supports a request for a reinstatement with change until May 31, 2008 to perform additional morbidity and mortality follow-up of the Pittsburgh field site cohort.

SUPPORTING STATEMENT

A. JUSTIFICATION

A.1 Circumstances Making the Collection of Information Necessary

The impetus for the current study was the Working Conference on Coronary Heart Disease in the Elderly held in Bethesda, September 1985. Conference participants recognized the need for epidemiological studies of atherosclerotic disease in a general elderly population. The study objectives of the CHS are clearly within the National Heart, Lung, and Blood Institute mandate and the Institute is uniquely capable of coordinating this complex study over an extended period of time. The NHLBI mandate is described in the PHS Act, Section 421 (42USC 285b-3) and specifies provision of "investigation into the epidemiology, etiology and prevention of all forms and aspects of heart, blood vessel, lung, and blood diseases, including investigations into the social, environmental, behavioral, nutritional, biological, and genetic determinants and influences involved in the epidemiology, etiology, and prevention of such diseases."

Cardiovascular disease is a major public health concern because it is a leading cause of death and a major source of illness and disability. It has an adverse effect on the quality of life of patients and their families. More than one-third of all deaths are attributed to cardiovascular disease. Other measures of the public health importance of cardiovascular disease are the major burden it imposes on health care personnel, medical institutions and resources. One of the roles of the NHLBI, Division of prevention and Population Sciences (DPPS) is to plan and direct epidemiological studies and projects for disease prevention, and health promotion in heart

diseases. The CHS is one of many ongoing studies that help to fulfill that role and address the public health concerns described above.

The main objectives of the CHS include objectives for long-term follow-up. In a population of men and women aged 65 and older, the CHS is designed to meet the following objectives:

1. To quantify associations between conventional and hypothesized risk factors and coronary heart disease (CHD) and stroke.
2. To assess the associations of non-invasive measures of atherosclerosis, cardiac structure and function, and pulmonary function with the incidence of CHD and stroke.
3. To quantify the associations of risk factors with non-invasive measures of atherosclerosis, cardiac structure and function, and pulmonary function.
4. To characterize the natural history of CHD and stroke, and identify factors associated with clinical course.
5. To describe the prevalence and distributions of risk factors, atherosclerosis, abnormalities of cardiac structure and function and pulmonary function, and CHD and stroke.
6. To identify the risk associations with clinical disease by accumulation of events.
7. To determine whether presence or progression of subclinical disease (abnormalities detected non-invasively without signs or symptoms) are better predictors of clinical disease than traditional risk factors.
8. To identify determinants of change in subclinical disease.
9. To identify characteristics of subgroups at low risk for developing CVD (in whom

preventive measures may be unnecessary).

Long-term follow-up of the CHS cohort is essential to permit adequate estimates of cardiovascular risk utilizing the extensive measurements performed during examinations. The present request for reinstatement of information collection activities through May 31, 2008 will help enable NHLBI to complete the renewal aim of the study: to determine longer-term risk of development and progression of cardiovascular disease in the elderly. Ascertainment of additional incident and recurrent events is needed to increase study power and stabilize risk estimates in key subgroups such as minorities, women, the very elderly, and those with other co-morbid conditions such as diabetes and kidney disease.

This is a request for reinstatement with change of CHS' OMB approval, 0925-0334, which expired 9/30/2007. Contract support for events follow-up and ascertainment efforts ended at most CHS sites in May 2005 but continue via investigator-initiated grant funding. However, contract support for data collection for events at the Pittsburgh field site continued via a no-cost extension of the University of Pittsburgh contract that was scheduled to end on August 31, 2007. In August, the NHLBI and the University of Pittsburgh reviewed the status of funds in that contract and determined that an additional no-cost extension was feasible. A modification was executed on August 15, 2007 to extend the period of contract performance until May 31, 2008, making the University of Pittsburgh the only CHS field site still contracted by the Federal government to collect new events ascertainment. The determination and execution of this contract extension were completed too late to meet the optimal submission schedule for an OMB extension request. The 60-Day Notice was published when it was realized that extending data

collection activities through the no-cost contract extension required continued OMB clearance.

A.2 **Purpose and Use of the Information Collection**

Other prospective epidemiologic studies sponsored by the NHLBI have not focused on discovering associations of etiological importance in cardiovascular disease among exclusively older populations. Some of the risk factors identified (i.e., serum cholesterol and cigarette smoking) have not been as predictive of disease in older persons. This may be a result of these factors losing their associations with cardiovascular disease with increasing age. The ability to study these associations by age or other subgroups such as sex, race, or co-morbidities has been limited by the lack of adequate statistical power to detect differences because the number of cardiovascular events to date in some subgroups has been small. Risk factors for clinical cardiovascular disease in an older population where atherosclerosis and co-morbid conditions are prevalent are being shown to differ from those related to the development of atherosclerosis in younger populations.

This study will continue to provide information on factors that may induce clinically overt disease in the elderly. It will do so by assessing the prediction of clinical disease from traditional and novel cardiovascular disease risk factors and from measures of subclinical disease, such as carotid atherosclerosis measured by ultrasound, left ventricular impairment by echocardiography, cerebrovascular disease by magnetic resonance imaging, peripheral vascular disease by ankle-brachial index, and arrhythmias or episodes of myocardial ischemia by Holter monitoring. It will also test for genetic associations with these outcomes. Since cardiovascular events may occur in the elderly as a result of health or life circumstances which may have

changed in the months preceding the event, the study will contact participants at 6-month intervals to evaluate their status with respect to concurrent diseases and recent hospitalizations. Expansion of the knowledge of the correlates for atherosclerosis and the precipitants of clinical manifestations of cardiovascular disease would make possible longer, more functional and active lives for the elderly.

The primary purpose of CHS is to conduct sound research to meet its stated objectives and to disseminate results to the scientific community. Preliminary data from the baseline examination became available in September 1990 for initial cross-sectional analyses of prevalence and correlates. Currently, data on eleven years of follow-up are available for analysis. A total of 511 manuscripts has been published to date, which indicates the actual use NHLBI has made of the information received from the current collection. Attachment 1 includes a list of CHS manuscripts published since the last OMB revision request in 2004.

CHS incidence and prevalence data have also been used to plan new NHLBI initiatives, such as the Cholesterol Reduction in Seniors Project (CRISP [CE 90-5-02]), the Clinical Trial of Coronary Disease Prevention in High-Risk Hypertensives (CE 94-10-01), the Family and Genetic Studies of Cardiovascular Disease (0925-0399, expiration 01/31/96), the Evaluation of Prevention and Treatment Strategies in Peripheral Arterial Disease (CE 93-07-03), the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (CE 93-11-01), the Multi-Ethnic Study of Atherosclerosis (CE-99-11-08), and the Hispanic Community Health Study – Study of Latinos (submitted 09/30/2007 for OMB review). As new factors are identified, NHLBI brings this knowledge to the attention of the health profession and the public

by making recommendations and disseminating information by publication of results in appropriate scientific journals (e.g., New England Journal of Medicine, American Journal of Epidemiology, Stroke, Circulation) and by presentation at scientific meetings (e.g., American Heart Association, Council on Cardiovascular Epidemiology, American Public Health Association). After full scientific evaluation, results will be presented as policy recommendations by the NHLBI using public education and prevention programs.

A.3 **Use of Information Technology and Burden Reduction**

CHS will continue to use state-of-the-art data entry and management systems that maximize data accuracy and minimize respondent burden. Trained interviewers obtain information from the respondent and enter this information directly into the computer. This computer assistance rapidly directs the interviewer to the relevant sections of the interview for the particular respondent and provides for very rapid interviewer action, thus lessening the respondent burden. This system has been very successful in the preceding years of CHS, and it will continue to be used when telephoning the respondent for the follow-up interviews.

A.4 **Efforts to Identify Duplication and Use of Similar Information**

CHS contains many features that are not present in other epidemiologic studies; thus, CHS does not duplicate other research efforts. The focus of CHS is on the precipitants of clinical cardiovascular diseases in an elderly population. Other NHLBI-sponsored cohort studies have complementary but different aims, including measuring associations of established and suspected risk factors with the development of atherosclerosis and onset of cardiovascular disease in middle-aged populations (Atherosclerosis Risk in Communities (ARIC) [0925-0281, expiration

05/31/2010]) , studying the evolution and distribution of CVD risk factors in young adult populations (Coronary Artery Risk Development in Young Adults (CARDIA), CE 94-10-01), or identifying characteristics of subclinical cardiovascular disease and risk factors that predict its progression (Multi-Ethnic Study of Atherosclerosis (MESA), CE-99-11-08); other studies are not broadly geographically representative (The Framingham Study [0925-0216, expiration 12/31/2007]; The Jackson Heart Study, CE 99-11-09). The only other prospective, multicenter, population-based study of the elderly to date, the Established Population for Epidemiologic Studies of the Elderly (EPESE) [0925-0147, -0149, -0150, expired 08/31/83], sponsored by the National Institute on Aging (NIA), was designed "...to identify predictors of mortality, hospitalization, and placement in long-term care facilities and to study risk factors for chronic diseases and for disability in the elderly."[1] The EPESE was a series of household and telephone interview surveys, with limited physical examination components (urine, blood pressure, physical functioning). It did not utilize the special biomedical technologies (i.e., echocardiography, carotid ultrasonography, cerebral magnetic resonance imaging (MRI), ambulatory ECG monitoring) essential to the study of atherosclerosis and cardiovascular disease that have been used in CHS. Because of the high proportion of expected events, both prevalent and incident, CHS has and will continue to contribute information on the natural history and subsequent disability from CHD and stroke. By utilizing previously collected data, CHS will also continue to investigate the predictive value of preclinical disease using cerebral MRI, carotid ultrasonography, echocardiography, retinal photography, and blood lipids, lipoproteins, coagulation and other factors to investigate their relationships to the development and

1 Cornoni-Huntley et al (eds): Established Populations for Epidemiologic Studies of the Elderly, Resource Data Book, U.S. Department of Health and Human Services, Public Health Service, National Institute of Health, 1986. NIH Publication No. 86-2443, p.1.

progression of clinical cardiovascular disease. The ability to identify genetic polymorphisms related to cardiovascular disease has also opened up new opportunities for innovative research using the CHS data.

The unique features of this study (as described above) preclude the use or modification of similar data. CHS has and will continue to collect new information on incidence and recurrence of cardiovascular disease in a diverse elderly population. This information will further our understanding of cardiovascular disease in the elderly, and will be used to develop cardiovascular disease prevention strategies.

A.5 **Impact on Small Businesses or Other Small Entities**

No businesses or other small entities are burdened by this study. Previously, physicians were requested to provide medical information on patients identified by the study as having died or experienced cardiovascular events for which they were not hospitalized. However, events ascertainment procedures have been simplified, and this is no longer being done.

A.6 **Consequences of Collecting the Information Less Frequently**

All annual clinic visits for the CHS cohort have been completed. The only data collection currently in place and requested through May 2008 concerns surveillance for clinical events. Phone calls are made every six months to facilitate participants= memory in recalling events and to make the collection of hospital, physician and proxy data current enough to increase efficiency in answering the questions. Semi-annual contacts with participants are necessary because of the high expected event rate, the complexity of accompanying illness, and the frequent use of medical care. The CHS protocol has proven to be successful based on the

retention rate of participants, greater than 85% overall and 90% at the Pittsburgh field site in particular. These data are presented across study years in Attachment 2.

A.7 **Special Circumstances Relating to the Guidelines of 5 CFR 1320.5**

The protocol designed for the CHS does not include any special circumstances that would cause information collection to be conducted in a manner outside of the guidelines of 5 CFR 1320.5.

A.8 **Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency**

The agency's 60-day notice in the *Federal Register* soliciting comments on the information collection prior to submission to OMB of this revision to the study was published on September 12, 2007, on page 52155. One comment has been received in response to this notice and is attached (Attachment 3).

This project initiative was initially reviewed and recommended for approval by the Clinical Applications and Prevention Advisory Committee to the Division of Epidemiology and Clinical Applications, National Heart, Lung and Blood Institute on February 26, 1992 (Attachment 4). A list of the membership of the committee is attached. A new contract award to support study infrastructural functions to extend from June 1, 2005 until May 31, 2008, with the understanding that morbidity and mortality follow-up would also continue through a variety of funding sources, was approved by a meeting of the NHLBI Advisory Council on October 30, 2003. Most recently, at its June 5, 2007 meeting, the NHLBI Advisory Council approved a renewal of this contract to extend an additional three years, from June 1, 2008 through May 31, 2011. The

relevant Council minutes can be found as Attachment 5.

In addition, the study has in the past actively sought input from the study participants. The Field Centers periodically scheduled seminars into which all participants were invited. At these gatherings, results of the study were presented and participants were asked to comment on their experience with advice for improvements to the study. Two Field Centers (Washington County and Pittsburgh) developed Participant Advisory Boards made up of CHS participants who have met periodically to provide input on the study. In addition, a newsletter was sent out twice yearly to participants, in which comments and questions were solicited. These activities have ceased in recent years as the study cohort has grown older and less able to participate. Current and planned future contacts with participants include only semi-annual telephone calls; however, participants' questions and suggestions will continue to be welcome.

A.9 **Explanation of Any Payment or Gift to Respondents**

CHS does not provide direct payment to participants for taking part in the study. While reimbursement for transportation expenses was done during the period of clinical examinations, this is no longer necessary. Only telephone calls are now used to contact participants.

A.10 **Assurance of Confidentiality Provided to Respondents**

A.10.1 IRB Certification

The CHS contract stipulates that research involving human subjects is subject to an annual review to be submitted each year with a properly completed certification of Institutional Review Board review and approval of the protocol in accordance with 45 CFR 46. A copy of the most

recent certification from the contract relevant to this submission, the University of Pittsburgh, is included in Attachment 6.

The information obtained by the CHS has been established and maintained in computer data files and is also stored in paper record files and is subject to the Privacy Act. This collection of records is included in the records system 09-25-0200, entitled, "Clinical, Basic and Population-based Research Studies of the National Institutes of Health (NIH), HHS/NIH/OD," as published in the *Federal Register*, Vol. 67, No. 187, pp. 60776-60779, September 26, 2002.

All CHS Principal Investigators and their institutions have agreed to comply with the Privacy Act of 1974 as part of their contractual agreement with the NHLBI. The contract stipulates that research involving human subjects cannot be conducted until: (1) the protocol has been approved by NHLBI, (2) written notice of such approval is provided by the Contracting Officer, and (3) each CHS Contractor provides the Contracting Officer with a properly completed certification of Institutional Review Board (IRB) review and approval of the protocol. Each investigator has undergone requisite training on protection of human research participants, as mandated by the NIH (see NIH Guide Notice OD-00-039).

A.10.2 Informed Consent

Each participant has been provided with written assurances that all individual data collected in the study will be kept confidential to the extent provided by the Privacy Act. Each center that has data with personal identifiers will continue to provide file security so that confidential data are not released. The participants were informed at study entry and during informed consent

processes periodically during the study (and continue to be reminded in semi-annual phone calls) that their participation is voluntary and that they are free to withdraw at any time. Verbal consent continues to be collected at telephone calls, and medical records releases continue to be obtained in order to collect information from hospital records. All Field Centers are in compliance with current HIPAA regulations, and the Coordinating Center has been granted a waiver of the Authorization requirement from its institution's IRB.

A.10.3 Data Security

The field centers at Pittsburgh and the three other locations included in their pre-examination packets a statement describing the level of confidentiality. Participants have been advised of the protection that has been instituted by the study centers to assure their privacy. They have been and will continue to be reminded that no participant names, only codes numbers, are used to identify their files. All computerized information is protected by a series of access codes known only to the principal investigator and his/her designated deputy. No data are transmitted or published with participant names. All Field Center staff are trained to keep participants' information confidential, and have been informed of the penalty for breach of confidentiality. Data files are currently transmitted to the Coordinating Center by Internet E-mail. Files that have been transmitted but not yet received by the CHS Coordinating Center can only be accessed via the account to which they have been addressed. Both username and password must be supplied before gaining access.

Only CHS Coordinating Center staff has access to the Coordinating Center's personal computers, thus simplifying security arrangements. Access to IBM PCs is protected by individual unit keys

to prevent tampering or unauthorized access to the units. Use of a Local Area Network (LAN) provides two additional levels of security in the unlikely event of an unauthorized user finding a machine unattended or unlocked. The LAN restricts access to the Database files via passwords, and the Database itself requires a password before files may be opened. No Internet connections to these databases have been made.

In order to promote use of the data collected in CHS, system files in SPSS format have been made available to CHS investigators for use in analyses. Currently, data from baseline through Year 17 are available on the CHS internal homepage on the Internet. The internal CHS homepage requires a user name and password provided to each CHS Principal Investigator for their site. In order to access the CHS data files, an investigator must obtain permission from his/her site PI and then call the CHS Coordinating Center for a second password that is changed weekly.

A.11 **Justification for Sensitive Questions**

While clinic visits are no longer being implemented, telephone interviews continue. These include calls to participants regarding morbid events and to friends or relatives regarding deaths. Staff members at all sites have undergone specialized training, including grief training, to help them understand the special needs of the elderly. These efforts are intended to promote rapport and to make participation in the study a positive experience for the participants, as well as to be sensitive to issues of grief following the death of a loved one.

The Informant Interview will be asked of informants previously designated by the participant to determine the circumstances surrounding the participant's death, but only in those cases where no other information about the death is available. (Note: an informant is defined as a proxy who can discuss a participant's health after he or she is deceased.) This information is critical in determining whether or not a death was due to cardiovascular causes, which is the primary endpoint of the study.

A.12 **Estimates of Hour Burden Including Annualized Hourly Costs**

A.12.1 Respondent Burden

Respondent burden has been calculated utilizing number of projected responses and time per response. The estimate is lower than that reported in the 60-day Notice in that the burden to physicians has been removed. This is because the Physician Questionnaire has been eliminated from the simplified events ascertainment protocol. The revised estimate is presented below:

Estimates of Hour Burden				
Type of Respondents	**Estimated Number of Respondents**	**Estimated Number of Responses per Respondent**	**Average Burden Hours per Response**	**Estimated Total Annual Burden Hours Requested**
Participants	346	1.2	0.5	208
Participant proxies	121	1.2	0.5	73
Total	467	1.2	0.5	281

Event rates and estimated contacts for each type of disease outcome were calculated based on CHS' events surveillance to date.

A.12.2 Annualized Cost to Participants

Annualized Cost to Respondents					
Type of Respondents	**Number of Respondents**	**Frequency of Response**	**Hourly Wage Rate**	**Average Burden Hours per Response**	**Annual Respondent Cost**
Participants	346	1.2	$18.65	0.5	$3,872
Participant proxies	121	1.2	$18.65	0.5	$1,354
	467				$5,225

The annualized cost to the participants and proxies consists only of the cost of their time, for which no remuneration is given. To estimate cost to those agreeing to provide information to the study, wage rates from the 2000 U.S. Census were used.

A.13 **Estimate of Other Total Annual Cost Burden to Respondents or Record Keepers**

There are no additional costs associated with the study. There are no capital, operating, or maintenance costs to report.

A.14 **Annualized Cost to the Federal Government**

The average annualized cost to the U.S. Government for the information collection in CHS at the University of Pittsburgh site is $173 thousand per year. The annualized cost of monitoring the project by the National Heart, Lung, and Blood Institute is estimated at $80 thousand.

A.15 **Explanation for Program Changes or Adjustments**

CHS event surveillance is an ongoing collection of information. The program has been streamlined since the 2004 Supporting Statement submission. As explained in A.1 above, only the Pittsburgh field site will continue to collect new information under a no-cost extension of a CHS contract due to end on May 31, 2008; the estimated number of respondents has been adjusted accordingly. The data collection protocol has also been simplified, such that the Acute Precipitants and Medications questionnaires are no longer being administered in follow-up calls to participants, and physicians are no longer being contacted for information about potential non-hospitalized clinical outcomes. Even so, the advanced age of the study participants and their increasingly complicated hospitalization histories have required an estimated greater time burden for participant and proxy responses. The annualized cost to respondents has been calculated based upon more realistic current hourly wage rate estimates. Average annualized costs to the U.S. government have been adjusted to reflect that only one CHS field site continues to collect data under the contract.

A.16 **Plans for Tabulation and Publication and Project Time Schedule**

To achieve the ultimate goal of determining policy recommendations for cardiovascular disease prevention, the intermediate goal of presenting statistical results to the scientific and health community must be met. CHS has strived to present results by publishing in scientific journals (e.g., New England Journal of Medicine, American Journal of Epidemiology, Stroke, Circulation), by presentation at scientific meetings (e.g., American Heart Association, Council on Cardiovascular Epidemiology, American Public Health Association), and by compilation of special reports and monographs available to the scientific community. CHS has met its goal of

interim communication of study results as documented by the number of scientific manuscripts published to date. To date, a total of 511 manuscripts have been published in peer-reviewed journals, including 202 since the last OMB revision request (Attachment 1). They include analyses of baseline, longitudinal, events, and ancillary study data. In addition, 26 manuscripts have been submitted for publication or are in press, and over 300 other manuscripts are in progress. Over 375 presentations of CHS results to date have also been made at scientific meetings. The time schedule for the entire CHS project has been included as Attachment 7.

A.17 **Reason(s) Display of OMB Expiration Date is Inappropriate**

According to 5 CFR 1320.8(b)(1), the expiration date will be displayed.

A.18 **Exceptions to Certification for Paperwork Reduction Act Submissions**

There are no exceptions to the certification statement identified in Item 19, ACertification for Paperwork Reduction Act Submissions,@ of OMB Form 83-I.