Supporting Statement A for:

THE AGRICULTURAL HEALTH STUDY: A PROSPECTIVE COHORT STUDY OF CANCER AND OTHER DISEASE AMONG MEN AND WOMEN IN AGRICULTURE (NCI)

OMB Control Number: 0925-0406

(Anticipated Date to HHS)
June 30, 2008

Submitted by:

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A. JUSTIFICATION

A.1 Circumstances Making the Collection of Information Necessary

Since the late 19th century when the use of pesticides in the agricultural community was widely introduced, there has been a growing concern about the relationship between pesticide use and specific health outcomes among agricultural health workers. A number of studies have been conducted in the past with inconsistent results and differences in risk estimates due in part to differences in study design, population heterogeneity, problems with exposure assessment methods, and other limitations (Attachment: 1-6). To address some of these limitations, in 1992 the National Cancer Institute (NCI) initiated a 20-year prospective cohort study of approximately 90,000 registered pesticide applicators and their families in North Carolina and Iowa titled "The Agricultural Health Study (AHS)" (Attachment 1: 4; OMB#: 0925-0406/ exp. 11/2005). The National Cancer Institute (NCI) has collaborated with a number of different Institutes and Agencies for this study. NCI is primarily interested in cancer outcomes and determinants of exposure and National Institute of Environmental Health Sciences (NIEHS) is interested in other disease outcomes. Additionally, the Environmental Protection Agency (EPA) and the National Institute for Occupational Safety and Health (NIOSH) provide support for a limited exposure assessment effort.

The long-term prospective study design offers several advantages over retrospective cohort and case-control investigations. Occupational exposures, medical and family history, nutritional habits, and lifestyle factors related to cancer and non-cancer endpoints can be ascertained at a baseline time frame prior to the onset of cancer and other chronic diseases and updated on a periodic basis. Obtaining information on the use of chemicals, work practices, use of protective equipment, exposure to sunlight, diet, and other potential confounders at several

points in time reduces the dependence on recall and minimizes the potential for exposure misclassification. In addition, the information obtained from questionnaires is being linked to environmental and biologic measures that will strengthen the exposure classification. This study also offers the opportunity to evaluate other exposure-related non-cancer outcomes of interest, such as renal, reproductive, developmental, neurological, and immunologic endpoints.

Cohort enrollment began in the two selected study sites, Iowa and North Carolina, in December 1993 and January 1994 respectively (OMB initial approval #0925-0406, exp. 08/1996). Under the protocol of the first five years, the AHS was presented to applicators as they obtained or renewed their pesticide application licenses. The enrollment form gathered information on demographic characteristics, pesticide use, general health and health risk factors, and overall farming characteristics. The applicator was then given or sent additional questionnaires (an applicator questionnaire, a spouse questionnaire, and a female/family health questionnaire) to be completed by the applicator and spouse at home. These questionnaires focused on additional details on pesticide use, other agriculture exposures, work practices that modify exposure, as well as on other activities that may affect either exposure or disease risks (e.g., diet, exercise, alcohol consumption, medical conditions, family history of cancer, other occupations and smoking history). During the first five years 89,658 (1993-1998) respondents or approximately 80% of the target population were enrolled into the study; this includes private applicators, spouses of private applicators, and commercial applicators. This enrollment percentage is among the highest for prospective cohort studies conducted to date in the United States (Attachment 1: 7).

During phase II (1998-2003) of the study (OMB approval #0925-0406, exp. 11/2005), we interviewed 60,728 enrolled cohort members (3,241 had died; 5,735 were diagnosed with cancer;

4,872 migrated out of the state of Iowa and North Carolina, no longer applied pesticides, or left farming) resulting in a 80.1% response rate among eligible cohort members (N=75,810). Cancer incidence and mortality follow-up was completed on all but 650 (<1%) cohort members who were either lost to follow-up or who requested to be dropped from disease follow-up.

The focus of phase III (OMB approval #0925-0406, exp. 11/2008) is to continue to follow the cohort to determine disease incidence and mortality. The cohort continues to be followed through the cancer registries within Iowa and North Carolina, the Social Security Administration database, state vital statistics offices, the National Death Index, and various in-state databases, such as the listing of registered pesticide applicators. Updated information on pesticide and other agricultural exposures, health status, and residential histories will continue to be collected from cohort members in order to enhance information gathered during enrollment and to obtain information on possible pesticide exposures since the phase II interview.

Additionally, biomarkers of early biological effect can also be assessed to a limited degree to provide indicators of potential alteration in DNA function. Evaluation may include assessment of chromosomal aberrations, telomere shortening and epigenetic effects. The correlation of early biological effect and subsequent disease will be assessed. Buccal cells will be collected from approximately 1,000 additional study subjects to enable the later assessment of the effect of inherited polymorphisms and the interaction of environment and genomic predisposition. To date, 35,697 buccal cell collections have been made.

The continuation and completion of the phase III protocol will provide a valuable epidemiologic resource to help prevent cancers in the future by identifying risk factors in the rural/agricultural environment. Because more cases of important cancer outcomes occur in this cohort every year, potential cancer causes can be evaluated with increased statistical power.

Larger numbers of cases also allow for statistical control of confounding factors and more meaningful conclusions about cancer risk, and, for some relatively infrequent cancers, such as the lyphomas and leukemias, greater follow-up time is necessary to make any meaninful observations.

Under Section 411 of the Public Health Service Act (42 USC § 285a-2), the Division of Cancer Epidemiology and Genetics of the NCI is authorized to collect information to generate and test hypotheses concerning environmental and host determinants of cancer. The AHS continues to generate and test hypotheses regarding the association of specific agricultural, occupational, dietary, and other exposures and specific cancers and other chronic disease outcomes. This is a request for continuation so that the follow-up activities for phase III that began in 2005, can be concluded. Specifically, some of the respondents that were requested in the 2005 have not been interviewed and therefore, we are requesting a carry-over of those burden hours.

A.2 Purpose and Use of the Information

The Agricultural Health Study has six major objectives:

1. Identify and quantify cancer risks among men and women, whites, and minorities associated with specific direct pesticide exposures and exposures to other agricultural agents.
2. Evaluate non-cancer health risks associated with exposure to pesticides and other potential agricultural exposures, e.g., neurotoxicity, reproductive hazards, asthma and other respiratory diseases or symptoms, immunological toxicity, kidney disease, birth outcomes, and growth and development among offspring.

3. Evaluate the disease risks among spouses and children of farmers that may arise from 'indirect' contact with agricultural chemicals (e.g., ambient air drifts, pesticide residues on rugs, furniture, and other items, transferring chemicals) and 'nonoccupational' exposures (e.g., applications to pets, in homes, and on gardens).
4. Assess agricultural exposures using periodic interviews and environmental and biological monitoring.
5. Study the relationship between agricultural exposures, the occurrence of biomarkers of exposure, biological effect, and biomarkers of pre-clinical disease and genetic susceptibility factors relevant to carcinogenesis.
6. Identify and quantify cancer and other disease risks associated with dietary exposures and cooking practices and chemicals resulting from the cooking process.

A major benefit of a prospective study is that investigators can collect data on exposure and disease as they occur instead of relying entirely on recalled information. This approach reduces errors associated with recall of events that occurred prior to disease onset and will make scientific conclusions more valid. The phase I enrollment questionnaires (1993-1998; OMB#: 0925-0406/ exp. 8/1996) and phase II telephone interviews (1998-2003; OMB#:0925-0406/ exp.11/2005) administered previously gathered information on demographic characteristics, pesticide use, general health and health risk factors, diet, buccal cell samples, overall farming characteristics, other agriculture exposures, work practices that modify exposure, as well as on other activities that may affect either exposure or disease risks (e.g., diet, exercise, alcohol consumption, medical conditions, family history of cancer, other occupations and smoking

history). Investigators are currently comparing the number of cancer cases expected to the number that are actually identified through linkages with state cancer registries. They are also comparing disease risks in individuals exposed to specific occupational or environmental exposures to risks in unexposed individuals.

Data obtained from the study are being analyzed using standard procedures for cohort studies. Poisson and logistic regression will continue to be used to evaluate cancer risks from agriculture and other exposures using the EPICURE, STATA and SAS package of statistical programs. Data will be cross-classified by age, race, and sex, but analyses by race/sex specific groups will also be performed. Adjustments for confounding factors (e.g. smoking, alcohol, diet, etc.) will depend upon the exposures and cancers under consideration.

Analysis will proceed from the simple to the complex. The analyses of phase I involved comparing the mortality from various diseases among farmers with the mortality experience of the entire population of the states of Iowa and North Carolina. The disease incidence of individual farmers, their spouses, and commercial pesticide applicators compare the incidence rates among exposed subjects with rates among unexposed subjects. The objective of these detailed analyses is to evaluate the data with respect to the relationship between cancer risk and level, frequency and duration of exposure to specific chemicals. Currently, the analyses of phase I has been completed and is being replicated with the phase II data. The goal will be to replicate findings from the phase I data collection, when the combined data of phase I and II are analyzed. Below is an example of a sequential series of analysis for a selected cancer(s) and pesticide exposure(s).

1. Ever exposed to pesticides verses never exposed. This will include separate analyses of farmers (both men and women), spouses of farmers who may receive exposure indirectly, and commercial applicators.
2. For persons directly engaged in pesticide application i.e., farmers (both men and women) and commercial applicators, risks will be assessed by specific pesticides used by year of first use, application method, frequency of use, years of use, amount applied, use of protective equipment, frequency of mixing, time spent mixing and applying, use of tractors with and without cabs, and hygienic habits (washing, changing clothes). Continuous variables (e.g., frequency of exposure, amount applied, etc.) will be analyzed with and without categorization. Categories will be used to provide relative risks by limited number of strata and continuous measures provide excess relative risk per unit to exposure. For spouses of farmers who do not engage in direct application of pesticides, analyses will assess risk from handling pesticide contaminated clothing, pesticide drift from nearby fields, transporting pesticides, and household use of pesticides.

The analytic plan for non-cancer outcomes will be similar to that proposed for cancer with the addition of comparisons focusing on prevalence of symptoms and specific conditions at enrollment of the cohort.

Using national data bases such as the National Health and Nutrition Examination Survey (NHANES; OMB #: 0920-0237/exp. 3/2007), the National Survey of Family Growth (NSFG; OMB#: 0920-0315/ exp. 9/2003), and the National Household Interview Survey (NHIS; OMB#: 0920-0214/ exp.12/2007), and data from Centers for Medicare and Medicaid Services (CMS) and the United States Renal Disease System (USRDS; OMB#: 0938-0447/ exp. 1/2007), the prevalence of childhood and adulthood asthma, infertility, arthritis, hypertension, diabetes,

developmental delay, attention deficit disorder, kidney failure, and other conditions can be compared to that in the AHS cohort. The age-, race-, and sex-specific rates for these conditions in the national samples will be compared with the prevalence rates in the entire cohort and in subgroups of the cohort based on exposure to specific pesticides, work practices, and exposure level as defined by constructed exposure scales. In addition, the prevalence rates among "exposed" and "unexposed" subgroups of the cohort can be compared.

Mortality from specific chronic diseases such as kidney and neurologic diseases will be evaluated by calculating expected death rates based on age-, sex-, and race-specific rates in the two states being studied as well as based on rated in the US as a whole. Expected numbers of incident End-Stage Renal Disease (ESRD) cases will be obtained using data from the USRDS which covers the entire United States, and expected numbers based on state-specific incidence rates will be calculated using data from the CMS-funded renal disease networks in North Carolina and Iowa. These databases will also be used to prospectively ascertain cases in the study cohort. Again, the groups under study will range from the entire cohort (or subgroups defined as applicators or farmers) to specific subgroups defined by predetermined exposures scales, exposure to specific exposures, or intensity and duration of exposure.

As with the analysis of cancer outcomes, an attempt will be made to characterize risks by intensity and duration of exposure as well as by ever-exposure to pesticides and other agricultural agents. Data from the questionnaires on known disease risk factors, demographic factors, and information on other occupational demographic factors, and information on other occupational and environmental exposures will be used to adjust risk estimates as warranted. For example, an analysis of risk for chronic kidney disease might take into account history of

hypertension and diabetes, family history of kidney disease, use of analgesic medications, and exposure to solvents as well as age, race, and sex.

To date, we have published over 100 papers detailing study methods and exposure assessment methods (Attachment 1: 8-22), high pesticide exposure events (Attachment 1: 23-27), environmental measures (Attachment 1: 28-32), cancer and other health outcomes (Attachment 1: 33-55), and diet (Attachment 1: 56).

A.3 Use of Improved Information Technology and Burden Reduction

A structured questionnaire, Phase III CATI v.2, will be administered to all respondents by telephone using interviewers trained for this purpose (Attachment 2). Prior to administering the questionnaire, the respondent will be screened to ensure that the interviewer has contacted the correct respondent, and to gain verbal informed consent (Attachment 3A or 3B, depending on whether it is the Iowa or North Carolina Field Station). This initial screening and questionnaire will take, on average, 35 minutes to complete, including the additional request for buccal cells from a selected number of participants (N=1,000) (Attachment 4A or 4B). Computer-Assisted Telephone Interview (CATI) techniques will be employed. The interviews will be conducted at a time that is convenient to the subject. Every effort has been made to minimize the length of the questionnaire, and to format it in a manner that optimizes clarity and minimizes the burden on the respondents.

For the majority of respondents, the total amount of time required for this information collection is equal to 35 minutes**.** We will be asking a subset of participants to provide buccal cell samples in addition to completing the CATI interview. The time required to read and sign the informed consent form, read the sample collection instructions, and collect the sample is, on

average, 25 minutes. So for 1,000 participants, the time required for this information collection is equal to 60 minutes.

A Privacy Impact Assessment (PIA) was completed and submitted to NCI's Privacy Act Coordinator in November 2007. A PIA is designed to identify and protect employee and public citizens' personally identifiable information (PII) and it ensures that the government has considered necessary safeguards for the PII passing through or being collected, maintained, or disseminated in the AHS's IT systems. For reference, the name of the IT system used to collect data is titled, "IA Field Station Ag Health Study CATI", and the IT system used to store the data is titled, "IA Field Station Ag Health Study Subject Database".

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

There is no other source of similar information to that which will be collected in this effort. Most epidemiologic studies of farming and pesticides have been conducted, these studies have had many weaknesses. Most relied on rather crude indicators of exposure, such as farming or use of general pesticide classes, while very few have employed comprehensive, quantitative measurements of specific pesticides as we do in the AHS.

Control of confounding by cigarette smoking and other lifestyle factors has been a problem in almost all previous studies. These weaknesses make it difficult to draw reliable conclusions from past studies. Exposure assessment is particularly strengthened by the prospective design of the study and design of the questionnaires.

The investigators for AHS are members of an International Agriculture Consortium (Attachment 5), whose objectives are to determine interest in, and utility of, a consortium of

cohort studies on agricultural populations, characterize ongoing and planned studies, identify areas where pooling would be advantageous, and identify areas for replication of findings.

A.5 Impact on Small Businesses or Other Small Entities

Since this data collection involves farmers it will involve small businesses. Participation of all subjects is entirely voluntary, and scheduling of interviews is at the convenience of the participants to minimize disruption of personal or work time. In addition, we have structured the study so that interviewing of farmers shall be conducted during winter months (the "off-season"), to avoid interference with time required for planting, growing and harvesting.

A.6 Consequences of Collecting the Information Less Frequently

The protocol for phase III questionnaires and collection of buccal cells involves a one-time collection of data for each respondent. The design of the study requires an update on exposures and medical history every five years to minimize exposure misclassification and identify the occurrence of non-cancer endpoints which cannot be obtained by any other existing data system.

The investigators for AHS are not planning on contacting the cohort more that once during phase III. The request for this extension of phase III is so that the remaining applicators and spouses that were not contacted in the past three years of data collection, can be contacted to complete this phase of the study. There are approximately 20,582 respondents remaining to contact. Phase IV of the study is currently being finalized and may involve one additional contact with selected subsets of the cohort.

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

There are no special circumstances that require collection to be conducted in a manner inconsistent with Guidelines in 5 CFR 1320.5.

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

A 60-day Federal Register Notice of proposed data collection was published in the Federal Register on 4/30/2008 in Vol. 73 and Page No. 23473. Comments were solicited on the proposed information collection. No public comments had been received.

The investigators for this study consult with a National Advisory Panel (NAP) annually to get their views on the activities being conducted by the study. The last meeting was held on February 13, 2008. The NAP consists of epidemiologists, toxicologists, farmers, and pesticide educators (Attachment 6).

Additionally, the investigators for AHS are members of an International Agriculture Consortium (Attachment 5), whose objectives are to determine interest in, and utility of, a consortium of cohort studies on agricultural populations, characterize ongoing and planned studies, identify areas where pooling would be advantageous, and identify areas for replication of findings.

A.9 Explanation of Any Payment or Gift to Respondent

Materials to be utilized in the study are provided to the respondent (e.g., a small bottle of mouthwash to be used in the buccal rinse collection) and return postage for any materials to be returned to the Field Station or the Coordinating Center is provided via the use of pre-stamped

Business Return Permits on the return envelopes. We will provide each respondent who returns a buccal cell sample (N=1,000) with $5.00 as compensation for the time spent providing the sample. The $5 compensation is provided as an incentive to the respondent to accurately read and follow the instructions for the buccal cell collection.

A.10 Assurance of Confidentiality Provided to Respondents

Procedures have been developed to protect the confidentiality of the subjects. A Certificate of Confidentiality was obtained prior to onset of data collection, and has been renewed through 2009 (Attachment 7). Though data collection is not anticipated to extend past December 2009, if this does occur a renewed Certificate of Confidentiality will be submitted to OMB by applying for a 83-C, non-substantive change request and attaching the new certificate. The data collection is covered by NIH Privacy Act Systems of Record 09-25-0200, "Clinical, Basic and Population-based Research Studies of the National Institutes of Health (NIH, HHS/NIH/OD" (Attachment 8). In addition, all contractor staff sign a pledge agreeing that all information provided by the respondents will be accorded the highest degree of confidentiality allowable (Attachment 9). Subjects are informed of the measures taken to protect their confidentiality in the introductory letter. Two introductory letters are issued for applicators depending on whether they reside in Iowa (Attachment 10A) or North Carolina (Attachment 10B). A different version of the introductory letter has been developed for spouses of applicators who live in Iowa (Attachment 10C). All letters are sent out on Battelle or Iowa Field Station letterhead. Additionally, respondents are informed again of measures taken to protect their confidentiality prior to beginning the telephone interview. Since the questionnaires will be administered by telephone, informed consent will documented verbally (Attachment 3A or 3B).

An additional verbal consent will be administered for those respondents participating in the buccal cell collection who reside in Iowa (Attachment 4A) and those who reside in North Carolina (Attachment 4B).

Buccal cell specimens collected in phase II (1993-1998) and those collected in phase III will be stored without personal identifiers, in a manner that will permit efficient retrieval and optimum stability for later use. Genetic data resulting from analysis of the buccal cells will not be provided to the Field Stations. The procedure for collecting the buccal cells involves the use of a commercial mouthwash in a manner compatible with normal use of the mouthwash. This procedure causes little or no discomfort and has a minimal possibility of infection. The risks associated with the genetic analysis of these samples are considered to be minimal, as the analysis to be done within the AHS are not of a sensitive nature. Genetic analyses to be performed, address polymorphic normal genetic variants. The risks of disclosure of the genetic information have been minimized through the records handling precautions taken and the removal of personal identifiers from both the interview instrument and the biologic specimens.

Personally identifiable information (PII), such as Social Security Numbers (SSN) are being collected to provide tracing capabilities. Additional procedures to protect security for PII include:

1. All study subjects are assigned an I.D. number at the time of the study enrollment. Personal identifier data are kept by the Field Stations separate from the questionnaire data, which are held at the Coordinating Center. The I.D. number, not the participant name, is used to track participant activities throughout most phases of the study. Verbal permissions is obtained from the participants after they have been read a consent form that states, “The information you provide will

be kept confidential, and will not be disclosed to anyone but the researchers conducting this study, except as otherwise required by law." (Attachment 3A or 3B)

2. The computer data files with identifier information will be available to only a limited number Coordinating Center staff for a limited time. These data will be handled Privacy Act System of Record Notice, 09-25-0200, Clinical Research: Environmental Epidemiologic Studies in the Division of Cancer Epidemiology and Genetics, HHS/NIH/NCI (Attachment 8).
3. Previously collected hard copies of questionnaires that contain any personal information (primarily the female/family health questionnaires and selected follow-up questionnaires) are stored in locked rooms at the Coordinating Center. All personnel involved with the project have signed confidentiality agreements (Attachment 9). A Certificate of Confidentiality was obtained prior to onset of data collection, and has been renewed through 2009 (Attachment 7).
4. After the data are analyzed, personal identifiers will be kept by the Iowa and North Carolina Field Stations if another phase of the study is undertaken, otherwise the data will be destroyed. At the completion of the study, all personal identifiers will be removed from the data.
5. All collaborators allowed access to PII's for other studies are required to sign a confidentiality agreement (Attachment 11) indicating that data and/or PII will not be shared with individuals not covered by the confidentially agreements.

Extensive safeguards are in place to ensure the confidentiality of each subject is protected. Each subject is assigned a six-digit number; these IDs are used for any references to

subjects on an individual basis. Names and other identifying information are kept in separate databases maintained by the Field Stations. These data files are joined only for performing linkages to the mortality and cancer incidence databases. Contact of subjects occurs only through the Field Stations. Several layers of passwords exist to ensure unauthorized access to the electronically stored data is not permitted. Hard copies of questionnaires from phase I that contain any personal information (primarily the female/family health questionnaires and selected follow-up questionnaires) are stored in locked rooms at the Coordinating Center. All personnel involved with the project have signed confidentiality agreements.

Since the last IRB approval no participants have elected to withdraw from the Agricultural Health Study. Such requests are honored without question. There has been no indication of personal harm or injury to any of the participants in the study. Usually the request to discontinue participation is made due to a participant leaving agricultural employment and losing interest in participating in the study.

The original concept for the AHS was approved by the Board of Scientific Counselors of the Division of Cancer Etiology in March 1992. The questionnaires from which the follow-up questionnaires were developed were approved by the Epidemiology and Biostatistics Program for Technical Evaluation of Questionnaires (TEQ) on January 14, 1992. Phase II questionnaires received TEQ approval on May 14, 1998. Phase III questionnaires received TEQ review at the November, 2004 meeting. All comments and suggestions which came out of the TEQ review were incorporated into the questionnaire.

The protocol for the administration of the phase II questionnaires received initial NCI IRB approval on June 9, 1998. All materials for this proposed information collection (i.e., questionnaire, contact letters, telephone scripts) have been approved by the IRBs representing the

National Cancer Institute (Attachment 12A); Westat, Inc., the Coordinating Center for the study, (Attachment 12B); the University of Iowa; and Battelle Centers for Excellence in Public Health Research and Evaluation, Inc. Iowa Field Station initial IRB approval was received on March 13, 1998 and subsequent approvals every year through 2008 (Attachment 12C). The North Carolina IRB initial approval was received on September 18, 1997 and subsequent approvals every year through 2008 (Attachment 12D). Initial approval from Westat IRB required for processing of death certificates from the cohort was received on December 8, 1997 and subsequent approvals every year through 2008 (Attachment 12B).

A PIA was completed and submitted to NCI's Privacy Act Coordinator in November 2007. For reference, the name of the IT system used to collect data is titled, "IA Field Station Ag Health Study CATI", and the IT system used to store the data is titled, "IA Field Station Ag Health Study Subject Database".

A.11 Justification for Sensitive Questions

Most questions asked during phase III (2005-2008) are typically not considered sensitive. Questions include those on the handling of pesticides, fertilizers, farm operations, occupations other than farming, and source of drinking water since enrollment and medical history. Information on these factors has been collected in phase I and phase II and is now being updated in phase III.

Some questions, such as those about alcohol consumption, medical history, and reproductive health may seem sensitive to some respondents. However, these are important factors to evaluate as possible confounders, especially for breast cancer among women, lung cancer and oral cancer among men and women, reproductive difficulties and other chronic

diseases. These represent questions that are common to health studies. Verbal consent is obtained prior to the start of the interview. Respondents are informed that their responses will be kept confidential and they have the right to skip any questions even if they consent to the interview as a whole.

Personally identifiable information (PII) was collected in the form of SSN. Participant's SSN were collected in phase I and phase II and since all SSN are now known it will not be necessary to ask for this information again. Social Security Numbers are used for tracking vital status, cause of death, and cancer incidence in both states and the incidence of birth defects in Iowa utilizing registries. Participants were advised that SSN was requested to enable checking of health records, that disclosure is voluntary, and refusing to give the SSN will in no way affect any rights, privileges, or benefits the respondent or their family may have now or in the future.

Individuals who were enrolled into the study but who are not longer at the address given during enrollment (based on subsequent attempts at followup) have been submitted and will continue to be submitted (through NIOSH) in the standard format to the IRS under their Project 057 Taxpayer Address Request Program. Identifying data provided to the IRS include only SSN and the first four letters of the last name of the cohort member. IRS provides in return the most current address in IRS records if a match (SSN + all four letters of the last name) are found. The purpose of this effort is to identify members of the cohort who have moved out of state, to enable adjustment of person-years for incidence and mortality calculations. Persons who have moved out of state can be followed for vital status and cause of death, but not for cancer incidence.

A.12 Estimates of Annualized Burden Hours and Costs

The estimated annualized burden for phase III of the Agricultural Health Study is estimated to be 4,140 hours (see Table A.12-1). This amounts to a total of 12,420 hours over a three-year period. Based on a median hourly wage rate of $26.48, the total cost to participants will be approximately $328,895, which corresponds to an annualized average cost of $109,632 (Table A.12-2). The figures represent respondents that were not interviewed, burden hours that were not used, and costs that were not spent during the 2005-2008 data collection period.

Table A.12-1 Estimates of Annual Burden Hours

Type of Respondent	Instrument	Estimated Number of Respondents	Frequency of Response	Average Time Per Response (Minutes/Hour)	Annual Burden Hours
Private Applicators	Interview Only	2,920	1.00	35/60	1,703.33
	Interview & buccal cells	83	1.00	60/60	83.00
Spouses	Interview Only	2,680	1.00	35/60	1,563.33
	Interview & buccal cells	165	1.00	60/60	165.00
Commercial Applicators	Interview Only	930	1.00	35/60	542.50
	Interview & buccal cells	83	1.00	60/60	83.00
Totals		6,861			4,140.16

Table A.12-2 Annualized Cost to Respondents						
Type of Respondent	**Instrument**	**Estimated Number of Respondents**	**Frequency of Response**	**Average Time Per Response (Minutes/Hour)**	**Hourly Wage Rate**	**Respondent Cost**
Private Applicators	Interview Only	2,920	1.00	35/60	$26.48	$45,104.26
	Interview & buccal cells	83	1.00	60/60	$26.48	$2,197.84
Spouses	Interview Only	2,680	1.00	35/60	$26.48	$41,397.06
	Interview & buccal cells	165	1.00	60/60	$26.48	$4,369.20
Commercial Applicators	Interview Only	930	1.00	35/60	$26.48	$14,365.40
	Interview & buccal cells	83	1.00	60/60	$26.48	$2,197.84
Totals		6,861				$109,631.60

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

There are no capital costs, operating costs or maintenance costs to report.

A.14 Annualized Costs to the Federal Government

The total projected cost to the Federal Government to complete phase III for the Agricultural Health Study is $1,348,000 and the annualized cost is $449,333 over the three-year period (see Table A.14-1). This includes contract costs for Coordinating Center (Westat, Inc.), the University of Iowa, and to the Battelle Centers for Excellence in Public Health Research, Inc. Since the funding was delayed resulting in slower than anticipated data collection, a portion of the request made for the 2005 OMB submission was not used.

TABLE A.14-1. ANNUALIZED COSTS TO THE FEDERAL GOVERNMENT			
	Labor Hours	Wage Rate	Total Cost
Coordinating Center (Westat Inc.)	2,222	$30/hour	$66,660
University of Iowa	6,061	$22/hour	$133,342
Battelle Centers for Excellence in Public Health Research, Inc.	3175	$21/hour	$66,675
TOTAL CONTRACTOR COST			$266,677
NCI Staff	1667	$50/hour	$83,350
Other Costs including: Overhead Costs			$66,660
Equipment Costs			$6,660
Telephone List Compilation and Maintenance			$6,660
Editing, Coding, Tabulation and Analyses of Data			$16,660
Publication of Results			$666
Travel of staff to implement/monitor			$2,000
TOTAL ANNUAL COST			$449,333

A.15 Explanation for Program Changes and Adjustments

The phase III collection was scheduled for 3 years (November 2005 through October 2008). As it was stated in the prior submission, it was anticipated that "it may be necessary to extend data collection to a fourth year." The Field Stations have always been aware that conducting CATI interviews of farmers during the planting and harvesting season was potentially burdensome to the study participants, so data collection is suspended during those time periods, which vary from year to year depending on the weather. Budgetary issues created circumstances that made fewer resources available in a timely manner than anticipated for phase III, so questionnaire administration will take additional time rather than the three years required during phase II. Funding for the project was slowed down so it has become necessary to extend the length of time for data collection. Though this request represents respondents that were not interviewed, burden hours that were not used, and costs that were not spent during the 2005-2008 data collection period, a revision to this request is being ask due to a reduction in burden hours

from the previous OMB approval. This request will allow the Agricultural Health Study to complete phase III of its research.

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

Full-scale data collection, cleaning and analyses will be followed by publication in peer-reviewed, scientific journals. Our project time schedule for the completion of phase III is given in Table A.16-1.

TABLE A.16-1. PROJECT SCHEDULE FOR PHASE III

Component	Time after OMB approval
Data collection	1-14 months after approval
Data editing	2-60 months after approval
Data analysis	2-60 months after approval
Publication	2-60 months after approval

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

There are no reasons to preclude display of the OMB expiration date on the questionnaires.

A.18 Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification statement.