Supporting Statement B for:

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

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Submitted by:

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B.1 Respondent Universe and Sampling Methods

Cohort members considered eligible for contact for the phase III interview include all pesticide applicators who completed the Enrollment Questionnaire (and at least one other data collection form) and all spouses, who are alive, current residents of Iowa or North Carolina, cancer free at the time of the attempted phase III interview and have not yet been contacted during the initial phase III (2005-2008) time period. This is approximately 20,500 study subjects. The respondent universe, interviews conducted to date, and remaining proposed data to be collected are outlined in Table B.1-1. There has been 80% response rates achieved for both phase I and phase II of the study. As of March 3, 2008 the response rate for Phase III was 75% for the Computer Assisted Telephone Interviews (CATI) and a 70% response rate and completion of the buccal cell sampling.

TABLE B.1-1: Target Sample For Completion of Phase III			
	Iowa	North Carolina	Total
Private Applicators Enrolled	**31,877**	**20,518**	**52,395**
Eligible for Phase III	26,075	14,664	40,739
Contacted during 2005-2008	19,619	12,366	31,985
Phase III Private Applicator target population to complete (includes buccal cell sub-set)	6,581	2,423	9,004
Spouses Enrolled	**21,771**	**10,576**	**32,347**
Eligible for Phase III	20,680	9,681	30,361
Contacted during 2005-2008	13,975	8,345	22,320
Phase III Spouse target population to complete (includes buccal cell sub-set)	6,955	1,586	8,541
Commercial Applicators Enrolled	**4,916**	**NA**	**4,916**
Eligible for Phase III	3,037	NA	3,037
Contacted during 2005-2008	0	NA	0
Phase III Commercial Applicator target population to complete (includes buccal cell sub-set)	3,037	NA	3,037
Total Enrolled	58,564	31,094	89,658
Total Phase III target population	49,542	24,345	73,887
Total Phase III Target to complete (includes buccal cell sub-set)	16,573	4,00934	20,582

B.2 Procedures for the Collection of Information

Data collection began in the winter of 2005-2006 and is anticipated to continue through until December 2009. To date, the interim response rate is approximately 73% but we anticipate this will increase once data collection is completed. This request is to complete the remaining phase III interviews and biospecimen collection.

The cohort is divided into three groups; private applicators, spouses of private applicators, and commercial applicators. Each year, private applicators will be targeted for contact in the winter, spouses of private applicators in the summer, and the commercial

applicators in the fall. While private applicators and spouses come from both states, commercial applicators were recruited only in Iowa.

A few weeks prior to initiating telephone contact, each eligible cohort member who has not yet been interviewed (N=20,582) shall be sent an introductory letter describing the study's purpose and sponsors, and the volunteer nature of participation (Attachment 10A, 10B, or 10C). The letter will remind participants of the on-going nature of the AHS, the importance of their continued participation, and describes the planned follow-up call. Interviews shall be conducted by trained interviewers, and will be scheduled for times that are convenient for the respondents. Up to six attempts will be made to contact each respondent, and callbacks will be made at the respondent's request.

Since the interview is conducted over the telephone, a prepared script will be used to introduce the interview and gain verbal consent (Attachment 3A or 3B). At the Iowa field station, quality control is performed by tape recording the telephone interviews, a percentage of which are then reviewed by the interviewer supervisors. The North Carolina field station does not have the capability to record interviews. Instead, supervisors directly listen to a portion of the interviews in order to monitor interviewer performance. These activities (and differences) are acknowledged in the introductory telephone script. The interview is conducted by a trained interviewer at a time that is convenient for the respondent.

After administration of the CATI, selected participants (N=1,000) shall be asked if they would be willing to provide a saliva (e.g. buccal cell) sample (Attachment 4A, 4B, or 4C). The purpose of the buccal cell collection is to collect samples from highly exposed study subjects in order to have enough statistical power to evaluate gene-environment interactions. Participants will be selected based on their cancer status. Those who agree shall be mailed a buccal cell

collection kit which includes a cover letter (Attachment 15A or 15E), informed consent form (Attachment 14A or 14B), instructions for collecting the sample (Attachment 15B or 15F), and questions and answers regarding the buccal cell collection (Attachments 15C,15D or 15G). The collection protocol involves the use of a simple mouth rinse: a kit containing a small bottle of mouthwash and a 15 ml container. Participants will be asked to pour 10 ml of the mouthwash into a cup, rinse the mouth for approximately one minute, expectorate back into the cup, seal it with the enclosed cap, and return the cup using an enclosed shipping mailer that contains an absorbent pad. The shipping mailer will be pre-stamped and addressed for convenience. Each respondent who has not returned the buccal cell sample within 4 weeks of mailing the kit will receive a reminder telephone call (Attachment 16A or 16B).

B.3 Methods to Maximize Response Rates and Deal with Nonresponse

The overall response rate for eligible cohort members using the CATI techniques was 80.1 % in Phase II, and we expect a similar response rate for the completion of Phase III. At least six attempts shall be made to contact each eligible respondent. Changes in telephone numbers will be tracked and an additional six attempts will be made for each new number. Interviewers are trained in refusal conversion techniques. Refusals, no contacts, deceased, etc., will also be tracked.

The CATI tool itself has been programmed for ease of administration and efficiency. Certain information about each respondent will be pre-programmed into the CATI system. So it will be available to the interviewers at the appropriate sections of the interview. The rate of participation by the cohort has been excellent to date and the ongoing AHS has achieved a high

level of acceptance in the agricultural community, which we hope to continue through to the end of data collection in phase III.

To date, approximately 35,697 participants have supplied buccal cells. As had been done previously each eligible respondent who returns a buccal cell sample shall receive $5.00 as reimbursement for the time spent providing the sample. This provides an incentive and maximizes the response rates. An additional 1,000 participants during the extension of Phase III of the study will be selected to participate in the buccal cell collection. The participants targeted for the buccal cell collection will be those found to have selected cancers such as prostate cancer and non-Hodgkin lymphoma. In order for us to adequately examine gene-environment interactions in relationship to these selected cancers, we need to collect a relatively larger number of samples. To ensure compliance and take into account mishaps with the buccal cell collection, there are a number of additional scripts and letters that have been developed by the Iowa Field Station. The scripts include a script in which the buccal cell kit arrived without a signed consent form (Attachment 17A) and a script to re-contact those in which the buccal cells were either missing or arrived damaged (Attachment 18A). The additional letters include a pre-telephone letter for those who have been chosen to participate in the buccal cell collection (Attachment 13A for respondents with prostate cancer, and Attachment 13C for respondents with NHL), a cover letter and buccal cell kit for respondents who have been chosen but who have language difficulties and will not be contacted initially by telephone (Attachment 13B for respondents with prostate cancer, and Attachment 13D for respondents with NHL), a re-mailed consent form cover letter (Attachment 17B), and a re-mailed buccal cell kit cover letter (Attachment 18B).

B.4 Test of Procedures or Methods to be Undertaken

Phase II CATI methods, which proved to be very successful, will be employed again to complete data collection of phase III in the AHS. In order to test the phase III interview design and timing, pilot interviews were conducted with the following categories of respondents:

- 9 private applicators in North Carolina (active farmers)
- 9 private applicators in Iowa (active farmers)
- 9 spouses of private applicators in North Carolina
- 9 spouses of private applicators in Iowa
- 9 commercial applicators in Iowa

We tested 9 subjects from each respondent category, using a different questionnaire tailored for each type of respondent. As in the main study, each potential participant received an advance letter prior to initiating telephone contact. For efficiency and ease of administration, one version of the phase III questionnaire was developed for use with all respondent types on the basis of skip patterns. For example, of the type of respondent is a commercial applicator, the CATI program would skip questions about farming practices. To ensure that these skip patterns worked as programmed, we piloted the interview within each category of respondent type, and within each state. Results of the pilot study validated our questionnaire design and timing of administration, with an average of 35 minutes per interview, including initial screening. However, for ease of administration and data processing, we have combined each version of the questionnaire into a single document, inserting skip patterns into the CATI program, to differentiate the correct pattern of questions for each respondent type.

B.5 Individuals Consulted on Statistical Aspects and Individuals Collecting and/or Analyzing Data

The Biostatistics Branch of the NCI Division of Cancer Epidemiology and Genetics has a staff of biostatisticians who are experts in this type of study. Dr. Jay Lubin, Senior Investigator, (301/496-3356), a member of this branch, is a study investigator.

The Field Stations in Iowa and North Carolina will be responsible for data collection activities under this protocol:

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Iowa City, IA
(319/335-9633)
Charles Lynch, MD, Ph.D., Director

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Charles Knott, MPA, Director

The National Cancer Institute is responsible for overall study management and coordination and the analysis of the cancer endpoint data, and the National Institute for Environmental Health Sciences is responsible for analysis of the non-cancer outcomes. Federal scientific investigators conducting data analysis include:

Michael Alavanja, Senior Investigator, National Cancer Institute, (301/435-4720)
Gabriella Andreotti, Staff Fellow, NCI (301/496-9093)
Donna Baird, Senior Investigator, National Institute of Environmental Health Sciences, (919/541-2786)
Laura Beane-Freeman, Research Fellow, National Cancer Institute, (301/496-9093)
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