Supporting Statement A For:

Resource for the Collection and Evaluation of Human Tissues and Cells from Donors with an Epidemiology Profile (NCI)

November 2010
(Revised from August, 2010 based on OMB's Comments)

Glennwood E. Trivers, Ph.D.

Laboratory of Human Carcinogenesis
Center for Cancer Research
National Cancer Institute

Building 37, Room 3060D
37 Convent Drive
Bethesda, MD 20892-4258

Telephone: 301-496-2094
Fax: 301-496-0497
E-mail: triversg@mail.nih.gov

Table of Contents

LIST OF ATTACHMENTS

A. JUSTIFICATION

A.1 Circumstances Making the Collection of Information Necessary

The Public Health Service Act, Title IV, PART C, Subpart 1, Section 410 (42 USC § 285), Section 411 (42 USC § 285a), and Section 412 (42 USC § 285a-1) authorizes the Center for Cancer Research in the National Cancer Institute to conduct and support research programs to study the cause, detection, diagnosis, prevention and treatment of cancer resulting from occupational and environmental exposure to carcinogens, and to collect, identify, analyze and disseminate information on methods for the prevention and early detection of cancer and the identification of individuals with a high risk of developing cancer. The Laboratory of Human Carcinogenesis (established in 1983), a Clinical Laboratory Improvement Amendment certified laboratory with a record of assays designed for clinical application, uses integrative biology and translational research strategies to investigate the molecular epidemiology of human cancer.

The research involves assessment of inter-individual variation and carcinogen metabolism in primary human cells and tissue explant cultures, and immortalized normal epithelial cells to study the molecular mechanisms in carcinogenesis. *In vivo* investigations include the identification of cancer risk biomarkers and markers of disease outcome, using the case-control and case-only models for molecular epidemiology studies and the molecular analysis of human tumors. To acquire these tissues, in the early 1980's we initiated a resource contract for the collection of human tissues and cells from donors with an epidemiological profile **(ATTACHMENT #1).**

This is the second 5 year contract awarded that uses information collection from non-hospitalized, population controls. In the early 1990's OMB approved clearance for this resource that consisted of questionnaires that collected information from "third party" next-of-kin sources of non cancer patients donating tissues at the time of autopsy (OMB Number 0925-0152). During that period the project was considered clinically exempt (by Dr. Frank Balis. M.D., Chairman, Clinical Research Subpanel at NIH) with the exception of the collection of information from third party sources representing autopsied, non-cancer, shock-trauma donors recruited as sources of normal tissues. In 1995, Dr. Charles Mackay (Project Clearance Branch, NIH) determined that OMB clearance was no longer required when the collection of information from the next–of-kin sources for autopsy donors averaged less than 10/year due to the Medical examiner's denial of access to most families in trauma. He confirmed continuation of this exemption in 1998 and in 2001.

In 1996, the Laboratory initiated the currently ongoing programs that 1. collect patient tissues for case-only molecular epidemiology studies (within patient comparisons between malignant and non malignant tissues, using cell culture (*in vitro)* and bio-specimen (*in vivo)* assays and 2. recruit newly diagnosed cancer patients to donate specimens of tumor tissues, blood and urine for prospective epidemiological, case-control studies. The case control studies compare cancer patients and non-cancer normal controls and their specimens to test hypotheses of the environmental and social influences on the molecular mechanisms in human carcinogenesis **(ATTACHMENT #2)**. To pursue case-control studies of the molecular nature of human cancer, the laboratory requires a continuing and reliable source of patients with recently diagnosed cancers. Of

equal importance, we need an efficient and an economical method for recruiting normal, non-hospitalized, population controls. The contract for these resources has been re-competed several times for 3 to 5 year periods and is currently entering the third re-competition for an additional 5-year renewal.

Starting in 1998, the studies began to change from one of a simple multi-organ collection design to what are now case-control studies, involving four investigators instead of one principal investigator. In the period between 1998 and 2005, recruitments of non-cancer hospital patients and normal subjects from the local population were initiated to provide diverse controls with complete profiles. In 2005, another change occurred when autopsy sources were discontinued and we started to predominantly recruit normal, population controls, instead of non-cancer hospital patients. During this period, it was not apparent to the Project Officer and research staff that OMB clearance was needed, because in the past Clinical Exemption has been sufficient for collections from first-party information sources.

The liver pilot study was a pre-cursor study to the Liver Cancer Study **(ATTACHMENT #8)** which occurred in 2008 when it was assumed, wrongly so, that the pilot study did not need OMB clearance. It was not until the completion of the pilot study, revisions of questionnaires, and procedures were finalized when the Project Officer began preparation of the Request for Proposals (RFP) for a new contract to begin in 2010, that Clinical Exemption was sought. When NIH Clinical Exemption was awarded (CE# 2009-09-002) in October, 2009 for the patient population **(ATTACHMENT #4)**, it was clear that OMB Clearance would be needed for the case-control population. However, it was unclear about the limitations of the decision until a

subsequent meeting was arranged in December, 2009 with NIH, Project Clearance Branch. At the December, 2009 meeting, the Project Officer was informed to stop the recruitment of population controls. So from approximately 1998 through 2009, population controls were recruited for multiple studies.

Using patients recently diagnosed with cancer, the Laboratory program currently includes protocols for case-control studies of three of the more important cancers challenging human health: lung, prostate and liver cancer. Pancreatic cancer will be added in the new contract. Each of the case-control studies has been approved by the National Cancer Institute's Internal Review Board (IRB) and those of the contractor's Institutions, University of Maryland, Baltimore Veteran's Administration, and Johns Hopkins University **(ATTACHMENTS #3A-H)**. All data collection procedures and the instruments used for recruiting cancer cases for these studies have been granted Clinical Exemption **(ATTACHMENT #4**). The laboratory requires also non-cancer, normal controls as a comparison for the results obtained in cancer patients to demonstrate, when applicable, that its findings are unique to the diseases.

The patient source is a cohort of middle aged to elderly men and women (40 to 80 years of age) from Baltimore and the surrounding counties. The cohort for the potential volunteers as population controls are made up a database of randomly selected individuals identified from the State of Maryland Motor Vehicle Administration's driver's license database and frequency matched (by age, race. gender, and geographic location) to cancer patients already in the program. The Motor Vehicle Administration tapes are purchased from the State via the contractor (University of Maryland Medical School in Baltimore-UMB) and their prior authorization from the State for use of these

data for medical research. The eleven Counties including Carroll, Howard, Anne Arundel and west in Maryland and the City of Baltimore chosen as the source of the population controls represent the geographic areas in which the cancer patients reside before coming to the participating hospitals.

A.2 Purpose and Use of the Information:

This project collects three forms of data in three phases:

(1) Personal identification and demographic data from the States' Driver's License Database;

(2) Respondents personal information for the completion of three study questionnaires; and

(3) Test results obtained from assays of the respondents' biospecimens to detect and quantify various common and uncommon molecular constituents and conditions.

Phase 1: Personal Information from the States' Drivers' License Database

Demographic data from the drivers' licenses are used to identify and frequency-match potential controls to cancer patients in the studies. Those who qualify as population controls are chosen from the mixed populations found among licensed drivers in the same geographic regions producing the cancer cases and at a distribution level closely similar to that of their presence in the State **(ATTACHMENT #5).** The study cohort of cases, consist of adult and senior men and women, of Caucasian, African American, Hispanic or non Hispanic and Asian members of the public in and around Baltimore MD who possess adequate English speaking and or reading facility to be interviewed and complete the questionnaires.

Phase 2: Respondents personal information for completion of study questionnaires

Participants complete study questionnaires providing histories of their social (alcohol, smoking, etc.), occupational (industrial, chemical exposures, etc.) and health (diseases, medicines, surgeries, etc.) experiences. The Main Data questionnaire (#1: **ATTACHMENT #6**) was originally designed for use with African American and Caucasian men and women who develop lung cancer (Medical histories, alcohol and tobacco histories, reproductive histories, upper respiratory conditions, exposure to industrial chemicals, etc), and is now used also for the general background information of prostate cancer patients. In addition, the Supplemental Data questionnaire (#2: **ATTACHMENT #7)** seeks information specific to prostate cancer (conditions and circumstances or diseases specific for or unique to the male genitalia, the use of condoms during sexual intercourse, masturbation, enlarged prostate, etc.). The prostate study supplemental questionnaire requests additional information specific to hypotheses being investigated in that study: e.g., number of sexual partners, frequency of sexual intercourse, use of prophylactics, numbers and types of sexually transmitted diseases, etc., and is given only to African American and Caucasian men.

Recently, the Data Collection for Liver Cancer Study questionnaire (#3: **ATTACHMENT #8)** was developed to obtain information specific to the study of liver cancer and is given to the same two groups of men and women plus those of Asian descent. Asia is one of the two regions of the world (Africa is the other) where liver cancer is most prevalent (has its highest frequency and mortality). This questionnaire seeks information on exposure to, or practices involving, factors of known or suspected causes of hepatocellular carcinoma of the liver (HCC). For example, exposure to the chemical carcinogen Aflatoxin, the infectious agents hepatitis viruses B and C, inquiries

specific to the lifestyle of Asians such as dietary choices and possible travel in the East, and environmental exposures in Asian societies. Although incidence of HCC is low in this country, it is one of the most prevalent cancers in the world at large, especially in Asia and Africa, and it is now on the rise in this country.

Completed questionnaires provide the personal histories of the controls including socio-economic, nutritional, tobacco, alcohol, and family medical histories including experiences with cancer. They require about 60 minutes and are administered only once per subject. These data are used to construct the environmental, social and occupational profiles of the matching controls for statistical comparisons to cancer patients that determine the common and/or the unique nature of the conditions affecting the health experiences and exposures of the cancer patients; to provide insight into the answer to such questions as the effect of smoking on the risk for lung cancer.

Phase 3: Respondents' biospecimens

One of the important uses of information from this data collection activity is the development of individual and group biological profiles of the controls to compare with those constructed from the cancer patients. Participating controls provide specimens of blood or check cells from a mouthwash collection, serum, plasma, and urine that are tested for molecules and conditions that are believed or have been shown to be associated with the targeted diseases. The questionnaire data and the test results are compiled to test various hypotheses. The resulting environmental and biological data are used by investigators to analyze, interpret and report the success or failure of the differences found between noncancerous controls and cancer patients. Application of questionnaire data and biological assay results from population controls in a comparison to those from

cancer patients tests the validity of various hypotheses underlying ongoing research supported by the resource contract (Currently NO2-RC-2010-00117): salient tests that examine hypotheses designed to determine environmental and molecular contributions to the development and progression of specified cancers in human populations.

As noted, the major use of the data obtained from the questionnaires is the comparison of the personal information with that of the cancer patients. The researchers' formulate specific questions and or hypotheses as to the nature of the molecular entities and mechanisms that contribute to the cancer process. They then detect and measure levels of the hypothesized molecules (genes, messenger RNA, microRNA, polymorphisms, etc) or conditions (tobacco smoking, alcohol consumption, health status, occupational and environmental exposures, etc.) among controls as compared to those of the cancer patients. These are analytically tested for any significant differences and the findings are reported to the scientific community. Based upon the results from this resource contract, to date there have been multiple publications from the studies of lung cancer (the oldest protocol) alone and similar numbers of publications from studies on cancers in other organs **(ATTACHMENT #9)** including cancers of the prostate, breast and colon (the latter two diseases being studied using the case-case method rather than the case-control design, the subject of this application review): publications issued on the analyses performed using the data obtained via the support of this resource contract.

A few examples of the productive contributions of this resource to the mission of the National Cancer Institute included here demonstrate the values inherent in our being allowed to continue the use of the relevant instruments to recruit population controls for this research program.

Selected examples of the questions studied and reports published are as follows:

a. Lung cancer studies: (1) Are childhood exposures to second hand smoke and mannose polymorphisms associated with the risk of developing lung cancer? (2) Do microRNAs (miRs) play a role in lung cancers found in never smokers? (3) Do serum concentrations of cytokines associate with survival in Caucasian and African American lung cancer patients? (4) Are occupation, race, and gender factors that affect lung cancer risk? (5) Are mutations of genes related to cancer development detectable in the plasma of tobacco smokers? **(Publications #1, #4, #5, #7 and 12: ATTACHMENT #9)**

b. Prostate cancer studies: (1) What is the status of miR and messenger RNA regulation in prostate cancer patients? (2) Do expression patterns of genes associate with prostate cancer prognosis; (3) Are there immunological differences between African-American and European-American prostate patients **(Publications #15, #16, and 17: ATTACHMENT #9).**

ATTACHMENT 9 also contains reports from other case-control and case-case studies of several other cancers (colon, esophagus and breast) not currently the subjects of the active recruitment. All these studies help to elucidate the role of the targeted human molecular constituents and the social and environmental exposures as contributors to the human susceptibility to these diseases, their rates of progression and their responses to therapeutic compounds.

A.3 Use of Improved Information Technology and Burden Reduction

In addition to burden reduction resulting from the reduction of the numbers via the sharing of subjects from the pooled control population (see Supporting Statement B, Section B.2 for further explanation), we will also reduce the burden by reducing the time it takes to enroll individual volunteers. At the request of the government in this annual period, the contractor is finalizing the development of procedures and a design for converting paper questionnaires to an electronic completion process **(ATTACHMENT #10)**. Tablet computers and computerized questionnaires (electronic versions on Tablet Computers) **(ATTACHMENT #11)** are currently being field tested to allow touch-screen entries of participant information directly into computerized instruments for subsequent transfer of new data into the expanding control databases. Conversion of the questionnaires to electronic designs, the purchase of the Tablet computers, and the additional training to develop the necessary management skills required an investment of new funding. Conversion from paper to electronic questionnaires provides a potential decrease in both time and cost and an increase in the security of data collection and transfer (the data are immediately housed in a password protected environment). Although the initial period will employ both electronic and paper records to verify the success of the conversion, the plan is to soon produce only an electronic version in the field and routinely print-out a paper copy as a back-up for any special needs in the home site.

The Laboratory research data is stored in accordance with the procedures described in the NIH Systems of Record Notice (SORN) 09-25-0200, “Clinical, Basic and Population-based Research Studies of the National Institutes of Health (NIH),

HHS/NIH/OD" **(ATTACHMENT #12)** in the laboratory's customized research data management system. Information will be kept private to the extent permitted by law. As part of meeting Federal IT and IT security policies, a Privacy Impact Assessment (PIA) was completed and published on July 26, 2010 to the HHS website, http://www.hhs.gov/pia/nih.html. The IT system name is "LHC-CCR-Lab Manager for Human Studies Data." Additionally, a Certification and Accreditation (C&A) is in process and being completed.

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

To our knowledge**,** the questionnaires used in the collection of these data are unique to these investigation subjects and they have not been previously used in this population. While some questions similar in nature may be included in questionnaires in other study populations, these questions either have not been asked in this study cohort previously or are asked again in these questionnaire as a means of updating previous information (e.g., current weight). No other questionnaire or data could provide the information required for the prospective analyses being conducted for this study.

A.5 Impact on Small Businesses or Other Small Entities

No small businesses or other small entities will be involved in this data collection project.

A.6 Consequences of Collecting the Information Less Frequently

This project to recruit and profile population controls represents the efforts to service the needs of prospective studies in three (ultimately four) different types of cancer that have follow-up requirements (therapeutic efficacy and survival) only for the cancer

patients in the studies. Ideally, frequency "matched" population controls are recruited ASAP during and to coincide with the frequency of the recruitment of the cancer cases. The timing proximity of the matching is very important to the relevance of the controls to the matched cases. Therefore a schedule for less frequent (with respect to time in a period as opposed to proportion in a variable) collection of information on the would-be matched controls could prove problematic to the scientific objectives in the attempt at analyzing the study results. The completion of the informational questionnaires and the donation of biological specimens is a one time, single opportunity experience in the research effort.

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

No special circumstances are anticipated.

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

The 60-Day Federal Register notice soliciting comments on this study prior to initial submission to OMB was published on June 16, 2010 (75 FR 34146). One public comment was received on 7/16/2010 from a business informing us that they are able to provide a time-saving "batch processing service" to locate and verify "the most current addresses and phone numbers" of survey respondents. A response was sent on 7/26/2010 to the business which indicated the existence of similar devices and/or procedures in the current design of the project.

The Laboratory of Human Carcinogenesis (LHC) maintains a board of highly accomplished scientists **(ATTACHMENT #13)** recognized as experts in their fields of research, as advisors to the laboratory. These scientists advice and consent through

criticisms and consultations throughout the development and the conduct of the research supported by the contract, meeting periodically with the Principal Investigators and their staff investigators who qualify to use the resource. Additionally, NCI maintains a Board of Scientific Advisors composed of highly accomplished internationally acclaimed scientists also of world renown, well-equipped to advise NCI regarding the overall benefit of this resource and its future direction. Specifically, the NCI advisory board performs an evaluation function for all NCI laboratories, appointing a Site Visit Committee every four years to review and evaluate each laboratory on the design and management of its research program. The LHC Site Visit Committee **(ATTACHMENT #14)** reviewed and recommended the renewal of this resource in September of 2008.

A.9 Explanation of Any Payment or Gift to Respondents

Respondents, who agree to participate, complete the questionnaire and provide the required biological specimens, and receive $50 as a token of appreciation for their participation. Although administering the questionnaires requires about an average of 60 minutes per enrolee, enrolment requires approximately two hours of the participant's time. This would include reading of the introductory letter **(ATTACHMENT #15)**, participating in a telephone screening assessment **(ATTACHMENT #16)**, and completion of the questionnaire **(ATTACHMENT #6, 7, and 8)**. The questionnaires are administered to women who complete the Main Data Collection **(ATTACHMENT #6)**, with the reproductive section, and the Data Collection for the Liver Cancer Study **(ATTACHMENT #8)**. The men (Caucasians and African-Americans) complete the Main Data Questionnaire **(ATTACHMENT #6)**, without the reproductive section, the Supplemental Data for Prostate Cancer Study **(ATTACHMENT #7)**, and the Data

Collection for the Liver Cancer Study **(ATTACHMENT #8)**. If male and not Asian, the respondents will also complete the prostate supplement, a part of which they are required to fill out in private due to the sensitive, sexual nature of some of the questions (if masturbation, what frequency, number of sexual partners, frequency of intercourse per partner, and change in partners and frequency with time). Finally, the respondents contribute blood, buccal cells from a mouthwash collection, and urine. We estimate that this process can take as much as 1½ to 2 hours from the sometimes busy schedules of the younger responders or the relaxed private time of some of the older and not so active, unemployed or retired responders. Due to the nature of the questions and the invasiveness of the biological samples, we believe the $50 token of appreciation is justified.

It is typical for National Cancer Institute protocols where respondents are asked to go above and beyond completing a survey to receive monetary token for the time, energy, and/or expense involved. The Agricultural Health Study (OMB No. 0925-0406) was recently approved by OMB and provides $75 per respondent/per home visit for the completion of the interview and biospecimen collection. Respondents in the NICHD sponsored pilot study for California Health Interview Survey-Cancer Control Module (CHIS-CCM) (OMB No. 0925-0598) are offered $25 to weigh and measure the height of their child. The 24-Hour Dietary Recall Method Comparison Study and NCI Observational Feeding Study (OMB No. 0925-0605) offers respondents $52 and $120 (respectively, depending on which study they participated) for completing questionnaires about what they had eaten, eating meals at the study location, and participating in a dietary-related interview.

A.10 Assurance of Confidentiality Provided to Respondents

Participating hospitals need to have a source of confirmation of the accuracy of information transfer after keying-in the primary data from the completed questionnaires. Moreover, the respondents Social Security Numbers provide an assured method for preventing duplication of enrollment and a method for secure identification in the event it becomes necessary to locate and contact a subject at some point of time after their initial participation, e.g., as indicated in the Privacy Impact Assessment, the need to notify of any substantial change in the original protocol for use and application of the personal information acquired or the test results obtained from their specimens. Even after the completion of the incorporation of data into study datasets and when or before the study results have been analyzed, hard-copy records will be maintained as required by a contractor's local IRB. Updated contact information may have to be added to the collected data in the event a study design change is made to propose new applications of the biospecimen tests results or the participant personal information data. Such a change might require notification of all the affected subjects to allow them informed consent to accept or reject the new applications. At which time his or her data might have to be tagged with the restraints imposed by a participant's instructions to limit their accessibility in the contractor's permanent database. In the laboratory, an individual's study data is identified without personally identifiable information and retrieved by a study/accession number only.

Because the study is ongoing, respondent identifiers have been maintained and a number of controls who have been diagnosed with cancer were removed from the study. Thus, the identity of respondents is kept private to the extent permitted by law and the

responses to the initial study questionnaire are maintained. Control volunteers and their personal data are shared among studies for as long as the quantity of their biological specimens are adequate for a testing series, their information will be maintained for use in future studies (**ATTACHMENT #18**).

The contractor is responsible for storing the identifiers in a secure, password protected, and locked file according to Department of Health and Human Services ADP Systems Security Policy as described in DHHS ADP Systems Manual, Chapters 6-30 and 6-35. At the request of the Project Officer, the data from specified groups of questionnaires will be transferred periodically to a subcontractor at Georgetown University for analyses. A complete description of the procedures the contractor and sub-contractor will use to keep the information private and secure, to the extent permitted by law, for the control participant database is found in the Privacy Impact Assessment and the contractor's Security Plan **(ATTACHMENT #17)**.

The Introduction Letter to the population controls describes the privacy of the data and the fact that the intended purpose of the questions is as control information to be used for ongoing data analyses **(ATTACHMENT #15)**. Participants give consent **(ATTACHMENT #18)** after reading and signing of the form provided before the questionnaires are administered. A NIH Certificate of Confidentiality has been submitted but not yet approved.

In addition to managing the accumulating data in accordance with the assigned Privacy Act System of Records Notice (SORN) 09-25-0200, "Clinical, Basic and Population-based Research Studies of the National Institutes of Health (NIH), HHS/NIH/OD" (Published in the FRN on 9/26/2002, Vol. 67, p. 60776)

(ATTACHMENT #12), all patient information is obtained and managed via HIPPA authorization obtained from each participant in the studies including the controls **(ATTACHMENT #19)**. A statement pledging confidentiality is signed also by all persons hired to serve as a Study Coordinators (recruiters/phlebotomists) to enroll the population controls and all contract staff working with patient and study data. Access to study data is limited to the staff working on the study **(ATTACHMENT #20)**.

All computerized data is maintained in a manner that is consistent with the Department of Health and Human Services ADP Systems Security Policy as described in DHHS ADP Systems Manual, Chapters 6-30 and 6-35. No reports or data files sent to the NIH will contain personal identifiers. The data from this project will be maintained until the completion of the study or until no longer required for the research. Data will be destroyed as required by NIH Manual 1743 - Keeping and Destroying Records, when the laboratory research project terminates or the specimens collected are insufficient to be used for comparison to any additional cases.

The National Cancer Institute's Special Studies Institutional Review Board (IRB) reviewed and approved the Main Questionnaire on July 24, 2007, in accordance with 45 CFR 46. A copy of the IRB approval is found in **ATTACHMENT #3.**

A.11 Justification for Sensitive Questions

When conducting epidemiologic studies, it is important to be able to capture data on medical conditions, medical procedures, health behaviors and physical characteristics. The Prostate Supplemental Questionnaire **(ATTACHMENT #7)** includes sensitive questions related to sexual practices or selected health conditions. All respondents have the right not to answer particular questions without consequence.

Personally identifiable information (PII) is collected in the form of the respondent's name, home addresses, phone numbers, Social Security numbers, DOB, Motor Vehicle ID, race, sex and age. PII will be retained throughout the active three year clearance period and for a minimum of 10 years. The latter procedure is a possible limitation necessity to remain compliant with the requirements of the primary contractor who regulates the destruction of all personal files after a ten year period. The project design supports the use of participant materials and information for as long as the studies are ongoing or the biospecimens are exhausted, whichever comes first.

Social Security Numbers are being collected from patients and population-based controls in our studies to be able to conduct searches of the National Death Index (NDI). Currently, NDI searches are conducted annually to collect information on death and the causes of death, and to specifically find out if the cause of death is related to cancer and specific types of cancer. The collection of this information for controls is used to determine if controls were indeed non-cancer controls at time of recruitment or had occult cancer that developed into the clinical disease in subsequent years. It is a major aim in the studies to identify blood-based markers for risk and disease outcome by analyzing case and control samples. The NDI information is important because it can eliminate possible misclassification of controls, which can have critical importance in assessing the performance of a biomarker.

A.12 Estimates of Annualized Burden Hours and Costs

Table A.12-1 describes the annualized burden hours for these studies involving 3 different questionnaires (the Main questionnaire, the prostate supplement, and the liver supplement), a screener for eligibility, and a refusal questionnaire. It is estimated that

approximately 1700 respondents will complete the screen annually, and of those, 225 respondents will participate in the studies. Some respondents will complete the main questionnaire and liver supplement, and the male respondents will receive the main, liver and prostate questionnaires. The total number of *respondents* in Table A.12-1 more accurately reflects the total number of *responses* to various questionnaires. The annual burden is estimated to be 692 hours which amounts to a total of 2,076 hours over the course of three years.

TABLE A.12 – 1. ESTIMATES OF ANNUAL BURDEN HOURS

Type of Respondents	Survey Instrument	Number of Respondents	Frequency of Response	Average Time per Response (Minutes/Hour)	Annual Burden Hours
Adults (40-79 years old)	Telephone Screener (Attachment 16)	1700	1	10/60 (0.17)	283
	Main Questionnaire (Attachment 6)	225	1	60/60 (1)	225
	Prostate Supplemental Questionnaire (Attachment 7)	125	1	30/60 (0.5)	63
	Liver Supplement (Attachment 8)	225	1	30/60 (0.5)	113
	Refusal Questionnaire Form (Attachment 21)	225	1	2/60 (0.03)	8
Totals		2500			692

Table A.12-2 describes the annualized cost to respondents. The total number of responses (2500) includes those to the screener and those for documenting the refusals (totaling 291 hours), leaving 401 hours annually for those who enroll. At $22.97 per hour (Department of Labor: Mean wage for all occupations in the State), the total estimated annualized cost to all respondents is $15,895 (Table A.12-2) for an average of 1.5 hours ($34.46) per respondent: $6,684.27 for screening plus and the refusals, and $9,210.97 for the enrollees. This amounts to a total cost of $47,686 over the course of three years administration of the instruments developed for these case control studies.

Table A.12 – 2. ANNUALIZED COST TO RESPONDENTS					
Type of Respondents	Survey Instrument	Number of Respondents	Annual Burden Hours	Hourly Wage Rate	Respondent Cost
Adults (40-79 years old)	Telephone Screener (Attachment 16)	1700	283	$22.97	$6,500.51
	Main Questionnaire (Attachment 6)	225	225	$22.97	$5,168.25
	Prostate Supplemental Questionnaire (Attachment 7)	125	63	$22.97	$1,447.11
	Liver Supplement (Attachment 8)	225	113	$22.97	$2,595.61
	Refusal Questionnaire Form (Attachment 21)	225	8	$22.97	$183.76
Totals		2500	692		$15,895.24

*Wage rate found at the Department of Labor website: http://www.bls.gov/bls/blswage.htm

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

The estimated annualized cost to the government for the services of the study over the duration of the one-annual period is $118,510 (Table A.14-1). The capital costs include cost of maintenance and software development for Tablet computers used for in-the-field collection of participant profile data. Operational and maintenance components of the studies include purchasing MVA tapes (~$5,600/year), $50 as a token of appreciation for participants, formatting, printing, and mailing introduction letters and three questionnaires, as well as keying-in, coding, processing and storing the data files. It should be noted that materials and supplies for biospecimen collection are not included in this estimate since this request is for information collection.

A.14 Annualized Cost to the Federal Government

NCI staff time required to participate in planning and design activities, monitoring the study, and in analysis of this data is estimated to average 0.20 FTE for scientific staff over the 12-month study period. These figures correspond to an average annualized cost total of $25,400 over 12 months (Table A.14-1).

Table A.14-1. Annualized costs to the Federal Government

Annualized Capital/Start-up Cost	Amount	Operational/Maintenance and Purchase Components	Amount
Tablet for Questionnaire	$4,950	DMV Tapes	$5,600
		Participant Compensation	$20,360
		Contractor's Personnel Cost	$53,200
		NCI Personnel Costs	$25,400
		Mailing Introduction Letters and Questionnaires	$3,000
		Keying-in, coding, processing, and storing the data	$3,000
		Transportation	$3,000
TOTAL . . .	$4,950	TOTAL …	$113,560

Estimate of Other Total Annual Cost Burden: $118,510

Thus, the average annual cost to the government over a 12-month period is approximately $118,510. Over the course of three years, the total estimated cost to the Federal government is $355.530.

A.15 Explanation for Program Changes or Adjustments

This is an Existing Collection in Use without an OMB Number. OMB Clearance was originally approved (OMB Number 0925-0152) in the early 1990's for collection and

evaluation of human tissues and cells with an epidemiological profile. From 1998 through 2009, population controls were recruited for multiple studies (see Section A.1 for additional history).

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

Table A.16-1 outlines the general project time schedule based on a standard study. However, this resource project collects information and specimens from population controls for major components of the research programs of three different Principal Investigators in one research program that is ongoing and does not have a schedule for completion. The only time-lines are related to the resource's designed objective to obtain controls within a period reasonably proximal to the cases, and securing the consistency of the applicable and relevant environmental conditions. It provides the controls for the case-control studies for the achievement of the laboratory's research program.

This program is on-going and highly productive under the guidance, evaluation and authorization of the Internal Review Board and the Board of Scientific Advisors to the National Cancer Institute. The data collected is efficiently acquired, analyzed, and published ASAP to effectively compete with researchers doing similar studies in other laboratories and institutions world-wide. Specifically, and of paramount importance, is the need for rapid reports of new findings to the relevant public of active scientists and medical practitioners in the fields of cancer research and cancer patient management.

A.16 - 1 Project Time Schedule

Activity	**Time Schedule**
Introduction Letters sent to respondents	Immediately after OMB approval
Telephone/Screen respondents	0.5 -36 months after OMB approval

Field questionnaire and collect biological samples	0.5 -36 months after OMB approval
Completed field work	1 - 36 months after OMB approval
Validation	Continuously after OMB approval
Data Processing and Analysis	1 - 36 months after OMB approval
Report Results	6-36 Months after OMB approval
Estimated Publication Dates	8 - 36 months after OMB approval

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

All instruments will display the OMB expiration date.

A.18 Exceptions to Certification for Paperwork Reduction Act Submissions

No exceptions to the Certification for Paperwork Reduction Act Submissions are requested. The LHC was established 28 years ago with the authorization to study human cancer under the auspices of the directors of the CCR and the NCI.