Supporting Statement B For:

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

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Attachment #25: Description and Results of Pilot test for Prostate Case-Control Study

B. STATISTICAL METHODS

B.1 Respondent Universe and Sampling Methods

Eligible population controls are those who are either white or black; US-born; residents of Baltimore City, adjacent Maryland counties, or the Maryland Eastern Shore; able to speak English well enough to be interviewed; non-institutionalized; and never interviewed as a control for the study. For the upcoming Case Control Study of Liver Cancer, population controls that are self identified as Asian are also eligible as population control matches for the liver cases of that ethnicity.

Population controls are recruited from the same Maryland counties of residence as the cancer cases by screening information obtained from the Department of Motor Vehicles **(ATTACHMENT #5).** Potential participants are randomly selected from the MVA records. The data given to us from the MVA includes the MVA ID, name, street, city, county, state, zip, DOB, race, sex, and age (**ATTACHMENT #23).** The epidemiologist (Dr. Loffredo) randomly selects the needed MVA records using a SAS program that selects individuals from the MVA data set by age, race, and gender in the counties of interest. For example, in a given month we may need to recruit controls from Baltimore County as a comparison group to cases from that county, and the epidemiologist will then select a random group of potential controls from that county, of a given age and race/sex characteristics. Study subjects recruitment and matching are therefore an on-going process, and are adjusted as needed for matching to the cases that are enrolled. Each randomly selected potential participant is then given a study ID number and placed into the Maryland Lung Cancer Study (MLCS) population controls database. The drivers' license data, allows the contractor the time-saving step of matching with potential controls prior to their being

contacted for a decision as to whether or not to participate. The names of the matching control individuals are then put into search-engines (commercial and custom designs) to find their telephone numbers, with which they are contacted for their willingness to participate in our studies.

The current cohort of potential population controls consists of 687,903 licensed drivers (approximately 60% men and 40% women) from the 11 Counties sampled and Baltimore City **(ATTACHMENT #23)**. In an 11 month period of observation, of the 1697 telephone numbers found among drivers matched to cases recently enrolled, 1196 were contacted but only 182 were eligible. Of these, only 137 (11%) volunteered as controls for our studies (**ATACHMENT #24)**. Needless to say, even at this rate, the efficiency is much higher than one could expect from approaching strangers to perform demographic matches and subsequently solicit participation.

Since the beginning of the study we have searched for the telephone numbers of approximately 28,000 potential population controls that were sampled and imported into the study database. We have found the telephone numbers for 66%. Of those who were sent letters to introduce the study **(ATTACHMENT #15)**, and were then called **(ATTACHMENT #22)** for screening **(ATTACHMENT #16)**, 75% have participated, 20% were eligible refusals and 5% are still in the process of being contacted and screened. In the last 10 years we have therefore experienced exceptional response rates to participation and completion of the questionnaire in the population control group. Of those enrolled in the population control group, 98.7% completed the questionnaire.

The current population control group (N= 973) consists of 53% males and 47% females, with 59% report being White and 41% Black. Their overall mean age is (65), compared to the mean of (66) in the lung cancer cases, demonstrating our success in matching.

B.2 Procedures for the Collection of Information

a. Recruitment Procedures.

Using Motor Vehicle Administration records, the contractor's epidemiologist identifies individuals whose demographic data matches those of cancer patients. Once the potential participants are randomly selected, the data manager uses on-line commercial and customized search engines to search for the potential participant's telephone number. Each such subject is then mailed an introductory letter **(ATTACHMENT #15)** explaining the purpose of the study providing information about the confidentiality of their responses, and asking them to participate. After a week or 10 days they are contacted by telephone, given additional information and asked to participate. Each person is called at least three times. At least one call is made to each person during the day, night and weekend if needed. Each time a call is made, it is tracked in the data base in the call tasks tab for each person. An IRB-approved script for the telephone calls is used as a guide to the telephone contacts **(ATTACHMENT #22)**. The main areas discussed in the contact phone call are: a) the purpose of the study; b) screening for eligibility; c) setting up an interview where appropriate; and d) planning transportation and parking fee reimbursement needs. If they refuse they are asked to complete a refusal questionnaire (**ATTACHMENT #21**) to document their reasons for saying no.

If they accept, they are screened **(ATTACHMENT #16)** to determine eligibility (American born, English speaking, no cancer history, etc.) and if eligible, then scheduled for an interview. An interview is scheduled at a location of their choosing, usually in their home. All enrollees are required to read and sign an informed-consent document **(ATTACHMENT #18 for men and women)** prior to the interview to complete the questionnaires.

b. Questionnaire Administration and Biospecimen Collection Methods

As described in Supporting Statement A, Section A.2, the recruitment of population controls involves the use of three instruments for obtaining control information: the main questionnaire (#1, for lung, prostate, and pancreas studies); the supplemental questionnaire (#2, specific to the prostate study); and a second independent questionnaire (#3, specific to the liver study) **(ATTACHMENTS #6-8)**. All male controls, except Asian men, who do not get questionnaire #2, are surveyed using all three questionnaires (without the reproductive section in #1), each administered one time only. All women controls receive questionnaire # 1, with the reproductive section, and questionnaire #3.

In a step that reduces the potential burden by one third to one half, all controls are entered into a pool from which individual controls are assigned to one or more of the three ongoing studies, e.g., male controls, except those of Asian descent, are individually assigned to either of the three studies and frequently to more than one, possibly all three, the lung, prostate and the liver studies. Asian men and women are assigned only to the liver study. Therefore, whereas the lung and liver studies include both African-Americans and European-Americans, the liver study includes all three races, including those of Asian descent. Further, women receive only the basic and the liver questionnaires, but they too go into the pool for assignment to the lung or the liver study or both and soon also the pancreas study. Ultimately, while the liver and the lung studies include men and women subjects, obviously the prostate study accepts men only. After completing the questionnaires, the interviewer-phlebotomist will draw 65ml of blood, have the donors flush orally with 30 ml of mouthwash if no or inadequate amounts of blood is collected, and have them fill a container with a 30-60 ml volume of urine. All fluid specimens are aliquoted into 500 microliter (one half ml) volumes and stored at -80 degrees centigrade.

c. Rationale for Sample Size

The current case control studies of prostate cancer and lung cancer share the same population control group. The upcoming liver study will as well. In all of these disease-specific studies, the case-control design allows us to detect statistically significant differences in the frequency of genotypes between cancer patients and population-based controls, and the questionnaire provides data on relevant covariates of risk such as demographic variables (age, gender, race, and education) and known risk factors (such as tobacco smoking history). Given the study design and goals, we have ensured that the studies will achieve 90% statistical power to detect case-control differences at the 95% confidence level (alpha=0.05). An additional design feature is the stratification of case-control genetic factor associations by gender and race, such that each stratum (e.g. black females) is large enough by itself for us to observe statistically significant case-control differences. Therefore each of these strata has already achieved the recruitment of a minimum 200 cases and 200 controls (in the case of lung cancer) or is in the process of achieving this sample size (in the case of prostate cancer).

The targeted total number of controls in the combined, currently approved protocols for the new 5-year contract is approximately 1125 controls to be shared via multi assignments, men and women combined (225/yr; 113/gender/year). This amounts to approximately 1125 for lung (563 white; 563 black; 563 males; 563 females); 600 for prostate (300 white males; 300 black males); 500 for liver (200 white; 200 black; 100 Asian); and 500 for pancreatic (250 white; 250 black; 250 males; 250 females). The assignment of controls, and like-wise their information and bio-specimen, for the three studies from a pool of the recruited participants simultaneously economizes the efforts in two specify directions: (1) It provides, to the fullest extent possible, sharing of participants and specimens to satisfy the numbers requirements for each of the three,

soon to be four, studies. Instead of approximately 3000 controls in 4 different study populations, a single population of approximately 1125 (225 controls per year) total participants will adequately serve the needs of the 4 studies, reducing the total recruited control population to two thirds to one half of the numbers needed in separate control populations. From the pooled population many of the controls (figuratively: actually their information and biospecimens) are assigned to participate in two or more of the three studies. (2) This design reduces the burden and the cost of obtaining these essential components of the research design. The Study Coordinators (recruiters/phlebotomists) in the field do not have to identify participants for one study or the other, except in the case of the Asian participants for the liver study. Administered all three Questionnaires, after processing, a given Caucasian or African-American male participant can be enrolled in the project and later assigned to the lung, the prostate and the liver studies, serving three studies at a cost equal to that required for one study, significantly reducing the costs. The same applies to female participants. The only controls that will not be shared will be those of Asian descent.

d. Quality Control

The contractor for this study has established and maintained quality control procedures to ensure standardization and a high level of quality of data collection and processing. The contractor monitors performance of the data monitoring activities, especially with regard to response rates and completeness of acquired data. The data is cleaned regularly though data base comparisons and analysis of raw data. Range and consistency checks are built into the data entry and coding system. Weekly conference calls are held between the NCI and the contractor and subcontractors. Regular communication is a part of the built in network of activities to ensure the quality of the data and all procedures completed for the study. Yearly Site visits are held at

the contractor site and are attended by all staff, investigators, subcontractors and NCI staff. Semi-annual and annual reports are provided to NCI. Additional requests for information from NCI are supplied on a regular basis.

B.3 Methods to Maximize Response Rates and Deal with No response

Our experience with the case-control studies of lung and prostate cancers is that potential participants appreciate the initial contact of an introductory letter prior to the telephone contact. We establish good rapport with the potential participants over the telephone by clearly describing what is being asked of each respondent during their participation in the study. We have also found that the contacted subjects appreciate knowing that the University of Maryland, whom many identify positively with as their State university system, is engaged in research on cancer that will help to prevent and control cancer in the future. The interviewers travel to over 80% of the respondents homes to complete the interview and specimen collection to make the enrollment as simple and convenient for the participant as possible (the other 20% come to the study offices to participate). Our experience over the last ten years has demonstrated an overall 75% participation rate in the population control group once we reach the respondent on the telephone, and a nearly 99% completion rate for the questionnaires and donated blood or mouthwash samples.

B.4 Test of Procedures or Methods to be Undertaken

Recruitment of population-based controls for our case-control studies had been ongoing and, until discontinued by order of the NIH (Project Clearance Branch), successfully serving the needs of our clinically exempt studies of the lung, the prostate, recently the liver, and soon to include the pancreas. We had previously conducted procedural tests on the recruitment results for the lung and the prostate **(ATTACHMENT #25)**.

Liver Pilot Study and Procedural Tests:

Specifically, during the 12-month pilot phase for the liver, the goal will be to recruit about 100 patients who either have a diagnosis of Hepatocellular carcinoma (HCC) or have risk factors associated with liver cancer development. Ultimately, we will also start recruiting controls that match the cases in age (5-year intervals), race and gender. We will recruit the cases at the 2 participating hospitals. Here, we offer the soon to be accumulating new results for the liver study as an ernest attempt to evaluate the functional efficiency of recruitment of the liver cases and the accompanying population controls, when approved, using the Main questionnaire, the supplemental questionnaires designed for the prostate and the liver studies.

We will assess the availability of liver cancer patients, Caucasian, African American, and Asian, willing to participate in the study, 2) provide blood or mouthwash specimen, and 3) provide specimens of their tumors. Also included (with OMB approval) would be the assessment of the availability of controls that are individually eligible for the lung, the prostate and the liver cancer study for frequency-matching with the cancer cases by age, race and gender.

The criteria that will be used to determine the success of the pilot will be 1) the accrual of 50 HCC cases, of 100 high risk non-cancer, chronic liver cases, 2) of 100 matched population-based controls, 3) the collection of 150 blood samples, and 4) the collection of 10 fresh-frozen tumor and non-tumorous specimens (20% of 50 cases). If major modifications are required to improve accrual rates or other aspects of the study, then the pilot study will be extended to address these issues. Otherwise, we will start recruiting for the main study at the projected rate of 50 HCC cases, 100 high risk non-cancer cases and 100 controls per year.

B.5 Individuals Consulted on Statistical Aspects and Individuals Collecting

The University of Maryland Medical School at Baltimore is the contractor doing the interviewing for these protocols. Dr. Loffredo and Lenka Goldman have been consulted on the statistical aspects of the design and analyzing the data.

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