DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

National Institutes of Health
National Cancer Institute
Bethesda, Maryland 20892

Date: *November 16, 2010*
(Revised from November 12, 2010 memo to account for changes made to the submission based on teleconference with OMB on November 15, 2010).

To: Office of Management and Budget (OMB)

Through: Seleda Perryman, DHHS Report Clearance Officer
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From: Glenwood E. Trivers, Ph.D.
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Subject: OMB Passbacks Questions and Responses re: "Resource for the Collection and Evaluation of Human Tissues and Cells from Donors with an Epidemiology Profile (NCI)"

This memo will address the questions that OMB outlined in the memo dated November 3, 2010.

1) OMB: SSA, A.11, page 16 need to provide a justification for collecting SSNs. Presuming the justification is that they are needed to link medical records.

In addition to the justification that was stated in SSA, A.10, p. 13-14, we have added text to the SSA that reads:

> "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" (SSA, A.11, p. 18).

2) OMB: SSB, however, raises a few questions about the history of this collection and whether we are in a bootleg situation. On page 7, Section B4, they refer to a study which had been ongoing "until discontinued by order of the OMB." What is this about? In the SSB, several parts are written in the past tense. It sounds like a portion of the collection has already taken place, is that correct?

We recognize that the wording in the SSB is inaccurate, and we have changed the wording to read, "Recruitment of population-based controls for our case-control studies had been ongoing and, until discontinued in October, 2009 by order of the NIH (Project Clearance Branch)…" (SSB, B.4, p. 7).

In terms of the history of this research, OMB Clearance was originally approved (OMB Number 0925-0152) in the early 1990's for our information instruments and procedures to be used for collection and evaluation of human tissues and cells with an epidemiological profile. In 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, as communicated by Ms. Ressa Nichols (NCI PRA Liaison). Confirmed continuation of this exemption in 1998 and in 2001 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.

Starting in 1998, our 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 our team that OMB clearance was needed, because in the past Clinical Exemption has been sufficient for collections from first-party information sources. Throughout this period the project received IRB reviews from all the participating institutions, including the NCI, but there was no mention to the study PI's of a need for OMB clearance. It was not until the completion of the pilot for the liver study and the revisions of questionnaires and procedures were finalized, when we began preparation of the Request for Proposals (RFP) for a new contract to begin in 2010, that Clinical Exemption was sought by contacting Ms. Vivian Horovitch-Kelley in June, 2009.

In June 2009, it was not clear whether this research, which involved both case-controls and population controls, would be fully or partially eligible for Clinical Exemption. To clarify, Marilyn Tuttleman (NIH) held a meeting with Dr. Trivers and, on September 9, 2009, determined that Dr. Trivers should submit an application for NIH Clinical Exemption Request. Dr. Trivers submitted Clinical Exemption request for review on September 15, 2009. Clinical Exemption was approved on October 28, 2009 for only the case-control population (patients) part of the research (Attachment 4 in the submission). The same day, Ms. Tuttleman informed Dr. Trivers that OMB clearance would be needed for the population controls and to stop

collecting information from the controls. So from approximately 1998 through 2009, population controls were recruited for multiple studies. Between November and May, 2010, Dr. Trivers worked on the draft of the OMB submission. In May it was reviewed by NIH and in June the 60-day FRN was published.

This submission was originally submitted as a "New" collection because the Project Officer had discontinued the collection of controls pending OMB approval. However, due to the above history and discussion with OMB during the teleconference call, it was decided to resubmit this collection as an "Existing Collection in Use Without an OMB number." The above history has also been documented in the SSA, A.1, p. 1-3.

3) OMB: SSB also appears to be seeking approval for a liver pilot study that was not discussed in Part A. Please explain the relationship between the two parts of the package.

The liver pilot study was a pre-cursor study to the Liver Cancer Study (mentioned in the SSA, and Attachment 8). It occurred in 2008 when it was assumed, wrongly so, that the pilot study did not need OMB clearance (see our response to #2, above).

At the request of OMB, the paragraph below has been removed from the SSB and the above paragraph inserted in the SSA, Section A.1.

> "The pilot study for the Case Control Study of Liver Cancer was designed and initiated. However, it is proceeding without the component designed for the evaluation of the recruitment of population-based controls. With OMB permission, we could include the test of the procedures for recruitment of the subjects for the liver as a demonstration of their use for population controls related to the conduct of this new study and the entire case-control project."

It might help to know that this project is a five-year contract that services the needs of four different Project Investigators. The Principle Investigator is Dr. Dean Mann and the project provides participants and human specimens for the case control studies of four Laboratory of Human Carcinogenesis (LHC) Principal Investigators: Drs. Curtis Harris, Stefan Ambs, Xin Wang and Perwez Hussain. They study, respectively, cancers of the lung, the prostate, the liver and the pancreas. This OMB submission, and the combined project, allows the PI's to collect and draw from a pool of population-controls that fits their research needs.

4) OMB: With respect to the race/ethnicity question in the screener – the "Other" category must not be read as an option to respondents – it is only to be used for coding if the respondent provides a different response than that associated with the 'approved' categories.

We have modified Attachment 16 (Q. 2) so that the "Other" response does not appear.

5A) OMB: Telephone script and SSA assure confidentiality. Please change to reflect the privacy information included at the beginning of the questionnaires.

A NIH Certificate of Confidentiality was applied for on October 19, 2010. Since we have not yet received the Certificate, we have modified the SSA (p. 10, 15, and 16), the Letter of Introduction (Attachment 15), Consent Forms (Attachment 18), and the Telephone Interview Script (Attachment 22) to read, "This information will be kept private to the extent permitted by law."

OMB questioned whether the SORN needs to be updated once the Certificate of Confidentiality is approved. Vivian Horovitch-Kelley will contact Suzy Milliard, NCI Privacy Act Coordinator, and respond to OMB with the answer to this question.

5B) This document also states that participants will be "paid". Similarly, the term "compensation" is used on page 13 of SSA and in the consent form. Please change these to state that participants will be given $50 as a token of appreciation for their participation. These two issues also apply to the introduction letter.

We have revised the SSA (p. 12, 13, 19), Introduction Letter (Attachment 15), Consent Forms (Attachment 18), and the Telephone Script (Attachment 22) based on your comments.

6) OMB: The data security and confidentiality plan should be about keeping data "secure" instead of "confidential".

Absolutely. We have changed the sentence in the SSA to read:

> "A complete description of the procedures the contractor and sub-contractor will use to keep the information private and secure for the control participant database is found in the Privacy Impact Assessment and the contractor's Security Plan" (SSA, A.10, p. 16).

7) OMB: Not all documents mention the collection of cheek cells. Please be consistent throughout.

We have added the use of mouthwash to collect cheek cells to the following documents:

- SSA (p. 7 and 14),
- SSB (p. 7 and 8),
- Introduction Letter (Attachment 15), and
- Telephone Interview Script (Attachment 22).

NOTE: As a result of a new contract for 2010, the attachments that included the previous contract #NO2-RC57700, have been modified to account for the new contract #NO2-RC-2010-00117.