Supporting Statement B For:

Follow-up of Kidney Cancer Patients from the Central European Multicenter Case-Control Study (CEERCC) (NCI)

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B. COLLECTIONS OF INFORMATION EMPLOYING STATISTICAL METHODS

B.1 Respondent Universe and Sampling Methods

The respondent universe is comprised of the specific population that was diagnosed with Renal Cell Carcinoma (RCC) in the original case-control study that was conducted in each of the 6 study centers. Therefore, to be eligible for the pilot study, or the follow-up survival study of RCC, patients needed to have participated as a histologically confirmed renal cancer case in our previous case-control study entitled Central European Renal Cancer Case-Control Study. From a subgroup of these subjects, we will first conduct a pilot study to determine the feasibility of collecting survival information including 5-year survival status, date of death, cause of death, and date of last follow-up if alive on 220 cases from the six collaborating centers. Information on 50 cases will be obtained from Olomouc and Moscow and 30 cases from the remaining centers (Bucharest, Prague, Brno, Lodz), using a list of cases provided to the centers by the NCI. The feasibility of abstracting additional information including surgical and medical treatment procedures used to treat primary disease, recurrence and progression of primary disease will also be determined. Abstracted information collected and translated into English, in addition to a report describing any obstacles to obtaining information requested will be provided by IARC to the NCI. If we can obtain information from 80% of cases in the feasibility study we will proceed with the full survival study.

For the survival study, we estimate that there will be 658 cases living at 5-years; and 439 cases dead at 5-years. Sample sizes were calculated based on the known number of cases in the original study and expected outcomes for survival and also known outcomes of other factors including, VHL gene mutation status, promoter hypermethylation and gene silencing, and

prevalence of known RCC risk factors such as smoking, BMI, hypertension, sex, and a range of genetic susceptibility allelic prevalences (10, 20, 30%). Sample size calculations are provided in Attachment 8. We are expecting a high participation rate (at least 80%) since all subjects were previous respondents of the case-control study.

B.2 Procedures for the Collection of Information

All subjects that will be contacted for this study were previous participants in the Central European Renal Cancer Case Control Study. The prevalence of covariates such as ethnicity, smoking history, BMI, hypertension, and family history of cancer have already been determined. To obtain information on survival status, treatment, disease recurrence, progression and a limited list of risk factors, forms have been created to abstract/record information from three potential sources. These include 1) vital statistics, 2) patient medical records, and 3) cancer registry information when available. The main method to obtain follow-up information is by linking the patients data obtained in the case-control study with vital statistics, cancer registry files, and medical records through active participation with patients' physicians from the previous study. We will use the information collected from the respondents as a gold standard to the other forms of data.

Before the interview, patients will learn about the study from their physicians during regular follow-up and participation will be requested by the physician. The physician will ask the subject whether they would prefer to be interviewed at home or at the hospital. The script that will be used when we contact the patient in included on page 1 of the attached questionnaire (Attachment 6).

All information collected from each method will be cross checked to determine and confirm the quality and completeness of data collected. After we distinguish the types of follow-up protocols used and procedures followed in each country, we will develop a definition of those cases confirmed to be disease-free using "high-confidence confirmation methods" (i.e. CT, PET scan, laboratory methods, other), from those for whom follow-up was not confirmed, incomplete, or undetermined ("low-confidence confirmation"), so that we will be able stratify by this variable and conduct restricted analyses.

For tobacco use post-diagnosis, interview of the patient [CE-08-05-01], or family interviews (no more than 9 will be interviewed) will be the most probable source of obtaining this information. It may be possible to assess tobacco use after cancer diagnosis through medical charts, but this is not expected to be consistent. The availability of tobacco information will be assessed in the pilot study.

In summary:

(a) Subjects in this study will be selected based on having prior participation in a case-control study conducted in this area.

(b) Subjects will be contacted by physicians during follow-up visits, by phone and by mail.

(c) All subjects enrolled in the previous study will be included; there are no exclusions if subjects met the criteria for cases in the previous case-control study of RCC risk factors conducted in this area.

(d) All discussion of risks and benefit to the subjects is described in the informed consent form which will be presented prior to the interview. The

text will be read as proposed in the introduction of the informed consent document.

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

Data collection procedures are designed to maximize response rates. Training of abstractors and interviewers will facilitate the process of data collection and ensure data quality. Training will be conducted at each center since the linking procedures and records available in each center are expected to be different. The principle investigator of each center will first try to gather a data report from the vital statistic office, cancer registry, and a set of medical records for the first several patients, to demonstrate how to collect the information requested. For interviews, the interviewers will be trained with material available from the original case-control study and as in the case-control study, physicians and trained medical professionals will abstract information from clinical records. For the purpose of this survival study, patients will either refuse to participate or will be lost to follow-up. Since these patients have already participated in our study we expect that participation will be high. However, of greater concern will be the percent of patients lost to follow-up. A patient will be considered lost to follow-up if the patients cannot be reached or tracked by any of the vital statistics records, cancer registry, and medical chart/pathology reports at the hospital, or available contact information. They will be considered lost to follow-up when all possible trails have failed to provide information on their status. We will also try to obtain information about the date last seen through the hospital or potential contacts or family members because this will tell us something about their cancer survivorship for a specific period of time, post treatment. For subjects that refuse to participate at this time, we will ask them to contact their physicians to discuss this project. If subjects still refuse to

participate, we will consider them living and will try to obtain other information we can through passive measures.

B.4 Test of Procedures or Methods to be Undertaken

There are no plans to test procedures or methods in this study.

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

The six study centers will be under contract from IARC and the NCI to serve as study centers and are responsible for data collection and data processing activities. Data will be analyzed by Dr. Lee E. Moore (Epidemiologist/Investigator) at 301-496-6427. Statistical Consultation has and will be provided by Dr. Ruth Pfeiffer (Statistician/Senior Investigator) at 301-594-7832. Additionally, Information Management Services, Inc. is under contract to NCI to provide analytic support.