

## **Attachment 4: Statement of Work**

Independently and not as an agent of the Government, the Contractor shall be required to furnish all the necessary services, qualified personnel, material, equipment, and facilities, not otherwise provided by the Government, as needed to support HREB with the simultaneous management of concurrent, multiple, domestic and international studies. The time line or schedule for support activities will be specified by the NCI Contracting Officer's Representative (COR) (or a designated representative—hereafter referred to only as the NCI COR) based on the study. The scientific design of studies and supervision of ongoing activities are the responsibility of HREB scientific staff. Requirements relating to biologic and environmental samples do not include laboratory analysis of samples; analysis of samples shall not be performed under this contract.

### **1. Initial Transition**

The Contractor shall ensure the orderly, efficient and safe transition from the previous Contractor ( if applicable) of all contract activities and materials within three (3) months of the inception of the contract, such as development and submission of an Initial Transition Plan for COR review and approval, conduct orientation briefings for contract technical and administrative staff, and participate in a one-day contract initiation meeting with the NCI COR, the Contracting Officer, other NCI staff designated by the NCI COR, the Program Director, and Contractor key personnel and if necessary, the incumbent Contractor at NIH.

The Contractor shall ensure that any transitioning of staff on tasks will be performed with minimal impact on support delivery and shall be discussed with the NCI COR requesting the work before such transitioning occurs in cases where it may be expected to negatively affect performance, budget, and/or delivery schedule.

### **2. Study Design**

- a) When necessary, help identify options by which the NCI COR can select unique or special populations for specific studies.
- b) Help identify potential collaborating institutions, organizations, and collaborators. Obtain necessary information to determine effective study resources (e.g., capabilities of collaborating institutions and laboratories, numbers of eligible study subjects, exposure information) and provide such to NCI COR upon request.
- c) Arrange for communications and meetings as needed between the NCI investigators, other NCI contractors, collaborating institutions, and/or agents for those whose cooperation or approval is necessary. Coordinate and attend such meetings, provide required background material, keep minutes of such meetings, and take appropriate actions on recommendations, as applicable.
- d) Coordinate with investigators at the study sites to develop methods as approved by the NCI COR for identifying study subjects who meet the NCI criteria for inclusion in studies and make recommendations on the feasibility of alternative selection and sampling schemes.

- e) Determine the feasibility of performing linkages to a variety of sources to define vital status, cancer status, medical history, census tract residence, etc. Linking should be done using a quality controlled method that has gone through rigorous testing. Linking should be able to handle partial and fuzzy data.
- f) Determine the parties whose cooperation or approval is necessary for implementation of the study (e.g., Federal, state, or local government agencies, including the Department of State; customs officials and other representatives of foreign governments; local institutions such as hospitals, clinics, physicians, private industry, industry associations, labor unions, extramural institutions and collaborators).
- g) Assist in compilation of protocols and completion of forms as may be required for various approvals and clearances to conduct studies, such as the DCEG's Technical Evaluation of Protocol Committee (TEP), the DCEG's Technical Evaluation of Questionnaires Committee (TEQ), Institutional Review Boards, Office of Management and Budget (OMB), Technology Transfer (TT), and Cooperative Research and Development Agreements (CRADAs). Attend meetings of such committees if requested by the NCI COR.
- h) Negotiate and manage all financial and administrative matters related to the collection, processing and storage of data and biologic samples, analysis of biologic samples with the various collaborating centers of other institutions or companies (e.g. developing subcontracts, purchasing supplies and equipment, providing other compensation). In consultation with the NCI COR, establish subcontracts with entities, within the United States and abroad, that are needed to meet study objectives, and assist subcontractors to meet logistical and other study requirements.
- i) Document each step of a study and maintain, in an orderly arrangement, all relevant material, so that any aspect of the study may be reviewed and evaluated by the NCI staff at any point in time. Involved are the following: prepare letters, forms, summaries of meetings, and other documents necessary for the conduct of the study; duplicate study documents when the original sources cannot be retained; maintain a filing system of all materials relevant to the study, cross-referenced in a manner so as to make all of the material easily accessible (these materials shall be maintained under security in accordance with requirements of the Privacy Act as it applies to Contractors); and maintain a log of decisions made during each study that affect the design, conduct, or analysis; each entry shall include a brief explanation and date of the problem, the decision made, and the name of the NCI investigator who authorized the change.

#### Development of Study Materials and Procedures

- a) Prepare, pretest, evaluate, and produce data collection forms (e.g., questionnaire, subject enrollment, medical record abstract, pathology and surgical report, anthropometric measurement recording, coding, follow-up, tracking, biospecimen collection, processing, and shipping forms) with guidance, input and approval from the NCI COR. Provide cost estimates for form development and data entry, comparing costs using different methods, including paper-based or computer-assisted (web-based and/or email-based) methods
- b) When multiple institutions are involved in a multi-center study, compile procedure manuals with the NCI COR approval to assure that the investigation is being conducted in a standardized way at all sites.
- c) Prepare procedure manuals for medical abstractors, coders, interviewers, phlebotomists, nurses, and

other personnel involved in data and specimen collection and management, with the NCI COR approval.

- d) As requested by and with the NCI COR input, prepare training programs and materials for interviewers, abstractors, laboratory personnel, medical abstractors, coders, and other study personnel for study sites.
- e) Provide and train abstractors, telephone screeners, coders, interviewers, tracers, nurses, phlebotomists, laboratory personnel, field supervisors, and others who are involved in studies in the United States and abroad.
- f) Work with clinical experts or study consultants to help train clinical personnel at study sites (including abroad), when necessary.
- g) Prepare manuals with NCI COR input for obtaining, handling, and abstracting medical records, pathology specimens and reports, and death certificates. Review and code these reports or specimens.
- h) Develop or adapt existing schemes of coding with NCI COR approval for categorizing information based on demographic, reproductive, medical, occupational, or other lifestyle factors as well as complex laboratory or genetic data.
- i) Make arrangements for translations and necessary transactions to monitor studies in foreign settings. Translate data collection instruments or manuals into appropriate languages for foreign studies. When requested by the NCI COR, back-translate either a portion of the material or all material into English to assure that the original meaning of the material has not been changed by the translation.
- j) Evaluate existing and/or develop new coding schemes for death certificates and medical and pathology records by appropriate nosologists, pathologists, or clinicians in accordance with criteria provided by the NCI COR.
- k) Given the similarity of activities across studies, design or use systems and approaches that can serve as a “shell” or “template” for future work in order to avoid reinventing such systems for each study or project. Determine data management needs for specific projects and implement an appropriate data management system that allows for use by multiple HREB projects. This system should facilitate the acquisition of required data, provide for quality control and entry of computer-readable forms, help monitor the progress and accuracy of field work and data acquisition, provide for rapid response and summary characteristics of data, and facilitate construction of data files for analysis.
- l) For studies with a heavy clinical component, help identify and order supplies and equipment and make arrangement for delivery to the study sites. For international studies, assist with obtaining customs clearance, as needed.

### **3. Study Conduct**

#### Subject Identification, Selection, and Tracing

- a) Coordinate with investigators at the study sites to implement methods as approved by the NCI COR for identifying study subjects who meet the NCI criteria for inclusion in studies.

- b) Demonstrate that the appropriate institutions have registered their Institutional Review Board (IRB) and maintain an approved Multiple Project Assurance (MPA) or a Federal-side Assurance (FWA) issued by the DHHS Office for Human Research Protections (OHRP).
- c) Based on criteria provided by the NCI COR, use methods to derive appropriate control series for use in case-control studies. This could include a variety of different types of controls, including (but not limited to) those derived from hospitals or clinics, random-digit dialing, area surveys, employer personnel or labor union records, or population rosters. Other techniques may be required. When methods such as random-digit dialing are performed, clear documentation shall be kept so that precise response rates can be determined for all phases of the telephone screening, and so that reasons and demographic characteristics can be summarized for subjects who refuse to participate or who are lost to follow-up.
- d) Acquire appropriate population rosters or files from sources such as motor vehicle departments and Medicare files to identify selected series of potential study subjects. For domestic and international studies, coordinate with local agencies and institutions, such as the census bureaus, to identify an optimal sampling frame or population roster for the selection of study subjects.
- e) Based on criteria provided by the NCI COR, trace study subjects to contact them to determine eligibility, introduce the study, determine their vital status, assess cancer incidence or obtain other information necessary to meet study objectives. For deceased or incapacitated subjects, it may be necessary to locate and interview next-of-kin or other proxy respondents.
- f) Assemble death certificates and records on cancer incidence. Have these certificates and records evaluated and coded by appropriate nosologists, pathologists, and clinicians.
- g) For follow-up of cases in previously conducted or ongoing NCI studies, obtain follow-up information from medical records and mortality databases. Arrange for National Death Index and National Death Index Plus searches for United States study populations and verify that the correct subjects have been matched to the death records. This may require additional follow-up with state vital records departments to obtain hard copies of death certificates. The Contractor shall be responsible for determining details and payment for death certificates.
- h) Monitor subject enrollment and response rates. Identify and suggest methods or systems to improve case ascertainment and subject participation rates, in particular for minority and underserved populations.
- i) With guidance and input from the COR, develop spreadsheet and internal monitoring systems to track the status of subject recruitment. The Contractor shall interact with recruitment sites on a regular basis, including conducting a periodic site visit to aid in monitoring and recruitment and study procedures.
- j) Remove personnel identifiers, create study participant IDs, retain the key, and use a pseudonymized ID for data sharing/analysis as needed.

#### Data Collection

- a) Oversee field activities in the U.S. and abroad that result in the acquisition of data that are identified with appropriate identifiers.

- b) Abstract, scan, photocopy, or obtain electronic copies of records (medical records, cancer treatment records, vital records, employment records, etc.). Maintain quality control over the abstracting or copying process. Verify a sample of abstracts by independent re-abstractation.
- c) Once NCI has obtained the necessary IRB and OMB approvals, interview subjects or surrogates using mail, telephone, computer-assisted, or personal interviews. Tape the interviews if specified. If requested, verify a sample of completed questionnaires by re-interviewing subjects. If verification indicates a problem, develop and implement ways to correct the problem.
- d) Obtain approvals to link data with state cancer registries to ascertain information on development of cancer among study subjects. As requested by the NCI COR, help obtain record linkage data from population-based in-patient and cancer registries in the United States or abroad for analytic studies. Determine ways of standardizing information across cancer registries to enable the pooling of data.
- e) With assistance from NCI COR, develop tracing management systems to generate participation and loss rates for all data collection efforts. With guidance and input from the COR, develop other management systems to describe document control.
- f) Purchase other data, materials, and/or services as requested by the NCI COR.
- g) Obtain all necessary pathology reports or other reports of cancer for study subjects. Provide English translations of selected foreign reports and documentation of pathologic diagnoses, as requested by the NCI COR.
- h) With guidance and input from COR, develop management tracking systems that can be utilized by multiple HREB projects to monitor the incoming flow of data, editing of data, and changing, and/or modifying of data, which can be subsequently summarized into descriptive reports.
- i) Make all necessary arrangements for transfer of data, including electronic transfers, and shipment of other material from (and to) the United States and to (and from) the country in which the work is being done for all international studies supported by this contract.
- j) Validate exposure or disease histories obtained in interviews by obtaining original records. This includes maintaining a management tracking system for the retrieval of such records.
- k) When requested by the NCI COR, obtain necessary scientific/medical expertise to collect data, such as abstracting data from pathology reports. When requested by the NCI COR, the Contractor shall act as a clinical liaison to collect clinical information for various types of studies in a timely fashion.
- l) With guidance and input from the COR, develop internal record-keeping procedures for assessing the progress of data collection, data preparation, and data entry. These record systems may be paper files or computer files.

#### **4. Biological Specimen Collection and Laboratory Aspects Involving Samples**

The Contractor shall perform support activities involving biological specimens and laboratory assays, such as specimen collection, repository monitoring, specimen storage, and specimen shipping.

Provide staff experienced in the arrangement of all aspects of biologic sample collection, handling,

transport, storage, and information processing.

#### Specimen Collection Manuals and Procedures

- a) With guidance and input from NCI COR, prepare procedure manuals for the collection, processing, short-term storage, retrieval, packing, shipping, and tracking of a wide range of biological samples, including (but not limited to) peripheral venous blood, saliva, buccal cells, urine, cervical cells, breast and prostate tissue, breast milk, and other tissue or biological fluids, from consenting study subjects.
- b) Research and provide recommendations for storage vials, labels, containers, and other supplies needed for biospecimens collection and storage as well as for shipment (e.g. mail courier services). When recommending vials/containers for specimen storage and shipment, consider what best maintains the integrity of the specimens, which sizes of storage vials would minimize repository storage costs, and what can be shipped in a timely manner. Coordinate with the NCI biorepository to ensure that storage vials and other containers selected for the study meet their requirements. Coordinate with field investigators and the biorepository to ensure that labels meet their requirements, including bar codes and storage temperature.
- c) Order supplies, prepare labels, and deliver to investigators in the field. These supplies should be selected only after obtaining consent from the NCI COR.
- d) Recommend and implement standard procedures that are adaptable to each site where work is being performed, and utilize standard approaches at all sites where possible in order to minimize sample variation. Document procedures to be followed in field manuals, including quality control procedures.
- e) Develop labeling schema for biospecimens and documentation of the condition of samples with input from COR.
- f) Develop collection and shipment methods to follow appropriate guidelines for biohazardous material and coordination with various laboratories/institutions with input from COR.
- g) Train phlebotomists and others in NCI protocols/procedures for collecting specimens.
- h) Develop management systems for tracking results as they derive from various contracting laboratories for assisting the NCI COR in rapidly evaluating laboratory performance on blinded quality control samples within lab batches and for rapidly communicating these results to the appropriate investigator.
- i) When requested by the NCI COR, the Contractor shall act as a clinical liaison to collect biological samples for various types of studies in a timely fashion.
- j) Provide recommendation on the feasibility of certain molecular approaches in the field, especially for studies abroad.
- k) Help identify hospitals or clinics that are willing to have an ongoing collaboration so that feasibility studies can be implemented readily to expedite the development of a cutting-edge full-scale study to test emerging hypotheses in a timely fashion. This includes obtaining permission to collect a wide range of biological samples from consenting subjects after IRB approval for testing and validation.

- l) With assistance from NCI COR, develop subcontracts with hospitals or clinics to conduct biospecimen collections under standard collection and operating procedures.
- m) As directed by the NCI COR, develop a specimen QC/QA plan, which may include a subcontract to a third party laboratory for periodic specimen testing.
- n) With COR input, develop procedures for anonymization of specimens and accompanying data, including de-linking and removal of personal identifiers, to simplify or eliminate the consenting process (i.e., IRB exemption) where applicable. Steps may include:
  - Re-labeling with NCI's Biospecimen Inventory (BSI) ID.
  - Link the NCI BSI IDs back to the Patient IDs and select records from the patient database for those linked IDs. The selected data records, along with the linked IDs will be sent back to the contractor.
  - The contractor will link BSI IDs to the data records. The Patient IDs will be stripped from the records. The links to the Patient IDs will be destroyed.
  - All of the data of interest (as described) on the file will be categorized. Frequency reports will be produced for each data item. Any category of data with a count less than a specified number (e.g., 10) will be collapsed into adjoining categories until no category contains a count of less than that specified number. This will ensure patients' anonymity by removing any potential unique identifier. The raw data values will be then destroyed to anonymize study subjects.

#### Sample Collection, Processing, and Shipping

- a) After obtaining necessary and appropriate informed consent, obtain biologic specimens (e.g., peripheral venous blood, urine, buccal cell mouth wash samples, saliva, breast milk) from study subjects. Process and divide samples, package them as necessary, and ship, transport or deliver them to a designated biorepository or laboratory(ies). Pertinent data (e.g., personal identifiers, collection date, etc.) concerning the specimen donor and processing procedures shall be collected and accompany every biologic specimen.
- b) Collect and deliver biologic samples to laboratories or individuals for storage and/or analysis. For domestic and international studies, help develop a shipping list and manifests and coordinate with local PIs and study staff for the transport of study samples from the field to the NCI repository. Such shipments require that the Contractor arrange for the following: appropriate government clearances required for transferring biologic specimens; appropriate shipping conditions and containers for perishable specimens; close monitoring of the shipment process so that perishable items arrive at their destination in useable condition within the allotted time frame. For international shipments of samples, help obtain necessary clearances for international shipping, monitor their arrival status and assure that they are appropriately cleared through customs and delivered to the required repository. Perform other general support activities involving collection, storage and/or shipment to laboratories.
- c) Report immediately to the NCI COR all irregularities, delays, losses, deteriorations, unplanned thawing, accidents, mishandlings, errors, discrepancies, and inefficiencies connected with any specimen collection, processing, delivery, storage, or testing activity, as well as keep a computerized record of such problems.

- d) Provide to the NCI COR support activities as specified by the NCI COR and coordinate with any NCI collaborating or contracting laboratories on tasks related to DNA extraction, aliquotting, and re-concentration of samples. Monitor the progress and quality of such activities.
- e) Prepare pathology slides for review by expert pathologists for both data collection and the creation of tissue microarrays. Prepare pathological specimen blocks and slides appropriately, accurately, and securely for shipments. When necessary, transport slides to appropriate collaborating investigators.
- f) Assist the NCI COR in obtaining necessary permissions to collect tumor and adjacent normal samples and other clinical specimens that are no longer needed for patient care as well as collect said specimens for retention and testing at NIH contracting and collaborating laboratories. Pertinent de-identified data related to the specimens and the donor shall be collected and accompany every biologic specimen.
- g) When necessary, provide support necessary to determine the best methods to collect certain biological specimens at the study sites.
- h) Maintain an inventory of specimens sent to laboratories for a wide range of HREB studies that may be a component of a project under this contract. Monitor discrepancies with field reports. Interface, use, and update the BSI NCI biorepository database system, the central biospecimens database of the HREB, to monitor the availability of, and manage the use of, biologic samples stored in NCI biorepositories from a large number of studies with previously collected samples.
- i) With guidance and input from the COR, develop spreadsheet and internal monitoring systems to track the status of specimens. Coordinate to ship specimens back to the NCI repository after the assays have been completed. On a regular basis, as directed by the NCI COR, verify the status of specimens at the repository.

#### Laboratory Assays

- a) Based on criteria set by the NCI COR, coordinate with NCI collaborators and contracting laboratories on a wide range of blood-based assays, including assays for hormones, cytokines, and infectious agents.
- b) For biomarker and molecular marker studies, assist in the selection and retrieval of samples for laboratory assays from the NCI repository and help make arrangement to deliver these samples to the collaborating laboratory.
- c) Monitor the progress of the assay and help obtain all necessary laboratory data and reports in a timely fashion. Generate data related to the QC of the data and process and deliver associated data immediately to the NCI COR. Obtain all necessary laboratory reports and process and deliver them immediately to the NCI COR. Merge laboratory results into primary study databases and carry out initial graphical and statistical analyses as requested.
- d) At the request of the NCI COR, help develop plans to collect or secure quality control (QC) samples to be incorporated into study sample sets for the determination of assay variation. This includes collection of samples from volunteers or purchase of already existing QC samples. For serum markers, this requires identification of volunteers who will consent to donate a large amount of blood (~100 ml) to be combined into sets of quality control pools. For studies involving genotyping, this

requires collection of DNA samples and preparation of multiple identical aliquots from several individuals.

## **5. Data Preparation and Processing**

- a) Provide available information on schemes for coding of medical, occupational, demographic, and genetic coding schemes. With input from COR, develop documentation of codes used and listings of unusual responses.
- b) Code or enter questionnaire responses, medical record data, and clinical and laboratory information into computer-readable form. Verify, by independent recoding, at least a 2% sample of the coding (the size of the sample shall be approved by the NCI COR). Recode as necessary. Summarize and describe differences between the two sets of data.
- c) Design and organize efficient computer systems to record and maintain the data in a manner that facilitates monitoring the progress of the field work, assuring quality control. Verify entry by 100% accurate re-entry. Re-enter as needed. Summarize and describe differences between the two sets of data.
- d) For laboratory data, work with collaborating or contracting laboratory staff to use state-of-the art technology to record or transfer data. When necessary, develop programs for web-based data entry for the lab or for directly downloading the data from the laboratory equipment to the computer.
- e) For data received from collaborators or laboratories, check for readability, completeness and errors, and verify the quality and consistency before making analytic files. Prepare datasets suitable for analyses for transfer to personal computers, as specified by the NCI COR.
- f) Maintain adequate backup of study data and secure storage of back up media. Frequency of backup may vary by specific study, but will be determined by COR. Report verification rates, discrepancy rates, and error rates for data collection, preparation and keying following the schedule agreed upon with the NCI COR. An unusual problem should be brought to the immediate attention of the NCI COR.
- g) Implement, maintain, and update secured network, server, computer databases and associated reporting software. When sharing data the information should be transferred with no link to subject information.
- h) Prepare and edit programs, including range and logic checks of data. Edit the data, and correct the computer files where necessary.
- i) Update the files with newly acquired data, follow-up data, error corrections, etc., as requested by the NCI COR. Maintain a clearly documented history of the development and updating of databases.
- j) Prepare and/or harmonize data sets for transfer to NCI investigators or other collaborators, including consortia, as specified by the NCI COR.
- k) Produce reports and develop analytic files based on collected data as requested by the NCI COR. Produce summary statistics and other analyses as specified by the NCI investigator. These may include simple descriptive statistics, such as frequencies or cross-tabulations, or other analyses. Most epidemiologic analyses will be performed elsewhere, but occasionally the Contractor may be

required to provide such service. For genotyping data and data from analysis of other biospecimens, when necessary, prepare a macro to verify the quality and consistency of the data, including testing for Hardy-Weinberg Equilibrium among controls and scatter plots of data, among other tasks.

- l) Provide cost-efficient methods for the **minimal (if any) storage** of large data files at the NIH/CIT computer facility. Avoid proliferation of datasets during conduct of epidemiologic studies. Develop and implement procedures for closing out studies and archiving data in an organized manner while retaining critical original data, analysis files, and programs.
- m) For laboratory data, after receipt of the data, check for consistency and provide quality control measures, such as the coefficient of variation and intra-class correlation for biomarker data and kappa statistics or percent of concordance for genotyping data, to the NCI COR to monitor the quality of the data. Prepare a summary report about quality control results.
- n) Report verification rates, discrepancy rates, and error rates for data collection, preparation, and keying, following the schedule agreed upon with the NCI COR. Any unusual problems should be brought to the immediate attention of the NCI COR.
- o) Prepare data sets in response to FOIA requests made to the NCI FOIA office, with special attention to protecting privacy and indirect identification of study subjects.

## **6. Final Transition**

In the event a new Contractor is selected for the recompetition of this contract, the current Contractor and the successor Contractor shall work together to carry out the transition activities. The transition of work from the current Contractor to the successor Contractor shall be completed within the last 30 days of the current contract. The current Contractor shall effect a smooth transition of the management and operations of the existing support to the successor Contractor without prolonged interruption of the normal day-today provision of support services. During this period, the current Contractor shall assume full responsibility for all essential activities, especially those that involve maintenance of existing study management. With guidance from the COR, the current Contractor will provide the successor Contractor with detailed briefings regarding the structure of data files, processing systems, and associated software. The schedule for transfer of actual data files, software, hardware, and documentation will proceed upon the request of the NCI COR and Contracting Officer. The current Contractor shall ensure that the data transfer is accurate, complete, and timely. The current Contractor, NCI COR, and key NCI staff will establish a schedule, with appropriate priority assigned to tasks, to accomplish the transition of all other activities.