

STATEMENT OF WORK

Preclinical PREVENT Cancer Program: Preclinical Efficacy and Intermediate Endpoint Biomarkers

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 perform the Statement of Work.

SCOPE

This contract shall support the development of potential cancer preventive agents or vaccines employing detailed preclinical pharmacological studies and determining pharmacodynamic efficacy, pharmacokinetic profile of agents and biomarkers, which parallel the effectiveness of a given agent. The primary endpoint of the efficacy studies shall be to prevent the development of invasive cancers whereas the biomarker studies will identify endpoints which correlate with the effectiveness of a given preventive agent or vaccine. These endpoints might be measured in body fluids, normal or at risk tissue from the target or in histopathologically altered tissue from the target organ(s).

The Contractor shall perform work in these Task Areas 1 and 2 as outlined below and specified in each Task Order.

NOTE TO OFFERORS: Task Orders shall range in duration from 2 years to 3 years. The number of animals required for a Task Order shall range from 350 animals per Task Order to 550 animals per Task Order.

NOTE TO OFFERORS: For proposal purposes Offerors shall assume that each Task Order will involve no more than two (2) compounds and no more than two (2) routes of administration.

A. TASK AREAS

TASK AREA 1 - CHEMOPREVENTIVE EFFICACY EVALUATION OF CHEMOPREVENTIVE AGENTS BY ANIMAL BIOASSAYS

Use of animal models as defined by the National Cancer Institute (NCI) for cancer prevention testing includes, but is not limited to mammary, bladder, lung, skin, esophagus, colon/intestinal tract, prostate, melanoma, trachea/bronchus, head and neck, brain, pancreas, ovary, and hematopoietic systems.

Contractor shall specifically:

1. Breed and maintain animal colonies of wild type rodents and transgenic rodents in sufficient numbers for efficacy testing purposes.
2. Procure the chemopreventive agent (unless provided by NCI).

3. Provide analysis of chemoprevention agents for purity and for homogeneity and stability of agent in administering vehicles.
4. Administer chemopreventive agents by different routes including diet, gavages, topical, inhalation, injection, or pellet implantation.
5. Administer vaccines and adjuvant(s) as required (typically intramuscular or subcutaneous route).
6. Administer carcinogens, promoters, hormones and/or chemopreventive agents to laboratory animals as needed.
7. Investigate different schedules of dosing regimen (such as intermittent or weekly).
8. Conduct studies monitoring tumorigenesis, body weight, and vital signs and appearance.
9. Conduct studies monitoring vaccine-mediated humoral and cellular immune responses.
10. Conduct gross necropsies in animals.
11. Conduct histopathological examination of selected tissues from selected groups in different strains and species of animals used.
12. Collect and preserve tissue, serum, and urine from laboratory animals in the study.
13. Perform formulation, pharmacokinetic study of agents as required.
14. Perform statistical analysis comparing treatment groups with control groups: for example, tumor incidence and tumor multiplicities, etc.
15. Present tumor inhibitor data in tabular or graphic form, as well as tumor incidence data and, where possible, multiplicity and latency data.
16. Collect tissues, plasma/sera or other body fluids, either fixed or frozen and maintain under appropriate storage conditions until utilized.

NOTE TO OFFERORS: The Offerors shall store collected tissues at either 4 degrees or -20 degrees or -80 degrees, according to the instructions of the experimental protocol on the specific Task Order issued. The Offerors shall keep plasma/sera or other body fluids at appropriate storage temperature (4 degrees, -20 degrees or -80 degrees) pursuant to the instruction or specification of the assay. The Offerors shall provide judicious estimation, based on the literature and/or previous validated protocol, on the number of specimens. For purposes of proposal preparation, the maximum number of specimens or tissue samples that require storage under this Task Order is 3,000.

17. Perform chemical analysis of feed or diet concerning preventive agents to be utilized.
18. Ship some or all of these samples with technical documentation to other investigators at the direction of the Task Order Contracting Officer Representative (COR).

TASK AREA 2 - EVALUATION AND VALIDATION OF INTERMEDIATE ENDPOINTS

The Contractor shall conduct intermediate endpoint assays in rodent tissues and perform studies utilizing NCI-supplied, de-identified human samples examining relevant intermediate endpoints. The relevant tissues shall be supplied to the Contractor unless otherwise specified in the Task Order. Intermediate endpoints that shall be examined include but are not limited to:

1. Genomic, proteomic and metabolomic assays performed on, but not limited to, relevant tissues, serum or urine.
2. Quantitative levels of specific genes or proteins (e.g. RT-PCR, quantitative IHC, Western

- Blotting) which are understood to be involved in the molecular mechanism of a given agent.
3. Pharmacokinetic endpoints directly related to the preventive agent e.g. levels of the parent compound or metabolites.
 4. Pharmacodynamic endpoints which may be directly modulated by the preventive agent or protocol but which are not necessarily related to the mechanism of action.
 5. Pharmacodynamic endpoints that may be directly modulated by the preventive agent or protocol but which may be directly related to mechanism of action of the protocol and which may serve as surrogate biomarkers.
 6. Immunologic assays, e.g. antibody levels, Elispot, CTL assays which demonstrate that a vaccine has elicited a relevant immune response against its intended target antigens.

As directed in the Task Order, the Contractor shall specifically:

1. Collect, and store and analyze tissue, serum/plasma, and urine from animals for use in biomarker studies. In addition, the Contractor shall store and analyze previously collected de-identified human samples for use in biomarker studies.
2. Process tissue, serum/plasma or urine for use in endpoints studies.
3. Perform biomarker studies using the tissues collected - the specific biomarker studies to be utilized will be determined as approved by the COR.
4. Perform endpoints studies.
5. Perform statistical analysis of endpoints studies.
6. Present endpoints results in tabular or graphic form, as well as offer a written commentary regarding the endpoints results.

B. GENERAL PROCEDURES/REQUIREMENTS

1. Animal Facility – The Contractor and any proposed subcontractor laboratories shall be accredited by or registered as follows:
 - a. The Contractor shall have an approved Animal Welfare Assurance for the Office of Extramural Research (OER), Office of Laboratory Animal Welfare (OLAW) (<http://grants.nih.gov/grants/olaw/olaw.htm>), Office of the Director, NIH, as required by Section I-43-30 of the Public Health Service Policy on Humane Care and Use of Laboratory Animals. The Contractor shall maintain such assurance for the duration of this contract, and any subcontractors performing work under this contract involving the use of animals shall also obtain and maintain an approved Animal Welfare Assurance.
 - b. The Contractor and any subcontractors performing work under this contract shall be fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) International or equivalent and maintain that accreditation for the life of the contract. Information about AAALAC accreditation is available at <http://www.aaalac.org/accreditation/>.

- c. The Contractor and any subcontractors performing work under this contract shall comply with the Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals (<http://grants.nih.gov/grants/olaw/references/phspol.htm>) and conduct work in compliance with recommendations established in the Guide for the Care and Use of Laboratory Animals (http://www.nap.edu/catalog.php?version=b&utm_expid=4418042-5.krRTDpXJQISoXLpdo-1Ynw.1&record_id=12910&utm_referrer=http%3A%2F%2Fgrants.nih.gov%2Fgrants%2Folaw.htm)
 - d. The Contractor and any subcontractors performing work under this contract shall comply with the Animal Welfare Act and Animal Welfare Regulations established by the United States Department of Agriculture (USDA) available at <http://www.aphis.usda.gov/wps/portal/aphis/ourfocus/animalwelfare>
 - e. Institutional Animal Care and Use Committee (IACUC) shall approve all animal procedures under this contract.
2. Animals - All animals for studies shall be furnished by the Contractor from established, reputable, known commercial breeders or shall be bred by the Contractor. The Contractor shall quarantine the animals for an appropriate period prior to placing them on test for studies and their release shall be documented by the attending American College of Laboratory Animal Medicine (ACLAM) veterinarian.
 3. Travel - One (1) staff member/Principal Investigator shall travel to a scientific meeting one (1) time in the final year of the Task Order for the purposes of presentation of the results for the Task Order.