

**STATEMENT OF WORK**  
**Preclinical Efficacy and Intermediate Endpoint Biomarkers**

**SCOPE**

This contract will support the development of potential cancer preventive agents or vaccines employing detailed preclinical efficacy studies and determining pharmacodynamic or efficacy biomarkers which parallel the efficacy of a given agent. The primary endpoint of the efficacy studies will be the development of invasive cancers whereas the biomarker studies will identify endpoints which correlate with the efficacy 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.

The Contractor shall perform work in these Task Areas as outlined in each Task Order:

**A. TASK AREAS**

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

Use of animal models as defined by the NCI for cancer prevention testing that may include, but are not limited to: mammary, bladder, lung, skin, esophagus, colon/intestinal tract, prostate, melanoma, trachea/bronchus, head and neck, brain, hematopoietic systems, pancreas, and ovary.

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 (intermittent, weekly);
8. Conduct studies monitoring tumorigenesis, body weight and clinical appearance
9. Conduct gross necropsies in animals;
10. Conduct histopathological examination of selected tissues from selected groups in different strains and species of animals used;
11. Collect and preserve tissue, serum, and urine from laboratory animals in the study;
12. Perform statistical analysis comparing treatment groups with control groups: for example: tumor incidence and tumor inhibitor;
13. Present tumor inhibitor data in tabular or graphic form, as well as tumor incidence data and, where possible, multiplicity and latency data;
14. Collect tissues, sera or other body fluids, either fixed or frozen and maintain under appropriate storage conditions until utilized;
15. Demonstrate expertise in the area of chemical analysis of feed or diet with regards to preventive agents to be employed;
16. Ship some or all of these samples with technical documentation to other investigators at the direction of the NCI.

## 2. TASK AREA 2 - EVALUATION AND VALIDATION OF INTERMEDIATE ENDPOINTS

The Contractor shall conduct intermediate endpoint assays in rodent tissues and may perform studies employing NCI-supplied, de-identified human samples examining relevant intermediate endpoints. In many task orders the relevant tissues shall be supplied to the Contractor. Intermediate endpoints that shall be examined include but are not limited to:

1. Large scale 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 mechanism of a given agent;
3. Pharmacodynamic 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 which 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.

Contractor shall specifically:

7. Collect, if required, and store and analyze tissue, serum, and urine from animals for use in biomarker studies. In a limited number of cases the Contractor may be asked to store and analyze previously collected de-identified human samples for use in biomarker studies;
8. Process tissue, serum or urine for use in endpoints studies;
9. Perform biomarker studies using the tissues collected - the specific biomarker studies to be employed will be determined as approved by the Contracting Officer's Representative (COR);
10. Perform endpoints studies;
11. Perform statistical analysis of endpoints studies;
12. Present endpoints results in tabular or graphic form, as well as offer a written commentary regarding the endpoints results.

## 3. GENERAL PROCEDURES

**A. Animal Facility** – The laboratories shall be accredited by or registered as follows:

1. The Contractor shall have an approved Animal Welfare Assurance for the Office of Extramural Research (OER), Office of Laboratory Animal Welfare (OLAW) ([://grants.nih.gov/grants/olaw/olaw](http://grants.nih.gov/grants/olaw/olaw)), 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.

2. The Contractor 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 [.aaalac.](http://aaalac.org)
3. The Contractor shall comply with the Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals ([://grants.nih.gov/grants/olaw/references/phspol.](http://grants.nih.gov/grants/olaw/references/phspol)) and conduct work in compliance with recommendations established in the Guide for the Care and Use of Laboratory Animals ([://www.nap.edu/openbook.php?record\\_id=](http://www.nap.edu/openbook.php?record_id=)).
4. The United States Department of Agriculture (USDA).
5. Institutional Animal Care and Use Committee (IACUC) shall approve all animal procedures under this contract.

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.