Sources Sought Notice No. HHS-NIH-RDSS-TSB-07011

Title: PRECLINICAL TOXICOLOGY OF DRUGS DEVELOPED FOR CANCER AND OTHER DISEASES

This is a Research and Development (R & D) Sources Sought notice. This is **NOT** a solicitation for proposals, proposal abstracts, or quotations. The purpose of this notice is to obtain information regarding the availability and capability of all qualified sources to perform a potential R & D requirement.

The Source Sought Notice (SS) for the above title is for information and planning purposes ONLY and not a solicitation or an obligation on the part of the National Cancer Institute (NCI). The above title will identify qualified small businesses including 8(a), HUBZONE, or Service-Disabled Veteran-owned business concerns that are interested in this requirement and capable of performing the work required for the "Preclinical Toxicology & Pharmacology of Drugs Developed for Cancer and Other Diseases". The NAICS code for this topic is Number 541710. The NCI does not intend to award a contract on the basis of responses nor otherwise pay for the preparation of any information submitted. However, the NCI may issue a Request for Proposal (RFP) based on the responses. THERE IS NOT A SOLICITATION AVAILABLE AT THIS TIME. In the event are requirement for this title should materialize, a claim against NCI shall not arise as a result of a response to this SS title or the NCI's use of such information as either part of the evaluation process or in developing specifications for any subsequent requirement. Additionally, if the requirement is fulfilled, it is anticipated that five or six multi-year, cost-reimbursement, completion type contracts would be awarded for base period of five (5) years.

The NCI is seeking qualified small businesses including: 8(a), HUBZone, or Service Disabled Veteran-owned business concerns to provide support to NCI's Toxicology and Pharmacology Branch (TPB), Development Therapeutics Program (DTP), Division of Cancer Treatment and Diagnosis (DCTD) to (1) develop approaches and methods; (2) perform experimental procedures; (3) record observations and data analyzing and interpreting findings; and (4) publishing results, interpretations and conclusions. The services include procedures, techniques, and activities directly supporting the conduct of R&D, involving innovative or standard methodologies to prepare or provide special materials, resources, or services integral to performing R&D projects, where the Offerors decision making process directs the work involved. Examples of direct support to R&D programs include; analyzing or interpreting experimental research data or information, or providing significant enhancements to scientific processes, existing equipment or systems.

Technical Evaluation Criteria include the following:

A. PERSONNEL

1. Availability and qualifications of a Program Director (Principal Investigator [PI]) with at least 5 years of relevant experience in managing an interdisciplinary team in the conduct of toxicology and pharmacology investigations of therapeutic agents. Suitability and adequacy of the PI's recent scientific accomplishments to this project as evidenced by bibliography and Curriculum Vitae (including study reports, published and accepted manuscripts).

2. Availability of Work Assignment Project Leaders (Study Directors) with leadership experience in performing team oriented studies of a similar nature to that to be performed under this contract.

Suitability and adequacy of recent scientific accomplishments to this project as evidenced by bibliography and Curriculum Vitae (including study reports, published and accepted manuscripts).

3. Suitability and adequacy of the training, experience and qualifications of other personnel in pathology, laboratory animal care, clinical pathology, analytical chemistry, pharmacokinetics, and quality assurance. In addition, describe the availability and suitability of personnel for performing in vitro assays, cardiotoxicity, immunotoxicity and neurotoxicity studies.

4. Extent of experience of the proposed staff functioning as a study team.

B. TECHNICAL APPROACH AND AWARENES

A realistic technical approach to the program as a whole and to each protocol, drawing upon recent experience in the conduct of toxicology and pharmacology studies including discussions on analytical chemistry, animal care, clinical pathology, histopathology, toxicity evaluations (drug versus nondrug related) and quality assurance. Understanding of the problems likely to be encountered in the studies as demonstrated by first-hand experience with diverse types of drugs.

Technical approach with regard to specialty studies such as in vitro assays, cardiotoxicity, immunotoxicity and neurotoxicity studies.

Evidence of ability to provide high quality data and service.

The means to provide interim data sets, raw data and derived parameters to the PO when needed in a consumable and integrative format.

C. FACILITIES AND EQUIPMENT

Availability and accessibility of suitable animal and laboratory space for the projected studies. Adequate capacity for multiple studies to be conducted simultaneously. Accessibility and adequacy of major equipment needed for the proposed work including analytical and computer equipment. Adequacy of library resources.

D. ORGANIZATIONAL EXPERIENCE

Extent of organizational ability to provide appropriate manpower and resources for each Work Assignment and meet turnaround times for reporting and data acquisition . Documented evidence of Q.C. procedures for study reports and data. Documented ability to handle increases and decreases in workload over the contract period. Adequacy of the safety and security procedures for the proposed work.

Additionally, all Offerors shall be AAALAC accredited at the time of initial proposal submission.

MANDATORY CRITERIA:

Proposals offered in response to any resultant RFP must meet the mandatory qualification of complying with all aspects of the Good Laboratory Practice (GLP) Regulations and the Confidentiality of Information Clause.

The GLP qualification must be met at the time of submission of the initial proposal. Since the toxicology studies will be used by the National Cancer Institute to satisfy the safety testing requirement of the Food and Drug Administration in the submission of an Investigational New Drug Application, the studies must be conducted and the data must be stored in accordance with the Good Laboratory Practice Regulations as outlined in the Federal Register Friday, December 22, 1978.

The NCI also signs legally binding agreements with certain suppliers (often pharmaceutical or chemical companies) which state that all information on the compounds submitted by the supplier must be held

confidential. The Contractor will be expected to evaluate the toxicity of such commercially confidential (discreet) materials. Therefore, the Contractor must be willing to sign a Confidentiality of Information Agreement at the time of award.

The National Institutes of Health (NIH) requires that prior to awarding of funds for contracts involving the use or intended use of animals in research; an acceptable assurance statement must be on file with the Office for Protection from Research Risks (OPRR).

Capability statements:

Interested qualified small business organizations should submit a tailored capability statement for this requirement not to exceed 20-single spaced pages (including all attachments, resumes, charts, etc.) presented in single-spaced and using a 12-point font size minimum, that clearly details the ability to perform the aspects of the notice described. Statements should also include an indication of current certified small business status; this indication should be clearly marked on the first page of your capability statement, as well as the eligible small business concern's name, point of contact, address, phone number and DUNS number.

Capability statements are due no later than November 23, 2009, at 2:00 PM EDT.
Please submit **one** (1) original and **three** (3) copies of your responses to:

POSTAL ADDRESS:

MaryAnne Golling
Contracting Officer
Treatment and Support Branch
Office of Acquisitions
National Cancer Institute at Frederick
Post Office Box B
244 Miller Drive, Room 118
Fort Detrick
Frederick, Maryland 21702-1201

COURIER ADDRESS:

MaryAnne Golling
Contracting Officer
Treatment and Support Branch
Office of Acquisitions
National Cancer Institute at Frederick
244 Miller Drive, Room 118
Fort Detrick
Frederick, Maryland 21702-1201

All responses must be received at NCI by the specified due date and time in order to receive consideration.

Any questions regarding this notice must be in writing and received by:
Tuesday, November 10, 2009, at 2:00 PM EDT.

POINTS OF CONTACT:
Dean Guidi
Contract Specialist
Email: guidid@mail.nih.gov

MaryAnne Golling
Contracting Officer
Email: gollingm@mail.nih.gov

STATEMENT OF WORK

Preclinical Toxicology of Drugs Developed for Cancer and Other Diseases

Independently and not as an agent of the Government, the Contractor shall furnish all the necessary services, qualified personnel, material, equipment and facilities, not otherwise provided by the Government as required to perform the Statement of Work below:

1. CONDUCT TOXICOLOGY AND PHARMACOLOGY STUDIES IN ACCORDANCE WITH THE COMPLETE PROTOCOL REQUIREMENTS DEVELOPED FOR EACH AGENT BY THE NCI PROJECT OFFICER.

It would be scientifically inappropriate to set rigid protocol guidelines that would be adequate for each compound that will be assessed, therefore, the guidelines below will be modified to account for data on the agent's *in vitro* cytotoxicity, biochemistry and schedule dependence as well as *in vivo* activity, if available. The types of studies that the Contractor will be required to perform includes, but is not limited to the following:

a. **Analytical Phase**: Drug identity analysis (*e.g.,* IR, NMR, MP, MS, or other emergent assay methodology designated by P.O.), validation of the procedures supplied by the NCI for dose concentration analyses and validation of the requisite methodology for assay of drug in biological fluids shall be initiated immediately upon receipt of drug.
b. **Pharmacokinetic Phase**: Plasma elimination kinetics shall be determined in one or more of the following species: dogs, rodents and non-human primates after single intravenous doses of drug. Other routes of administration such as oral, intraperitoneal, subcutaneous and intramuscular may be necessary to evaluate as well. Bioavailability of non-parenteral routes and plasma clearance rates shall be determined in order to establish the dose required to produce effective drug concentrations in plasma for future toxicity studies. The ability of a drug to cross the blood-brain barrier shall be assessed in dogs or non-human primates.
c. **Screening and Preliminary Phase**: For each drug, establish a maximum tolerated dose (MTD) and dose limiting toxicities (DLT) in both beagle dogs and rodents. The use of non-human primates as an alternative species may be required for certain agents under evaluation. The types of studies required in this phase shall be decided by the P.O. and may include the following:
    i. Short-term toxicity studies in rodents
    ii. Single or multiple dose range-finding studies in rodents, beagle dogs, or non-human primates.
d. **IND-Directed Toxicology Assesment Phase**: For each drug, establish toxicity and safety in relation to drug plasma concentrations or area-under-the-curve in both beagle dogs and rodents. The use of non-human primates as an alternative species will be required for certain agents under evaluation. The types of studies required in this phase shall be decided by the P.O. and may include the following:
    i. Single or multiple daily dose schedules such as Dx1, q3hr x 3, q8hr x 15, *etc*

ii. Continuous administration to mice via Alzet osmotic pumps and to beagle dogs, rats and non-human primates *via* infusion pumps for periods of from one hour up to 30 days.
iii. Twenty eight days or more of repeated administration of drug to rodents, beagle dogs and/or non-human primates
iv. Special studies such as cardiotoxicity, neurotoxicity, immunotoxicity may be requested as part of an existing study or in a separate study.

2. GENERAL AREAS OF WORK

The work assignments issued under this contract will have the following objectives. The Contractor shall:

a. Validate the analytical methodology to quantitate drug levels in dosing solutions, biological fluids, and tissues as required. Measure drug plasma levels in rodents, beagle dogs and/or non-human primates treated with the agent under study. Calculate and report all important pharmacokinetic parameters from the derived data.
b. Determine bioavailability of drug after oral and/or intraperitoneal, subcutaneous or intramuscular administration. Calculate and report all relevant pharmacokinetic parameters from the derived data.
c. Determine acute toxicity, (including, but not limited to, clinical observations, body weights, clinical pathology, histopathology) and plasma drug levels in rodents, beagle dogs and/or non-human primates over specified time periods.
d. Assess subacute toxicity (including, but not limited to, clinical pathology, hematology, histopathologic evaluation of tissues, clinical observations) in rodents, beagle dogs and/or non-human primates.
e. Assess cardiotoxicity, neruotoxicity, immunotoxicity in rodents, beagle dogs and/or non-human primates as specified by the P.O.

3. WORK ASSIGNMENTS

Multiple contracts will be awarded and each will be administered on a work assignment managed basis. Work assignments will be issued under contracts that result from this solicitation. Each work assignment will be issued after a cost estimate, labor and level of effort estimate has been received and found acceptable and agreement reached between the Government and the Contractor. The level of effort and cost of such a task shall not exceed that of the funded period.

4. GOVERNMENT FURNISHED PROPERTY/SUPPLIES

a. Animals, especially mice and rats, will be supplied by the Government when possible. Dogs, rabbits, non-human primates and specialty animals such as cathetered rats will be purchased by the contractor under this contract as specified by the P.O.
b. The test articles and some of the control articles used in these studies will be furnished by the Government.
c. Available analytical chemistry information including chemical identity data and methodology for dose concentration analysis, plasma drug analysis procedures, formulation information, available literature, *etc.* will be supplied by the Government.
d. Specialized equipment for infusion studies (pumps, jackets, collars, *etc*.) will be furnished by the Government.

5. PERIOD OF PERFORMANCE

The anticipated period of performance is anticipated to be five (5) years after the date of the award of the contract.

6. AAALAC ACCREDITATION

Accreditation by the American Association for Accreditation of Laboratory Animal Care (AAALAC) is highly desirable. Documentation of a lack of findings from one or more ALLAC inspections may also provided.

7. HUMAN SUBJECTS

It is hereby understood and agreed that research involving human subjects shall not be carried out under this contract, and that no material developed, modified or delivered by or to the Government under this contract, or any subsequent modification of such material will be used by the Contractor or made available by the Contractor for use by anyone other than the Government for experimental or therapeutic use involving humans without the prior written approval of the Contracting Officer. However, refuse human materials such as blood, serum, plasma, bone marrow, liver, kidney, other tissues, *etc.* may be necessary for use on this contract.

8. HEALTH AND SAFETY PLAN

Each agent will be considered potentially hazardous. Therefore, all necessary precautions must be taken to protect personnel and the environment against possible exposure to the agents being tested. The Contractor shall perform all work associated with this contract in accordance with all applicable Federal, State and local regulations including transportation and disposal of hazardous waste.

9. ACCESS TO DATA

The Government requires that all data accumulated under the projected contracts be immediately available for its review and that provisions be made to maintain confidentiality of all data. Authority to release data may be granted only by the Contracting Officer together with the Project Officer and must be in writing.

All individual animal data should be provided to the PO in a format that allows integration into DTP databases. Excel or other tab delimited file formats for are acceptable. Other formats will be considered but compatibility shall be confirmed.

10. CONFIDENTIALITY OF INFORMATION

Certain data provided to the Contractor under this contract must be treated confidentially. The data to be treated confidentially is associated with certain “discreet” compounds which are not available to the public. When compounds are assigned to the Contractor, these discreet compounds will be identified by the letter “D” as a prefix to

the compound NSC number. Under no circumstances are chemicals or drugs or any information associated with these chemicals or drugs to be released or divulged without prior written approval of the NCI COTR.

11. REPORTING REQUIREMENTS

a. **STUDY REPORTS**

The final report on each study will be due between 15 and 60 working days following completion of the in-life phase of the study. The due dates for reports on each segment of the study will be mutually agreed to at the time of study initiation. Each report must be acceptable to the Project Officer for filing as Attachment 6a of an Investigational New Drug Application with the Food and Drug Administration.

This report will accurately and completely describe the study design, procedures and findings, present an analysis and summary of the data followed by the conclusions derived from the analyses. Protocol modifications and/or deviations will be presented and discussed as well. The report will also include: (a) a cover page which will include the title, contract number, authors, laboratory name and address, dates of initiation and completion, and sponsor; (b) the NTIS Report Documentation Page, to be placed at the beginning of the final report; (c) a comprehensive summary to be placed after the NTIS page; (d) the dated signature of the Study Director and any others deemed necessary; (e) a table of contents; and (f) a statement prepared and signed by the Quality Assurance Unit which will refer to all phases of the study and where the raw data records, reports and samples are stored. In addition, the following items must be included in each report. Additional items may be required per Principal Investigator/Project Officer discussions.

1. Compound information
    a. Identity data
    b. Lot number
    c. History (dates received, on test and study completed)
    d. Stability
2. All data requested
3. Animal history (source, sex, age, weight, immunization, procedure used for unique identification, *etc.*)
4. Baseline data (pre-test)
5. Control animals

6. Vehicle controls (if requested)

7. Dose formulation information

8. Route of administration

9. Rate of injection

10. Urinalysis data, if specifically requested

11. Methodologies of all test procedures

12. Days of sacrifice

13. Time period from death to necropsy

14. Gross and microscopic pathology

15. Rationale and documentation of all deviations from protocol

16. Statistical methods for analyzing data

17. Corrections or additions to reports are to be submitted in form of amendment clearly identifying that part of report being added to or corrected, reasons for addition or correction and dated signature of person responsible

18. All portions of the studies and reports must be in compliance with the GLP Regulations as published in the Friday, December 22, 1978 Federal Register, Vol. 43, No. 247, pp.59986-60025.

b. **RAW DATA**

Data will be collected using the laboratory's in-house data management system. Final tabular data and raw data will be transmitted to the NCI for archival purposes. In addition, data can be transmitted electronically as part of the monthly report.

c. **MONTHLY REPORTS**

For each drug on test the contractor shall submit a monthly Status Report to both the Project Officer and the Contracting Officer between the 10th and 15th of each month. The report shall detail the status of the testing as of the reporting date, any problems encountered and the proposed means of resolution. Each monthly report shall NOT exceed 2 - 4 double spaced typewritten pages and may include charts and figures. The report shall include a listing of hours expended during the reporting period, cumulative work hours expended and work hours remaining for completion for each work

assignment as well as the total contract. Notwithstanding the requirement for monthly progress reports, the Contractor shall notify the Project Officer whenever the time allocated to a work assignment is expected to exceed the originally allocated time, a personnel change is necessary or the cost of the work assignment is expected to exceed the originally estimated cost. Revision of the time allowed, and of the cost allocated for deliverables can only be made by mutual agreement of the Contracting Officer and the Contractor.

d. **ANNUAL REPORTS**

The Contractor shall submit an annual progress report. This report shall include a cover page which shows the contractor's name, contract number, contract title, Project Officer and period being reported, a brief description of work performed during period reported, including the significant findings, any problems experienced, and the anticipated work plan for the following period. Each report shall contain as the first section a brief summary (not to exceed 200 words) of the salient results to date. The last portion of the annual report will contain a report on personnel and health and safety. This section should provide evidence that employees are properly instructed in the use of hazardous substances and have received appropriate medical history and physical examinations.

e. **SPECIAL BUSINESS REPORT**

On an annual basis the subject contract will have a merit technical review to evaluate the performance. Approximately 90 days prior to the expiration of each funded period, the Contractor shall submit to the Contracting Officer a status of funds, to included a breakdown of estimated costs and fixed fee for current year and a projection of expenditures needed for the next funding period. This report shall follow the same itemized format as the basic business proposal submitted hereunder and will serve as the basis for the allocation for funds under this contract, pursuant to the General Provisions thereof, entitled “Limitation of Funds”. The original and two (2) copies shall be submitted.

f. **FINAL REPORT**

The contractor shall submit a final report that documents and summarizes the results of the entire contract period of performance. This report shall be in sufficient detail to explain comprehensively the results achieved and shall contain a summary (not to exceed 200 words) of the salient results achieved during the performance of the contract. **REPORTS ARE REQUIRED AS FOLLOWS:**

Reports	Period Covered	Due Date (By 15th of each Month)	CO [1]	COTR [2]
Monthly	To Be Stated	To Be Stated	1 Copy	1 Copy
Study Report (Draft)	NA	35 working days from the end of the live phase	None	Electronic Copies
Study Report (Final)	NA	65 working days from the end of the live phase	None	Electronic signed Copies
1st Annual	To Be Stated	To Be Stated	1 Copy	2 Copies
2nd Annual	To Be Stated	To Be Stated	1 Copy	2 Copies
3rd Annual	To Be Stated	To Be Stated	1 Copy	2 Copies
4th Annual	To Be Stated	To Be Stated	1 Copy	2 Copies
5th Final	To Be Stated	To Be Stated	1 Copy	2 Copies
Business	To Be Stated	To Be Stated	2 Copies	1 Copy

Deliver To:

1 National Cancer Institute
TSB/OA/OD/NCI
244 Miller Drive, P.O. B
Ft. Detrick
Frederick, MD 21702
ATTN: Contracting Officer

2 National Cancer Institute
T&PB/DTP/DCTDC/NCI
6130 Executive Blvd.
EPN, Rm. 8034
Bethesda, MD 20892-7448
ATTN: Project Officer

12. LEVEL OF EFFORT

It is anticipated that five (5) or six (6) funded contracts will be awarded. Only one award will be made to an institution.

A "staff year" has been defined as 1880 hours per year exclusive of fringe benefits.

In actual practice, the complete evaluation of a promising therapeutic agent may require more or less effort than estimated above depending upon the number and complexity of the final protocols utilized. There may also be instances when studies on a drug will be terminated after the initial protocol. Conceivably, the laboratory may be required to perform a preliminary evaluation (one or two protocols) on a number of drugs prior to completely evaluating one drug for the purpose of filing an IND.

13. TRAVEL REQUIREMENTS

The Contractor should expect that the Principal Investigator and/or a senior scientist on the contract will attend one national scientific meeting a year. Plan on payment of registration fee, one day per diem and one-half of the air fare for this meeting. This travel must be approved in advance by the Contracting Officer.

Disclaimer and Important Notes. This notice does not obligate the Government to award a contract or otherwise pay for the information provided in response. The Government reserves the right to use information provided by respondents for any purpose deemed necessary and legally appropriate. Any organization responding to this notice should ensure that its response is complete and sufficiently detailed to allow the Government to determine the organization's qualifications to perform the work. Respondents are advised that the Government is under no obligation to acknowledge receipt of the information received or provide feedback to respondents with respect to any information submitted. After a review of the responses received, a pre-solicitation synopsis and solicitation may be published in Federal Business Opportunities. However, responses to this notice will not be considered adequate responses to a solicitation.

Confidentiality. No proprietary, classified, confidential, or sensitive information should be included in your response. The Government reserves the right to use any non-proprietary technical information in any resultant solicitation(s).