

**Program Announcement  
To DOE National Laboratories  
LAB 03-20**

***Low Dose Radiation  
Research Program -  
Biologically-Based Risk Modeling***

**SUMMARY:**The Office of Biological and Environmental Research (OBER) of the Office of Science (SC), U.S. Department of Energy (DOE), hereby announces its interest in receiving proposals for participation in a biologically-based risk modeling exercise, for the purposes of developing and evaluating different modeling/prediction strategies. Awardees will be asked to develop individual biologically-based models incorporating one or more phenomena such as adaptive response, bystander effects, genetic susceptibility, or genomic instability. A central aspect of this exercise will be the eventual modeling, by all awardees, of an artificially defined biological test system or archetype having a set of biological characteristics and radiation-induced endpoints for which exact probability values are either known or assigned. Please review the Supplementary Information and Proposal sections below for further details.

**DATES:** Preproposals (letters of intent) should be submitted by April 4, 2003.

Formal proposals are due 4:30 p.m. EDT, May 23, 2003, in order to be accepted for merit review and to permit timely consideration for award in Fiscal Year 2003.

**ADDRESSES:** Preproposals referencing Program Announcement LAB 03-20, should be sent to Ms. Joanne Corcoran by E-mail: joanne.corcoran@science.doe.gov, with a copy to Dr. Noelle Metting at: noelle.metting@science.doe.gov.

Formal proposals in response to Program Announcement LAB 03-20 are to be submitted as PDF files on CDs. Three complete copies (on separate CDs) should be submitted for each proposal. Color images should be submitted as a separate file in PDF format and identified as such. These images should be kept to a minimum due to the limitations of reproducing hardcopies. They should be numbered and referred to in the body of the technical scientific proposal as Color image 1, Color image 2, etc.

The three CDs, referencing Program Announcement LAB03-20, should be sent to: Life Sciences Division, SC-72/Germantown Building, Office of Biological and Environmental Research, Office of Science, U.S. Department of Energy, 1000 Independence Avenue, SW, Washington, D.C. 20585-1290, ATTN: Program Announcement LAB03-20.

When submitting by U.S. Postal Service Express Mail, any commercial mail delivery service, or when hand carried by the researcher, the following address must be used: Life Sciences Division, SC-72, Office of Biological and Environmental Research, Office of Science, U.S. Department of

Energy, 19901 Germantown Road, Germantown, MD 20874-1290, ATTN: Program Announcement LAB 03-20.

**FOR FURTHER INFORMATION CONTACT:** Dr. Noelle Metting, telephone: (301) 903-8309, E-mail: [noelle.metting@science.doe.gov](mailto:noelle.metting@science.doe.gov), Office of Biological and Environmental Research, U.S. Department of Energy, SC-72/Germantown Building, 1000 Independence Avenue SW, Washington, D.C. 20585-1290.

**SUPPLEMENTARY INFORMATION:** The Low Dose Radiation Research Program has the challenge of conducting research that can be used to inform the development of future national radiation risk policy for the public and the workplace. The Program has focused on quantifying and understanding the mechanisms of molecular and cellular responses to low dose exposures to radiation, currently 0.1 Gy (10 rads) or less, with a view toward the lower doses. Most scientists in the field would agree that not enough is yet known about the biological consequences of low dose radiation exposure to be able to completely model human health risk. However, it is timely to begin to systematically evaluate different approaches for modeling the diversity of available information on the biological effects of low dose radiation exposure.

We define biologically-based risk models as mathematical constructs of the key biological events involved in the production of an adverse health effect, e.g., cancer, in response to radiation across a range of doses of interest. Such models are likely to describe both stochastic and deterministic variables that range from probabilities of inducing key molecular events such as cell death, replication or specific gene expression, to the description of responses at the tissue level or even at the level of the entire organism. Mathematical predictors or estimators of radiation risk should ultimately be able to incorporate all available epidemiological and experimental information.

In this announcement, proposals are sought for participation in an interactive, biologically-based risk modeling exercise. The first activity for the awardees will be to participate in an initial Workshop for extensive discussions with experimental researchers and regulatory scientists. Awardees will then work to develop a biologically-based risk model that includes one or more characteristics important to low dose radiobiology.

Concurrently, awardees will participate in one or more workshops for the purpose of developing an artificially defined biological archetype. This biological archetype will become the core source of biological data, a biological test system for which exact probability values are either known or (temporarily) assigned. Quantitative information to be defined in the biological archetype will include definitions (specific probability values or ranges as a function of dose) for such attributes as:

- Amount of steady state endogenous DNA damage
- Yield of radiation-induced DNA damage (specific lesions)
- Efficiency of repair of radiation-induced DNA damage for specific lesions (repair capacity, saturation level, error rate)
- Radiation-induced gene expression
- Radiation-induced genomic instability

- Radiation-induced bystander effects (cell-cell communication)
- Radiation-induced adaptive responses
- Genetic susceptibility - for a population of individuals
- Current epidemiological information
- Etc...

The biological archetype will eventually be modeled by each funded awardee, for the ultimate purpose of comparing the different modeling/prediction strategies. Please note that the biological archetype will be a composite of what is presently established, supplemented where needed by best-guess, made-up data.

The long term goals of this exercise are the following: 1) to discover which mechanistic data are usable and which are the most critical inputs for development of biologically-based models to predict human health risks for low dose exposures (the exercise thus may help to define future experimental research needs); and 2) to provide new insight into how to extrapolate between different levels of biological organization (from molecules to cells to tissues to organisms) and from observations *in vitro* to biological responses *in vivo*.

Researchers should demonstrate knowledge of and expertise in risk modeling. They should discuss general strategies for, or demonstrate expertise in the use of, biological mechanistic data in the development of risk models. Ideally, the proposal should exhibit some familiarity with relevant radiation biology literature, but prior work in this field is not a prerequisite. **The Project Description must contain the following:**

1. A proposal to develop a biologically-based model taking account of one or more phenomena such as adaptive response, bystander effects, genetic susceptibility, or genomic instability. A hierarchical scheme may be proposed for developing a series of simple to complex biologically-based risk models that include successively higher numbers of biological parameters.
2. A discussion of model validation strategies, as well as a general discussion of error estimation strategies, should be included. (Of great importance will be the determination of how much error can be tolerated in each of the critical inputs.)
3. Briefly, the researcher's ideas on how one would begin to design a "biological archetype" that could be used to compare different models. (What type of biological archetype would be most useful at the present time--single cell, cell culture, tissue, mouse, man? In the future? Which characteristics of the biological archetype should be defined? Which characteristics are known at the present time?)

Information on the Low Dose Radiation Research Program can be found on the web site: <http://lowdose.tricity.wsu.edu>.

**PROGRAM FUNDING:** It is anticipated that up to \$1,500,000 will be available for approximately 8 two-year awards, contingent upon the availability of funds. Each award will be no more than \$200,000, total costs per year. If the exercise is judged productive by

administrative review, some or all awards may be extended an additional year. DOE is under no obligation to pay for any costs associated with the preparation or submission of proposals if an award is not made.

## **THE PROPOSAL**

### **(Please Note Information Below On Page Limits)**

Adherence to type size and line spacing requirements is necessary for several reasons. No researchers should have the advantage of providing more text in their proposals by using small type. Small type may also make it difficult for reviewers to read the proposal. Proposals must have 1-inch margins at the top, bottom, and on each side. Type sizes must be 10 point or larger. Line spacing is at the discretion of the researcher but there must be no more than 6 lines per vertical inch of text. Pages should be standard 8 1/2" x 11" (or metric A4, i.e., 210 mm x 297 mm). Proposals must be written in English, with all budgets in U.S. dollars.

Researchers are asked to use the following ordered format:

- **Field Work Proposal (FWP) Format** (Reference DOE Order 5700.7C) (DOE ONLY)
- **Project Abstract Page;** single page only, should contain title, PI name, and abstract text
- **Budget page** for the one year project period (using DOE F 4620.1)
- **Budget Explanation**
- **Project Description; ten (10) pages or less.** The proposal should contain the following:
  - a. A proposal to develop a biologically-based model taking account of one or more phenomena such as adaptive response, bystander effects, genetic susceptibility, or genomic instability.
  - b. A discussion of model validation strategies, as well as a general discussion of error estimation strategies, should be included.
  - c. Briefly, the researcher's ideas on how one would design a biological archetype that could be used to compare different models (approximately one page).
- **Literature Cited**
- **Collaborative Arrangements** (if applicable)
- **Facilities and Resources**
- **Biographical Sketches**
- **Current and Pending Support**
- **Letters of Collaboration** (if applicable)

Any recipient of an award from the Office of Science, performing research involving recombinant DNA molecules and/or organisms and viruses containing recombinant DNA molecules shall comply with the National Institutes of Health "Guidelines for Research Involving Recombinant DNA Molecules," which is available via the World Wide Web at:

<http://www.niehs.nih.gov/odhsb/biosafe/nih/rdna-apr98.pdf>, (59 FR 34496, July 5, 1994), or such later revision of those guidelines as may be published in the Federal Register.

DOE requirements for reporting, protection of human and animal subjects and related special matters can be found on the World Wide Web at:

<http://www.science.doe.gov/production/grants/Welfare.html>.

The instructions and format described below should be followed. Reference Program Announcement LAB 03-20 on all submissions and inquiries about this program.

## **OFFICE OF SCIENCE GUIDE FOR PREPARATION OF SCIENTIFIC/TECHNICAL PROPOSALS TO BE SUBMITTED BY NATIONAL LABORATORIES**

Proposals from National Laboratories submitted to the Office of Science (SC) as a result of this program announcement will follow the Department of Energy Field Work Proposal process with additional information requested to allow for scientific/technical merit review.

### **1. Evaluation Criteria**

Proposals will be subjected to formal merit review (peer review) and will be evaluated against the following criteria which are listed in descending order of importance:

- Scientific and/or technical merit of the project
- Appropriateness of the proposed method or approach
- Competency of the personnel and adequacy of the proposed resources
- Reasonableness and appropriateness of the proposed budget

The evaluation will include program policy factors such as the relevance of the proposed research to the terms of the announcement, the uniqueness of the proposer's capabilities, and demonstrated usefulness of the research for proposals in other DOE Program Offices as evidenced by a history of programmatic support directly related to the proposed work.

### **2. Summary of Proposal Contents**

Field Work Proposal (FWP) Format (Reference DOE Order 5700.7C) (DOE ONLY)  
Proposal Cover Page  
Table of Contents  
Abstract  
Budget and Budget Explanation  
Project Description  
Literature Cited  
Other support of investigators  
Biographical Sketches  
Description of facilities and resources  
Appendix

### **3. Detailed Contents of the Proposal**

Proposals must conform to the following three requirements: the height of the letters must be no smaller than 10 point with at least 2 points of spacing between lines (leading); the type density must average no more than 17 characters per inch; the margins must be at least one-half inch on all sides. Figures, charts, tables, figure legends, etc., may include type smaller than these requirements so long as they are still fully legible.

#### **3.1 Field Work Proposal Format (Reference DOE Order 5700.7C) (DOE ONLY)**

The Field Work Proposal (FWP) is to be prepared and submitted consistent with policies of the investigator's laboratory and the local DOE Operations Office. Additional information is also requested to allow for scientific/technical merit review. Laboratories may submit proposals directly to the SC Program office listed above. A copy should also be provided to the appropriate DOE operations office.

#### **3.2 Proposal Cover Page**

The following proposal cover page information may be placed on plain paper. No form is required.

Title of proposed project  
SC Program announcement title  
Name of laboratory  
Name of principal investigator (PI)  
Position title of PI  
Mailing address of PI  
Telephone of PI  
Fax number of PI  
Electronic mail address of PI  
Name of official signing for laboratory\*  
Title of official  
Fax number of official  
Telephone of official  
Electronic mail address of official  
Requested funding for each year; total request  
Use of human subjects in proposed project:  
    If activities involving human subjects are not planned at any time during the proposed project period, state "No"; otherwise state "Yes", provide the IRB Approval date and Assurance of Compliance Number and include all necessary information with the proposal should human subjects be involved.  
Use of vertebrate animals in proposed project:  
    If activities involving vertebrate animals are not planned at any time during this project, state "No"; otherwise state "Yes" and provide the IACUC Approval date

and Animal Welfare Assurance number from NIH and include all necessary information with the proposal.

Signature of PI, date of signature

Signature of official, date of signature\*

\*The signature certifies that personnel and facilities are available as stated in the proposal, if the project is funded.

### **3.3 Table of Contents**

Provide the initial page number for each of the sections of the proposal. Number pages consecutively at the bottom of each page throughout the proposal. Start each major section at the top of a new page. Do not use unnumbered pages and do not use suffices, such as 5a, 5b.

### **3.4 Abstract**

Provide an abstract of no more than 250 words. Give the broad, long-term objectives and what the specific research proposed is intended to accomplish. State the hypotheses to be tested. Indicate how the proposed research addresses the SC scientific/technical area specifically described in this announcement.

### **3.5 Project Description**

The narrative comprises the research plan for the project and is limited to 10 pages. **Please follow instructions for the Project Description found in the Supplementary Information above.**

### **3.6 Literature Cited**

List all references cited in the narrative. Limit citations to current literature relevant to the proposed research. Information about each reference should be sufficient for it to be located by a reviewer of the proposal.

### **3.7 Budget and Budget Explanation**

A detailed budget is required for the entire project period, which normally will be three years, and for each fiscal year. It is preferred that DOE's budget page, Form 4620.1 be used for providing budget information\*. Modifications of categories are permissible to comply with institutional practices, for example with regard to overhead costs. A written justification of each budget item is to follow the budget pages. For personnel this should take the form of a one-sentence statement of the role of the person in the project. Provide a detailed justification of the need for each item of permanent equipment. Explain each of the other direct costs in sufficient detail for reviewers to be able to judge the appropriateness of the amount requested. Further instructions regarding the budget are given in section 4 of this guide.

\* Form 4620.1 is available at web site: <http://www.sc.doe.gov/production/grants/Forms-E.html>

### **3.8 Other Support of Investigators**

Other support is defined as all financial resources, whether Federal, non-Federal, commercial or institutional, available in direct support of an individual's research endeavors. Information on active and pending other support is required for all senior personnel, including investigators at collaborating institutions to be funded by a subcontract. For each item of other support, give the organization or agency, inclusive dates of the project or proposed project, annual funding, and level of effort devoted to the project.

### **3.9 Biographical Sketches**

This information is required for senior personnel at the laboratory submitting the proposal and at all subcontracting institutions. The biographical sketch is limited to a maximum of two pages for each investigator.

### **3.10 Description of Facilities and Resources**

Describe briefly the facilities to be used for the conduct of the proposed research. Indicate the performance sites and describe pertinent capabilities, including support facilities (such as machine shops) that will be used during the project. List the most important equipment items already available for the project and their pertinent capabilities. Include this information for each subcontracting institution, if any.

### **3.11 Appendix**

Include collated sets of all appendix materials with each copy of the proposal. Do not use the appendix to circumvent the page limitations of the proposal. Information should be included that may not be easily accessible to a reviewer.

Reviewers are not required to consider information in the Appendix, only that in the body of the proposal. Reviewers may not have time to read extensive appendix materials with the same care as they will read the proposal proper.

The appendix may contain the following items: up to five publications, manuscripts (accepted for publication), abstracts, patents, or other printed materials directly relevant to this project, but not generally available to the scientific community; and letters from investigators at other institutions stating their agreement to participate in the project (do not include letters of endorsement of the project).

## **4. Detailed Instructions for the Budget**

(DOE Form 4620.1 "Budget Page" may be used)

### **4.1 Salaries and Wages**

List the names of the principal investigator and other key personnel and the estimated number of person-months for which DOE funding is requested. Proposers should list the number of



postdoctoral associates and other professional positions included in the proposal and indicate the number of full-time-equivalent (FTE) person-months and rate of pay (hourly, monthly or annually). For graduate and undergraduate students and all other personnel categories such as secretarial, clerical, technical, etc., show the total number of people needed in each job title and total salaries needed. Salaries requested must be consistent with the institution's regular practices. The budget explanation should define concisely the role of each position in the overall project.

## **4.2 Equipment**

DOE defines equipment as "an item of tangible personal property that has a useful life of more than two years and an acquisition cost of \$25,000 or more." Special purpose equipment means equipment which is used only for research, scientific or other technical activities. Items of needed equipment should be individually listed by description and estimated cost, including tax, and adequately justified. Allowable items ordinarily will be limited to scientific equipment that is not already available for the conduct of the work. General purpose office equipment normally will not be considered eligible for support.

## **4.3 Domestic Travel**

The type and extent of travel and its relation to the research should be specified. Funds may be requested for attendance at meetings and conferences, other travel associated with the work and subsistence. In order to qualify for support, attendance at meetings or conferences must enhance the investigator's capability to perform the research, plan extensions of it, or disseminate its results. Consultant's travel costs also may be requested.

## **4.4 Foreign Travel**

Foreign travel is any travel outside Canada and the United States and its territories and possessions. Foreign travel may be approved only if it is directly related to project objectives.

## **4.5 Other Direct Costs**

The budget should itemize other anticipated direct costs not included under the headings above, including materials and supplies, publication costs, computer services, and consultant services (which are discussed below). Other examples are: aircraft rental, space rental at research establishments away from the institution, minor building alterations, service charges, and fabrication of equipment or systems not available off-the-shelf. Reference books and periodicals may be charged to the project only if they are specifically related to the research.

### **a. Materials and Supplies**

The budget should indicate in general terms the type of required expendable materials and supplies with their estimated costs. The breakdown should be more detailed when the cost is substantial.

### **b. Publication Costs/Page Charges**

The budget may request funds for the costs of preparing and publishing the results of research, including costs of reports, reprints page charges, or other journal costs (except costs for prior or early publication), and necessary illustrations.

### **c. Consultant Services**

Anticipated consultant services should be justified and information furnished on each individual's expertise, primary organizational affiliation, daily compensation rate and number of days expected service. Consultant's travel costs should be listed separately under travel in the budget.

### **d. Computer Services**

The cost of computer services, including computer-based retrieval of scientific and technical information, may be requested. A justification based on the established computer service rates should be included.

### **e. Subcontracts**

Subcontracts should be listed so that they can be properly evaluated. There should be an anticipated cost and an explanation of that cost for each subcontract. The total amount of each subcontract should also appear as a budget item.

## **4.6 Indirect Costs**

Explain the basis for each overhead and indirect cost. Include the current rates.