

## DEPARTMENT OF ENERGY

Office of Science Financial Assistance  
Program Notice 03-20; Low Dose  
Radiation Research Program—  
Biologically-Based Risk Modeling

AGENCY: Department of Energy.

ACTION: Notice inviting applications.

**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 applications 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 Application sections below for further details.

**DATES:** *Preapplications* (letters of intent) should be submitted by April 4, 2003. *Formal applications* 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:** *Preapplications* referencing Program Notice 03-20, should be sent to Ms. Joanne Corcoran by E-mail: [joanne.corcoran@science.doe.gov](mailto:joanne.corcoran@science.doe.gov), with a copy to Dr. Noelle Metting at: [noelle.metting@science.doe.gov](mailto:noelle.metting@science.doe.gov).

Formal applications referencing Program Notice 03-20 must be sent electronically by an authorized institutional business official through DOE's Industry Interactive Procurement System (IIPS) at: <http://e-center.doe.gov> (see also <http://www.sc.doe.gov/production/grants/grants.html>). IIPS provides for the posting of solicitations and receipt of applications in a paperless environment via the Internet. In order to submit applications through IIPS your business official will need to register at the IIPS website. The Office of Science will include attachments as part of this notice that provide the appropriate forms in PDF fillable format that are to be submitted through IIPS. Color images should be submitted in IIPS 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 them. They should be numbered and referred to in the body of the technical scientific application as Color image 1, Color image 2, etc. Questions regarding the operation of IIPS may be E-mailed to the IIPS Help Desk at:

[HelpDesk@pr.doe.gov](mailto:HelpDesk@pr.doe.gov), or you may call the help desk at: (800) 683-0751. Further information on the use of IIPS by the Office of Science is available at: <http://www.sc.doe.gov/production/grants/grants.html>.

If you are unable to submit the application through IIPS, please contact the Grants and Contracts Division, Office of Science at: (301) 903-5212, in order to gain assistance for submission through IIPS or to receive special approval and instruction on how to submit printed applications.

**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, DC 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 solicitation, applications 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