

**Program Announcement
To DOE National Laboratories
LAB 04-21**

***Low Dose Radiation Research Program
- Molecular Mechanisms and Pathways***

SUMMARY: The Office of Biological and Environmental Research (OBER) of the Office of Science (SC), U.S. Department of Energy (DOE) and the Office of Biological and Physical Research (OBPR), National Aeronautics and Space Administration (NASA), hereby announce their interest in receiving proposals for new research to develop a better scientific basis for understanding exposures and risks to humans from low doses or low fluences of ionizing radiation. Research must support the DOE/OBER Low Dose Radiation Research Program, and may include complementary research of direct interest to the NASA/OBPR Space Radiation Health Program of sufficient scientific merit to qualify for partial NASA support. To be considered for funding, research must focus on elucidating exact molecular mechanisms and pathways involved in radiobiological responses to low dose exposure; exclusively phenomenological studies will not be considered. Scientists working in rapidly developing areas of biological sciences not necessarily associated with the study of radiation are also encouraged to consider the contributions that their field of study can make. Research employing genome-wide or proteome-wide high-throughput screening methods is especially encouraged.

DOE/OBER also announces its interest in receiving proposals for special awards to support new collaborative work between two or more laboratories, one or more of which is already funded by the DOE Low Dose Program. These "glue awards" are primarily designed to support post-doctoral or graduate-student research that will enable laboratories with complementary expertise to develop and apply innovative new approaches to low dose research. **Please review the Supplementary Information sections below for further discussion of programmatic needs, and for details on format for the two types of proposals.**

DATES: Preproposals (letters of intent), including information on collaborators, areas of research, and a one-page summary of the proposed research, should be submitted by July 15, 2004.

Formal proposals submitted in response to this solicitation must be received by 4:30 p.m., Eastern Time, September 15, 2004, in order to be accepted for merit review and to permit timely consideration for award in Fiscal Year 2005.

ADDRESSES: Preproposals referencing Program Announcement LAB 04-21, should be sent to Ms. Kim Laing by E-mail: kim.laing@science.doe.gov, with a copy to Dr. Noelle Metting at: noelle.metting@science.doe.gov.

Formal proposals in response to Program Announcement LAB 04-21 are to be submitted as 2 paper copies of the proposal and one CD containing the proposal in PDF format. 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 2 copies of the proposal and the CD, referencing Program Announcement LAB 04-21, should be sent to: Ms. Joann Corcoran, Office of Biological and Environmental Research, SC-72, 19901 Germantown Road, Germantown, MD 20874-1290, ATTN: Program Announcement LAB 04-21.

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: Ms. Joann Corcoran, Office of Biological and Environmental Research, SC-72, Office of Science, U.S. Department of Energy, 19901 Germantown Road, Germantown, MD 20874-1290, ATTN: Program Announcement LAB 04-21.

FOR FURTHER INFORMATION CONTACT: Dr. Noelle Metting, telephone: (301) 903-8309, E-mail: 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. For specific information on NASA/OBPR interests, contact Dr. Walter Schimmerling, telephone (202) 358-2205, E-mail: wschimmerling@hq.nasa.gov, NASA Headquarters, Mail Code UB, Washington, DC 20546-0001.

SUPPLEMENTARY INFORMATION

I. Specifics for the Low Dose Radiation Research Program (DOE)

II. Specifics for Glue Awards (DOE)

III. Specifics for the Space Radiation Health Program (NASA)

I. Specifics for the Low Dose Radiation Research Program (DOE)

The DOE/OBER 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. This research program will be a success if the science it generates is useful to policy makers, standard setters, and the public. Successful researchers will be expected to effectively communicate research results through publication in peer-reviewed journals. Any data and results generated through the investigations that are appropriate to share with the broader scientific community should, where possible, be provided in a format amenable to deposition in databases. Successful researchers will also be encouraged to communicate with the wider community of concerned persons, so that current thinking and the public debate is better able to reflect sound science.

Mechanisms and Pathways. In order to be considered for this solicitation, the proposed project must focus on elucidating exact molecular mechanisms and pathways involved in radiobiological responses to low dose exposure. Proposals to perform exclusively phenomenological studies will not be considered for funding.

Gene knock-out or knock-in technologies have already shown usefulness in studies of protein function and molecular pathways; newer molecular techniques such as RNA interference, SAGE (serial analysis of gene expression), and other sequence-based approaches and proteomics techniques may also prove useful. Another approach for elucidation of molecular pathways might be to characterize topological, physical, and chemical characteristics that underlie cellular responses to low dose radiation exposures. Intracellular organization is undoubtedly necessary in order for the various cellular components to efficiently mediate their appropriate pathways. Hence, studies of cellular internal organization using existing technologies are encouraged.

The linkage of data from low dose experiments to downstream health outcomes that might occur in humans (e.g., carcinogenesis) has not yet been accomplished. Defining the patterns of expression and functions of genes from tissues or tissue constructs containing several different cell types, after low dose exposures, may be critical to making this linkage. Therefore, research projects that extend basic mechanistic research in simple *in vitro* systems to look at more complex cell microenvironments (thus leading to greater understanding of radiobiological responses in intact human tissue) are strongly encouraged.

Information on regulatory, metabolic, and signaling pathways is growing rapidly, and proposals should point out, wherever possible, how the proposed research might clarify or extend this information.

Doses and dose rates. DOE/OBER is chiefly concerned with very low doses of low Linear Energy Transfer (LET) radiation (high energy electrons and protons, x- and gamma-rays). The focus of research should be on doses of low LET radiation that are at or near current workplace exposure limits. In general, research in this program should focus on total radiation doses that are less than or equal to 10 rads (0.1 Gray). Some experiments will likely involve selected exposures to higher doses of radiation for comparisons with previous experiments or for determining the validity of extrapolation methods previously used to estimate the effects of low doses of radiation from observations made at high doses. Low dose rate studies are also desirable, but the total dose delivered must be low.

Not all research on the biological effects of low doses of radiation will be equally useful for the development of radiation risk policy, though the path from basic radiation biology research to radiation risk policy is admittedly not clear at this time. In the present context, the research considered to be most useful will focus on biological responses that are known to be induced at low doses of radiation, have the potential to directly impact (i.e., increase or decrease) subsequent development of cancer or other harmful health impacts, are quantifiable, could potentially be linked to the development of a biologically based model for radiation risk, and could potentially lead to the development of biological predictors (biomarkers) of individual risk.

Alternatively, a biological response of interest could meet all of the above criteria only at high doses but may actually be absent (as opposed to simply undetectable) at low doses of radiation. Since evidence is accumulating that the mechanisms of action after high doses of radiation may be different from the mechanisms of action after low doses, such studies would help define these mechanisms. Defining the doses where these mechanisms shift is of critical importance.

Keeping in mind the above statements of programmatic needs, suggested topics for which the Program desires additional research include, but are not limited to, endogenous oxidative damage versus low dose radiation-induced damage, radio-adaptive responses, bystander effects, and individual genetic susceptibility to low dose radiation exposure. A brief description of each follows:

a) Individual genetic susceptibility to low dose radiation. A major goal of the Low Dose Radiation Research Program is determining the existence of genetic differences that result in increased risk for radiation-induced cancer in sensitive individuals or sub-populations. Knowledge of genetic susceptibility is also one of the Critical Questions used by NASA to define research priorities; this knowledge is required to properly define individual radiation risk for spaceflight crew members. Accordingly, high priority will be given to support of research that seeks to identify patterns of genetic polymorphisms significantly impacting radiation sensitivity or resistance to low dose exposures, and to characterize their mechanism of action. The ability to exploit genome-wide or proteome-wide high-throughput screening methods that have a chance of ultimately detecting complex, multi-gene patterns indicative of or related to susceptibility is of particular interest. Radiation sensitivity is already well known in individuals with particular gene polymorphisms or mutations that affect one or more of their DNA repair systems. It is very likely that many other gene anomalies and combinations of anomalies will be found to be implicated in human susceptibility to disease

In addition to an individual's genetic makeup or genotype, carcinogenesis occurs as a function of all the forces and phenomena that go into the production of that individual's phenotype. These include current and historical aspects of diet, physical exercise, and exposures to chemicals and radiation. Where appropriate, research design should consider these and other external factors that could influence susceptibility to low doses of radiation.

A new resource that is now available to all Low Dose Program investigators, but might be of particular interest to those proposing research in the area of genetic susceptibility, is a tissue repository containing cells from patients who developed second cancers following total body irradiation and hematopoietic stem cell transplantation (HSCT). Presently there are EBV-transformed cell lines from 25 individuals exposed to radiation, which subsequently developed a skin tumor, and an equal number from exposed individuals that have not yet developed a second cancer. A much larger tissue resource will be available in the future. Please contact directly Dr. Jeffrey L. Schwartz, Associate Professor of Radiation Oncology, University of Washington, (206) 598-4091, E-mail: jschwart@u.washington.edu, for collaborative opportunities.

b) Endogenous oxidative damage in relation to low dose radiation induced damage. A key goal of this research program is the study of similarities and differences between endogenous oxidative damage and damage induced by low levels of ionizing radiation, in order to distinguish any associated health risks. This information will underpin our interpretation of all other biological effects of exposure to low doses of ionizing radiation. Although qualitative descriptions of differences and/or similarities between the

types of damage induced under both conditions have been useful in the design and interpretation of experiments in other parts of the program, there is also a need for quantification of the levels of damage induced by normal oxidative processes and incremental increases due to low dose irradiation.

c) Radio-Adaptive Response Induction. This is the ability of a low dose of radiation to induce cellular changes that alter the level of subsequent radiation-induced or spontaneous damage. New research is sought to characterize the exact molecular mechanisms that are involved in radiation induced adaptive response. There is overwhelming evidence that the phenomenon does exist, although its applicability to different cell tissue types has not been fully explored, nor has quantification over a range of priming doses, dose rates, and time constants of action been completed. Nevertheless, it is crucial to focus on mechanism. The presumed DNA damage sensors: poly(ADP-ribose) polymerase (PARP), DNA-dependent protein kinase (DNA-PK), the protein product of the ataxia telangiectasia mutated (ATM) gene, and the tumor suppressor, p53, have each been individually implicated in the induction pathway, as have such apoptosis-related enzymes as Ras, ceramid-activated protein kinase, phospholipase-C, and phosphatidylinositol 3-kinase. There is evidence that the final mode(s) of action could be DNA repair up-regulation, heightened immunity, and/or heightened anti-oxidant production. However, no clear consensus of opinion on the mechanisms of adaptive response has emerged. High priority will be given to studies to discover the exact molecular mechanisms involved in all steps of the induction of radio-adaptive response.

d) Bystander effects. These are biological responses observed in cells that are not directly traversed by radiation but are neighbors of an irradiated cell. New research is sought to characterize the exact molecular mechanisms that are involved in radiation induced bystander effects. Multiple studies of cell monolayers in a wide variety of human and rodent cell types and strains have presented clear evidence for an effect; bystander cells have already been shown to respond with gene induction and/or production of clastogenic changes such as mutations, sister chromatid exchanges, chromosomal aberrations, oncogenic transformation, and apoptotic cell death. However, ongoing studies are only beginning to address the issue of whether different levels of bystander effects occur in three-dimensional tissues in contrast to corresponding monolayer cultures. Hence, additional proposals that address effects in tissues, or in tissue-like models, will receive high priority. Investigators are also encouraged to propose bioimaging for in situ quantification in tissues

General information resources. Information on the Low Dose Radiation Research Program can be found on the web site: <http://lowdose.tricity.wsu.edu>. Prospective proposers are also encouraged to visit the National Center for Biotechnology Information (NCBI) website: <http://www.ncbi.nlm.nih.gov/>, for information on techniques and resources, and especially its Science Primer web site: <http://www.ncbi.nlm.nih.gov/About/primer/snps.html>, for an introduction to single nucleotide polymorphisms (SNPs).

The DOE Low Dose Program is currently funding several projects that have developed micro-irradiation devices capable of delivering low doses of low LET radiation to individual cells or to

specific parts of individual cells. Investigators are encouraged to use these irradiators, as appropriate, through collaborative means, and funds are available to assist in the collaborative use of these or comparable tools (see also the information on glue awards, below). Information on the microbeam irradiators can be found at: <http://lowdose.tricity.wsu.edu>.

II. Specifics for Glue Awards (DOE)

The Low Dose Radiation Research Program is also interested in receiving proposals for the purpose of supporting collaborative work between two laboratories, one of which should be currently funded by the Program. These small awards are primarily designed to support post-doctoral or graduate- student research that will enable laboratories with complementary expertise to develop and apply innovative or collaborative approaches to low dose research, although comparative studies between laboratories already using similar experimental approaches are also encouraged. At least one of the research partners must hold a DOE award focusing on low dose studies, and both research partners must have at least 1 year of support remaining on their core awards at the time of award (~November 2004). Collaborative glue awards can be set up with laboratories funded by such diverse agencies as DOE, NIH/NCI, NASA, DOD, EPA, the European Union, Canada, France, or Japan, but in any case the proposed research must be of interest to the DOE Low Dose Radiation Research Program. Proposals for these small awards should review the sections above on programmatic needs, and must also follow the instructions in IIPS for electronic submission. **Please note: the Project Description for the glue award proposal should not exceed ten pages.**

III. Specifics for the Space Radiation Health Program (NASA)

The NASA/OBPR Space Radiation Health Program is charged with providing input for the determination of health risks to humans visiting the space radiation environment. NASA is especially interested in human exposure to low fluences of high-energy particulate ionizing radiation (protons and heavy ions). Proposals whose principal focus is on low LET radiation are encouraged to include complementary research with high-energy particulate ionizing radiation that leverages progress, resources, and technology used for the low LET radiation research. Investigators with currently funded low dose projects may also apply for supplementary funding to address closely related research of interest to NASA.

The primary area of emphasis of the NASA/OBPR Space Radiation Health Program is the development of mechanistic insights into biological effects of space radiation that account for radiation risks. Proposals are required to be hypothesis-driven and are expected to obtain their data in ground-based experimental radiobiology studies with protons and high-energy heavy ion beams in the energy range corresponding to space radiation. This is mainly a ground-based program using accelerator facilities to simulate space radiation. In addition to the research topics already described above this includes research on non-phenomenological predictors of late cell and tissue effects and the control and modification of radiation effect mechanisms

A short description of the current Space Radiation Health Strategic Program may be found at: http://spaceresearch.nasa.gov/common/docs/1998_radiation_strat_plan.pdf. Activities of OBPR, including research opportunities, descriptions of previous tasks, and other relevant information

can be found at: <http://SpaceResearch.nasa.gov>. A description of the ground-based facilities and experimental program at Brookhaven National Laboratory can be found at: <http://server.c-ad.bnl.gov/esfd/nsrl/index.html>. The proton therapy facilities at Loma Linda University Medical Center are described at: <http://www.llu.edu/llu/ci/nasa/>. The critical questions of concern to NASA radiation research are part of the NASA Bioastronautics Critical Path Roadmap; it can be downloaded at: http://research.hq.nasa.gov/code_u/bcpr/index.cfm. Scientists working in rapidly developing areas of biological sciences not necessarily associated with the study of radiation are particularly encouraged to consider the contributions that their field of study can make to Radiation Health. Proposals are required to provide evidence for expertise in radiation, either by reference to the Principal Investigator's work or by inclusion of active collaborators expert in radiation research. Hypotheses should be substantiated by presentation of preliminary data wherever feasible, or by adequate references to the published literature. Experimental proposals should include a clear discussion of the relevant aspects of the required radiation dosimetry and an estimate of the statistical power of the expected results.

Research proposals to which NASA will assign high priority:

- a.** Studies that increase the confidence in the accuracy of extrapolating the probability of radiation-induced genetic alterations or carcinogenesis from rodents to humans.
- b.** Determination of carcinogenic risks following irradiation by protons and HZE particles.
- c.** Determination if exposure to heavy ions at the level that would occur in deep space poses a risk to the integrity and function of the central nervous system.
- d.** Studies likely to result in the development of biological countermeasures in humans that could lead to prevention or intervention (including genetic or pharmacological agents) against effects of radiation damage in space.

Research that can lead to future space flight investigations will be welcome, and should take into account the impact of gender, age, nutrition, stress, genetic predisposition, or sensitivity to other factors of importance in managing space radiation risks. However, it should be noted that this announcement does not solicit space flight experiments.

NASA envisions that the selected proposals will be structured and operated in a manner that supports the country's educational initiatives and goals (including historically black colleges and universities and other minority universities), and in particular the need to promote scientific and technical education at all levels. NASA envisions that the selected proposals will support the goals for public awareness and outreach to the general public. The selected investigators are invited to participate in NASA-funded educational programs.

The proposals represent an opportunity to enhance and broaden the public's understanding and appreciation of radiation effects, as specified in the DOE Low Dose Program emphasis on communication of research results and the OBPR Policy for Education and Public Outreach. Therefore, all investigators are strongly encouraged to promote general scientific literacy and public understanding of radiation induced health risk research through formal and/or informal education opportunities. If appropriate, proposals should include a clear and concise description of the education and outreach activities proposed. Examples include such items as involvement

of students in the research activities, technology transfer plans, and public information programs that will inform the general public of the benefits being gained from the research, and/or plans for incorporation of scientific results obtained into educational curricula consistent with educational standards.

Where appropriate, the supported institution will be required to produce, in collaboration with NASA, a plan for communicating to the public the value and importance of their work.

The particles of interest to the Space Radiation Health Program are protons with energies between 20 and 1000 MeV, and nuclei of elements with atomic numbers between He and Fe, with energies between 50 and 3000 MeV/nucleon. Fluences of interest are of the order of 1-2 particles per cell; studies with higher fluences will need to be justified by compelling arguments, including an explanation of how the results can be applied in the low fluence regime. NASA has developed facilities for use of protons at Loma Linda University Medical School and high-energy heavy ion beams at the NASA Space Radiation Laboratory (NSRL) at Brookhaven National Laboratory. Proposals should not budget for the use of beams at these facilities, which is paid by NASA. NASA will cooperate with DOE to provide the range of technical resources available for experimentation and analysis of experimental results at Brookhaven.

Program Funding

It is anticipated that \$2 million will be available from DOE/OBER for new basic research awards during FY 2005, contingent upon the availability of funds. Multi-year funding of awards is expected, and is also contingent upon the availability of appropriated funds, progress of the research, and continuing program need. Additional funds of up to \$0.5M will be available from NASA for joint funding of new research in Fiscal Year 2005, also contingent upon the availability of funds. Funds will be available from DOE to assist in the collaborative use of certain microbeam irradiators. NASA provides beam time at the NSRL and the Loma Linda proton accelerator; investigators will not be required to pay for the beam time. It is expected that most awards will be from 1 to 3 years and will range from \$100,000 to \$500,000 per year (total costs). Glue awards should range between \$75,000 and \$110,000 per year, and run from 1 to 3 years. DOE is under no obligation to pay for any costs associated with the preparation or submission of proposals if an award is not made.

Collaboration

Researchers are encouraged to collaborate with researchers in other institutions, such as universities, industry, non-profit organizations, federal laboratories and Federally Funded Research and Development Centers (FFRDCs), including the DOE National Laboratories, where appropriate, and to incorporate cost sharing and/or consortia wherever feasible. Additional information on collaboration is available in the Application Guide for the Office of Science Financial Assistance Program that is available via the Internet at: <http://www.sc.doe.gov/grants/Colab.html>.

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)**
- **Proposal Cover Page**
- **Project Abstract Page**; single page only, should contain:
 - Title
 - PI name
 - Abstract text should concisely describe the overall project goal in one sentence, and limit background/significance of project to one sentence. Short descriptions of each individual aim should focus on what will actually be done.
- **Relevance Statement**; single page only, should identify DOE- or NASA-relevant research that each specific aim is intended to address
- **Budget pages** for each year and a summary budget page for the entire project period (using DOE F 4620.1)
- **Budget Explanation**
- Budget pages and budget explanation for each **collaborative subproject**, if any.
- **Project Description, 20 pages or less**, exclusive of attachments. Proposals with Project Descriptions longer than 20 pages will be returned to researchers and will not be reviewed for scientific merit. (**NOTE: Project Descriptions for Glue Awards should not exceed 10 pages.**) The project description should be a clear statement of the work to be undertaken and should include: objectives for the period of the proposed work and expected significance; relation to the longer-term goals of the principal investigator of the project; and relation to the present state of knowledge in the field, to work in progress by the investigator under other support, and work in progress elsewhere. The statement should outline the general plan of work, including the broad design of experiments to be undertaken, and an adequate description of experimental methods and procedures.
- **Literature Cited**
- **Biographical Sketches** (please limit to 2 pages per senior investigator, consistent with NIH guidelines)
- **Facilities and Resources** description
- **Current and Pending Support** for each senior investigator
- **Letters of Intent** from collaborators (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 policy requires that potential researchers adhere to 10 CFR 745 "Protection of Human Subjects" 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/grants/Welfare.html>.

The instructions and format described below should be followed. Reference Program Announcement LAB 04-21 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. The following guidelines for content and format are intended to facilitate an understanding of the requirements necessary for SC to conduct a merit review of a proposal. Please follow the guidelines carefully, as deviations could be cause for declination of a proposal without 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 and the Department's programmatic needs. External peer reviewers are selected with regard to both their scientific expertise and the absence of conflict-of-interest issues. Non-federal reviewers may be used, and submission of an proposal constitutes agreement that this is acceptable to the investigator(s) and the submitting institution. Proposals found to be scientifically meritorious and programmatically relevant will be selected in consultation with DOE and NASA selecting officials depending upon availability of funds in each agency's budget. In the course of the selection process, projects will be identified as addressing DOE requirements, NASA requirements, or both. The selected projects will be

required to acknowledge support by one or both agencies, as appropriate, in all public communications of the research results.

2. Summary of Proposal Contents

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

2.1 Number of Copies to Submit

Formal proposals in response to Program Announcement LAB 04-21 are to be submitted as 2 paper copies of the proposal and one CD containing the proposal in PDF format. 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.

3. Detailed Contents of the Proposal

Proposals must be readily legible, when photocopied, and 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 Narrative

The narrative (Project Description) comprises the research plan for the project and is limited to 20 pages (10 pages for Glue Awards). It should contain the following subsections:

Background and Significance: Briefly sketch the background leading to the present proposal, critically evaluate existing knowledge, and specifically identify the gaps which the project is intended to fill. State concisely the importance of the research described in the proposal. Explain the relevance of the project to the research needs identified by the Office of Science. Include references to relevant published literature, both to work of the investigators and to work done by other researchers.

Preliminary Studies: Use this section to provide an account of any preliminary studies that may be pertinent to the proposal. Include any other information that will help to establish the experience and competence of the investigators to pursue the proposed project. References to appropriate publications and manuscripts submitted or accepted for publication may be included.

Research Design and Methods: Describe the research design and the procedures to be used to accomplish the specific aims of the project. Describe new techniques and methodologies and explain the advantages over existing techniques and methodologies. As part of this section, provide a tentative sequence or timetable for the project.

Subcontract or Consortium Arrangements: If any portion of the project described under "Research Design and Methods" is to be done in collaboration with another institution, provide information on the institution and why it is to do the specific component of the project. Further information on any such arrangements is to be given in the sections "Budget and Budget Explanation", "Biographical Sketches", and "Description of Facilities and Resources".

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.