Program Announcement
To DOE National Laboratories
LAB 01-18

Low Dose Radiation Research Program
Basic Research

The Office of Biological and Environmental Research (OBER) of the Office of Science (SC), U.S. Department of Energy (DOE), hereby announces their interest in receiving proposals for research that supports the DOE/OBER Low Dose Radiation Research Program.

Research is sought by the DOE/OBER Low Dose Radiation Research Program for studies involving low LET radiation, in the following areas:

(1) Bystander effects
(2) Genomic instability
(3) Adaptive responses
(4) Endogenous oxidative damage versus low dose radiation-induced damage
(5) Genetic factors that affect individual susceptibility to low dose radiation

Proposals for well-justified research in other areas (see Supplementary Information below) will also be accepted. These Programs use modern molecular tools to develop a better scientific basis for understanding exposures and risks to humans from low doses of low LET radiation that can be used to achieve acceptable levels of human health protection at a reasonable cost.

SUPPLEMENTARY INFORMATION:

Description of Research Program Areas

The DOE/OBER Low Dose Radiation Research Program is faced with 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. For the present solicitation, DOE/OBER is chiefly concerned with very **low doses** of low LET radiation (x and gamma rays). There are three biological responses of specific interest for this solicitation that are most likely to meet the criteria outlined below. These include bystander effects, induction of genomic instability, and adaptive responses. Proposals proposing the use of additional biological responses will be considered only if the biological responses proposed for investigation can be reasonably demonstrated to meet the criteria outlined below. All proposals focused on the characterization of

specific biological responses, e.g., bystander effects, etc., should identify how the response of interest meets these criteria. There is also considerable interest in determining whether these biological responses can be extended from studies in isolated cells to tissues or to more complex tissue-like systems. These responses are discussed here:

Bystander effects - *The biological response observed in cells that are not directly traversed by radiation but are neighbors of an irradiated cell.* Bystanders have been shown to respond with gene induction and/or production of potential genetic and carcinogenic changes. It is important for the DOE/OBER Low Dose program to determine if these so-called bystander effects can be induced by exposure to low LET (linear energy transfer) radiation delivered at low total doses or dose-rates. If such an effect is demonstrated and quantifiable, it could, potentially, increase estimates of risk from low dose radiation. This bystander effect, in essence, "amplifies" the biological effects (and the effective radiation dose) of a low dose exposure by effectively increasing the number of cells that experience adverse effects to a number greater than the number of cells directly exposed to radiation. Research is sought to:

- characterize the nature of bystander effects at low doses of low LET radiation
- determine the relationship between radiation dose and the bystander effects at low doses of low LET radiation
- quantify the induction and extent of the bystander effect at low doses of low LET radiation
- determine the mechanism of the low LET radiation-induced bystander effect

Genomic Instability - *The loss of genetic stability, a key event in the development of cancer, induced by radiation and expressed as genetic damage many cell divisions after the insult is administered.* Current evidence suggests that DNA repair and processing of radiation damage can lead to instability in the progeny of irradiated cells and that susceptibility to instability is under genetic control. However, there is virtually no information on the underlying mechanisms and how the processing of damage leads to instability in the progeny of irradiated cells several generations later. Further, while there has been considerable speculation about the role of such instability in radiation-induced cancer, its role in this process remains to be determined. Research is sought to:

- characterize the induction of genomic instability by low doses of low LET radiation
- determine the relationship between radiation dose and the induction of genomic instability by low doses of low LET radiation
- quantify the induction and extent of genomic instability induced by low doses of low LET radiation

- determine the mechanism for the induction of genomic instability by low LET radiation

Adaptive Response *- The ability of a low dose of radiation to induce cellular changes that perturb the level of subsequent radiation-induced or spontaneous damage.* If low doses of radiation regularly and predictably induce a protective response in cells to subsequent low doses of radiation, or to spontaneous damage, this could have a substantial impact on estimates of adverse health risk from low dose radiation. The generality and the extent of this apparent adaptive response in cells irradiated with small doses of ionizing radiation needs to be quantified. Studies of the adaptive response typically focus on cellular responses to high "test" doses of radiation following low "priming" doses. However, this solicitation is mainly interested in studying the lower limits for test doses and endpoints that show adaptive response phenomenon. Research is sought to:

- characterize the adaptive response induced by low doses of low LET radiation
- determine the relationship between radiation dose and the adaptive response induced by low doses of low LET radiation
- quantify the induction and extent of the adaptive response induced by low doses of low LET radiation
- determine the mechanism for the induction of adaptive responses by low LET radiation

In addition to the three specific biological responses just described, the Program has great interest in understanding endogenous versus low dose radiation induced damage, and the mechanisms underlying individual genetic susceptibility to radiation damage.

Endogenous versus low dose radiation induced damage. A key element of this research program will continue to be the development of an understanding of the similarities and differences between endogenous oxidative damage and damage induced by low levels of ionizing radiation, as well as an understanding of the health risks from both. This information will underpin our interpretation of the biological effects of exposure to low doses of ionizing radiation. Although always needed, this information was not previously attainable because critical resources and technologies were not available. Today, technologies and resources such as those developed as part of the human genome program, e.g., coupled capillary electrophoresis and mass spectrometry systems and DNA sequence information, have the potential to detect and characterize small differences in damage induced by normal oxidative processes and low doses of radiation. A significant investment in technology development will be required to expand current capabilities for identifying and quantifying small amounts of oxidative or radiation induced damage. Radically new technologies are likely not

needed but current technologies will need to be modified. Methodologies having high sensitivity as well as high signal-to-noise ratio will be critical in this effort.

A significant research effort will be required to characterize and quantify normal oxidative damage in cells and the incremental increases induced by low doses of ionizing radiation. Preference will be given to the formation of partnerships between laboratories involved in characterization and quantification of radiation and oxidative damage and groups with expertise in or developing new technology to facilitate progress in both areas simultaneously. Although qualitative descriptions of differences and/or similarities between the types of damage induced under both conditions will be useful in the design and interpretation of experiments in other parts of the program, levels of damage induced by normal oxidative processes and incremental increases due to low dose radiation should be quantified.

Genetic factors that affect individual susceptibility to low dose radiation. The Low Dose Radiation Research Program is interested in determining if genetic differences exist making some individuals more sensitive to radiation-induced damage since these differences could result in sensitive individuals or sub-populations that are at increased risk for radiation-induced cancer. Research should focus on:

- identification of genes involved in the recognition, repair, and processing of damage induced by ionizing radiation
- determining the frequencies of polymorphisms in these genes in the population
- determining the biological significance of these polymorphisms with respect to cancer and radiation sensitivity.

Research in these areas will strongly complement ongoing initiatives at the National Institutes of Health (NIH). DOE/OBER staff will work with staff at the NIH to ensure that research in the Low Dose Radiation Research Program is complementary to and not duplicative of research funded by NIH programs.

The National Human Genome Research Institute (NHGRI) is funding research to identify common variants in the coding regions of the majority of human genes identified during the next five years with the goal of developing a catalog of all common variants. The NHGRI is also working to create a map of at least 100,000 single nucleotide polymorphisms (SNPs), the most common polymorphisms in the human genome representing single base-pair differences between two copies of the same gene. These SNPs will be a boon for mapping complex traits such as cancer, cancer susceptibility, and susceptibility to low dose radiation.

The National Institute of Environmental Health Science (NIEHS) is funding research as part of its Environmental Genome Project to understand the impact and interaction

of environmental exposures on human disease. The NIEHS project includes efforts to understand genetic susceptibility to environmental agents that will allow more precise identification of the environmental agents that cause disease and the true risks of exposures. The principal focus of NIEHS research will be on chemicals, so the focus on radiation in the Low Dose Radiation Research Program is highly complementary. Initially, the Environmental Genome Project will focus on categories of genes including: xenobiotic metabolism and detoxification genes, hormone metabolic genes, receptor genes, DNA repair genes, cell cycle genes, cell death control genes, genes mediating immune and inflammatory responses, genes mediating nutritional factors, genes involved in oxidative processes and genes for signal transduction systems.

Identification of potential susceptibility genes and polymorphisms in those genes is only the first (and perhaps the easiest) step in the program to characterize and understand genetic susceptibility. Determining the biological significance of these genetic polymorphisms with respect to cancer and radiation sensitivity is the ultimate goal and the more difficult task. The international human genome project, structural biology research, and the NHGRI and NIEHS efforts described above play important roles determining which polymorphisms are most likely to influence gene function. Population genetics and computational biology approaches will be required to estimate the potential impact on estimates of population and individual risk. Genetic epidemiology approaches will also be needed to relate specific polymorphisms and combinations of polymorphisms with cancer risk. Inbred mouse strains and other model organisms with well- characterized differences in susceptibility to radiation-induced cancer are also important tools for identifying significant polymorphisms. Direct assessment of the biological significance of candidate "susceptibility genes" can also be undertaken using animal models such as knockout and knock-in mice, mice with specific genes removed or added.

Background information on the Low Dose Radiation Research Program can be found in the research program plan at http://www.lowdose.org/index.html. A list of currently funded projects can be found at http://lowdose.org/research.html.

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. It is our belief that the most useful research will focus on biological responses that:

- are known to be induced at low doses of radiation,
- have the potential to increase or decrease the biological effects of radiation if they occur at low doses of radiation,
- have the potential to directly impact (i.e., increase or decrease) the subsequent development of cancer or other harmful health impacts,

- are potentially quantifiable, and
- could potentially be linked to the development of a biologically based model for radiation risk (see DOE Office of Science Program Announcement LAB 01-17).

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 the mechanisms of action may be different after high versus low doses of radiation, such studies would help define these mechanisms. Defining the unique doses where these mechanisms shift is important.

The focus of research in the Low Dose Radiation Research Program should be on doses of low linear energy transfer (LET) radiation that are at or below 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.* 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. Research that principally focuses on radiation doses greater than 10 rads, high LET radiation or non-ionizing radiation will not be considered without substantial justification.

The program is currently funding a number of projects to develop micro-irradiation devices capable of delivering low doses of low LET radiation to individual cells or to specific parts of individual cells. For links to currently funded "microbeam" projects see http://lowdose.org/99meeting/abstracts/tool.html – projects 26, 28, 29 and http://lowdose.org/99meeting/abstracts/response.html – project 3. Investigators are strongly encouraged to use these or similar tools, as appropriate, in the design and conduct of their research. Funds are available to assist in the collaborative use of these or comparable tools or, in some cases, to provide low-cost micro-irradiation devices to individual investigators.

DATES: Potential proposers should submit a one page preproposal referencing Program Announcement LAB 01-18 by 4:30 P.M. E.S.T., February 15, 2001. Receipt of preproposals sent by email will be acknowledged by a return message. An E-mail response to preproposals discussing the potential program relevance of a formal proposal generally will be communicated by February 22, 2001.

The deadline for receipt of formal proposals is 4:30 P.M., E.D.T., May 15, 2001, in order to be accepted for merit review and to permit timely consideration for award in FY 2001 and FY 2002.

ADDRESS: Preproposals referencing Program Announcement LAB 01-18, should be sent by E-mail to joanne.corcoran@science.doe.gov. Preproposals will also be accepted if mailed to the following address: Ms. Joanne Corcoran, Office of Biological and Environmental Research, SC- 72, U.S. Department of Energy, 19901 Germantown Road, Germantown, MD 20874-1290.

Formal proposals, referencing Program Announcement LAB 01-18, should be sent to: U.S. Department of Energy, Office of Science, Grants and Contracts Division, SC-64, 19901 Germantown Road, Germantown, MD 20874-1290, ATTN: Program Notice 01-18. This address must be used when submitting proposals by U.S. Postal Service Express, commercial mail delivery service, or when hand carried by the proposer.

FOR FURTHER INFORMATION CONTACT: For general information, contact Dr. David Thomassen, telephone: (301) 903-9817, E-mail: david.thomassen@science.doe.gov, Office of Biological and Environmental Research, SC-72, U.S. Department of Energy, 19901 Germantown Road, Germantown, MD 20874-1290.

Program Funding

It is anticipated that up to $4.0 million will be available from DOE/OBER for new awards during FY 2001 and FY 2002, contingent upon the availability of funds. Multiple year funding of awards is expected, and is also contingent upon the availability of appropriated funds, progress of the research, and continuing program need. It is expected that most awards will be from 1 to 5 years and will range from $200,000 to $400,000 per year (total costs). Proposals requesting more than 3 years of funding will need to clearly justify the benefits of the additional years of research to the goals of the low dose radiation research program. Please note that funds are available from DOE to assist in the collaborative use of certain microbeam irradiators. 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

Proposers are encouraged to collaborate with researchers in other institutions, where appropriate.

Preproposal

A preproposal should be submitted. The Preproposal should contain a title, list of investigators, address, telephone, fax and E-mail address of the Principal Investigator, and no more than a one page summary of the proposed research, including project

objectives and methods of accomplishment. Responses to the preproposals, encouraging or discouraging formal proposals, will generally be communicated within 7 days of receipt. Notification of a successful preproposal is not an indication that an award will be made in response to the formal proposal.

Proposals

PLEASE NOTE CRITICAL INFORMATION BELOW ON PAGE LIMITS

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 Project Description must be 25 pages or less, exclusive of attachments. **Proposals with Project Descriptions longer than 25 pages will be returned to proposer** and will not be reviewed. The proposal must contain an abstract or project summary, letters of intent from collaborators, and short curriculum vitaes consistent with NIH guidelines.

Adherence to type size and line spacing requirements is necessary for several reasons. No proposers should have the advantage, or by using small type, of providing more text in their proposals. 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 proposer 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).

Proposers are expected to use the following ordered format to prepare proposals in addition to following instructions in the GUIDE FOR PREPARATION OF SCIENTIFIC/TECHNICAL PROPOSALS TO BE SUBMITTED BY NATIONAL LABORATORIES below. Proposals must be written in English, with all budgets in U.S. dollars.

- Face Page (DOE F 4650.2 (10-91)).
- Project Abstract (no more than one page).
- Budgets for each year and a summary budget page for the entire project period (using DOE F 4620.1).
- Budget Explanation.
- Budgets and Budget explanation for each collaborative subproject, if any.
- Project Description (The Project Description must be 25 pages or less, exclusive of attachments. Proposals with Project Descriptions longer than 25 pages will be returned to proposer and will not be reviewed.)
- Goals

- Background
- Research Plan
- Preliminary Studies and progress (if applicable)
- Research Design and Methodologies
- Literature Cited
- Collaborative Arrangements (if applicable)
- Biographical Sketches (limit 2 pages per senior investigator)
- Description of Facilities and Resources
- Current and Pending Support for each senior investigator

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.

The instructions and format described below should be followed. Reference Program Announcement LAB 01-18 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, 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
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

An original and seven copies of the formal proposal/FWP must be submitted.

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 comprises the research plan for the project and is limited to 25 pages. 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.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.