Program Announcement
To DOE National Laboratories
LAB 04-32

Genomics:GTL

SUMMARY: The Office of Biological and Environmental Research (OBER) and the Office of Advanced Scientific Computing Research (ASCR) of the Office of Science (SC), U.S. Department of Energy (DOE), hereby announce their interest in receiving proposals for research from large, well integrated, multidisciplinary research teams (see Supplementary Information below) that support the Genomics:GTL research program (http://www.doegenomestolife.org/). A central theme of the entire Genomics:GTL program is to develop the necessary experimental and computational capabilities to enable a predictive understanding of the behavior of microbes and microbial communities of interest to DOE. To this end, proposals that integrate strong experimental biology and computational science research components are strongly encouraged.

DATES: Statements of intent to apply, including information on collaborators and areas of proposed research and technology development should be submitted by Monday, October 25, 2004.

Formal research proposals are due by 4:30 PM Eastern Time Tuesday, January 18, 2005.

ADDRESS: Statements of intent to apply should be sent to Ms. Kim Laing by email at: kim.laing@science.doe.gov with copies to Dr. David Thomassen at: david.thomassen@science.doe.gov and Dr. Gary Johnson gary.johnson@science.doe.gov.

Formal proposals in response to Program Announcement LAB 04-32 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 04-32, 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 04-32.

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 04-32.

FOR FURTHER 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, SC-72/Germantown Building, 1000 Independence Avenue SW, Washington, DC 20585-1290 and Dr. Gary Johnson, telephone: (301) 903-5800, E-mail: gary.johnson@science.doe.gov, Office of Advanced Scientific Computing Research, SC-31/Germantown Building, 1000 Independence Avenue SW, Washington, DC 20585-1290.

SUPPLEMENTARY INFORMATION

This solicitation will support the establishment of large, well integrated, multidisciplinary (e.g., biology, computer science, mathematics, computational science, engineering, informatics, biophysics, biochemistry) research teams. Researchers are invited to include, where appropriate, partners from multiple institutions, including DOE National Laboratories, universities, private research institutions, and companies. Successful proposals will include a detailed management plan describing the responsibility of and relationship between all participating institutions and investigators, a strategy for maximizing communication and exchange of information between investigators, a data and information management plan, and project milestones.

Research partners at individual universities, private research institutions and companies, and DOE National Laboratories may be funded directly by DOE but will be reviewed as part of the overall research proposal submitted by the lead research institution. To facilitate funding of individual research partners each proposal should include a complete set of forms for each research institution as described in the instructions contained in the Grant Application Guide, available on the web at: http://www.science.doe.gov/grants/Colab.html. This includes:

- Appropriate Face Page for submitting institution
- Budgets for each year, (using DOE F 4620.1)
- Budget Explanation
- Biographical Sketches (limit 2 pages per senior investigator)
- Description of Facilities and Resources
- Current and Pending Support for each senior investigator
- Other institutional forms as described

Research partners at DOE National Laboratories do not need to complete a signed face page or the "other institutional forms" included in the Grant Application Guide.

Research Focus

Research funded here will cut across components of each of the goals described in the Genomics:GTL program plan, available on the web at: http://www.doegenomestolife.org and is intended to complement and advance ongoing research in the Genomics:GTL program (see http://www.doegenomestolife.org/research/index.shtml#research).

Microbes of Interest to DOE. The focus of Genomics:GTL is on nonpathogenic microbes (including fungi) directly relevant to DOE mission needs in energy (cleaner energy, biomass conversion, carbon sequestration, and the global carbon cycle both terrestrial and ocean) or the

environment (immobilization of metals and radionuclides at DOE sites). When possible, research should take advantage of and focus on microbes whose complete DNA sequence is already known or microbial communities of interest to, directly relevant to, or that would contribute substantially to an ability to address DOE mission needs. Researchers should identify proposed high throughput DNA sequencing needs, if any, in their proposal. Researchers should also provide a clear, scientifically justified description for their choice of microbe(s) in the context of DOE mission needs as outlined above.

Data and Other Results. Data and results that are generated through these investigations that are appropriate to share with the broader community should be provided in timely, open, and machine-readable format where possible. At a minimum, data should be freely distributed to academics, including the right to redistribute. Accepting a licensing agreement that requires proper attribution is allowable. Microbial DNA sequence data will be publicly released according to the "Data Release Requirements: Microbial Genome Sequencing Projects" (http://www.sc.doe.gov/production/ober/EPR/data.html). Research plans should be included that describe the procedures and policies the teams will institute to make the data and results available and interoperable with other significant sources of relevant data. Teams should be amenable to the adoption of open data standards and interoperability requirements, as they evolve and are specified by the Genomics:GTL program.

Software Development and Distribution. Software developed by research teams that is appropriate for distribution beyond the developing team shall be made available to the biological and computational community. It is the intent of the GTL Program that this software be accessible, useful, affordable, and interoperable with other software and data to the maximum extent possible. At a minimum, executables need to be distributed freely to academics. A licensing requirement for proper attribution prior to distribution is allowable. Proposals should include plans for assuring availability, stating whether: the software will be available as binary or source code, a fee will be charged for the use of the software, some users (e.g., commercial) will be charged while others not, in what way derivative products will be treated, etc. Statements such as that by the International Society for Computational Biology on Bioinformatics Software Availability, http://www.iscb.org/pr.shtml, may be used for reference.

High Throughput Analysis of Microbial Multi Protein Complexes.

The vast majority of the processes and functions of living systems involve the interactions of multiple proteins. In some cases proteins work in an independent yet coordinated manner. However, in many cases, likely the majority, proteins work as part of multi protein complexes comprised of small to large numbers of proteins and perhaps other molecules. Some complexes are tightly bound and others only loosely associated with components coupled for widely varying times. Understanding the role of individual proteins in a biological system and the overall processes and functions carried out by that system requires that we have the research tools to identify and characterize all of the multi protein complexes used by a given biological system to carry out its various processes and functions. We also need computational tools, based on experimental data that enable us to predict the functions and behaviors of complex biological systems beginning with genome sequence data.

Research is sought to demonstrate the feasibility of establishing high throughput approaches for the isolation and characterization of microbial multi protein complexes. Researchers should describe a strategy designed to increase the throughput of complex isolation and characterization in their research project so that:

- >5,000 attempts to isolate and analyze complexes per year are made after three to five years, and/or
- at least 85% of the stable multi protein complexes in a single microbe can be identified and characterized within a single year.

Researchers should consider the following items when preparing their proposals though it is not expected that all items will be included in a proposal, that all items will be given equal weight, or that this is an exclusive list of topics for consideration:

- Methods to quantitate a cell's proteins as a function of state or time.
- Alternative methods for isolating multi protein complexes since no single method is likely to be effective for all complexes.
- Methods for stabilizing the components of unstable complexes.
- Methods for identifying the individual components that comprise a complex.
- Methods for characterizing the stoichiometry of the components that comprise a complex.
- Strategies for determining whether all the individual components required for function are present in a complex following its isolation.
- Methods for isolating and characterizing difficult complexes such as those that are short-lived or that are found embedded in membranes.
- Methods for determining the overall quaternary structure of complexes (Note: it is not the intent of this solicitation to support research on high resolution atomic-level structure determination of individual proteins or multi protein complexes though established techniques may be used in a supporting role in proposed research).
- Experimental and computational methods for determining the function of complexes.
- Methods for determining the temporal and spatial relationships of complexes within microbial cells over time and under different conditions.
- Development of predictive models or "rule sets" that can be used to predict the number and nature of multi protein complexes that a microbe is likely to form based on its genome sequence.
- Strategies for automating the isolation and analysis of complexes.
- Strategies for managing data flow, data analysis, data sharing, and sample and process management.

Milestones of annual research progress and success as well as overall project milestones should be included as part of the research plan.

Genome-Scale Analysis of Biochemical Pathways in Microbes and Microbial Communities

Microbes have capabilities and carry out processes of direct interest and importance to DOE that include energy production, the remediation of contaminants found at former weapons sites, and their central role in the global carbon cycle. Microbes or microbial communities exist that:

- normally carry out these various functions with differing efficiencies;
- can be stimulated, with the addition of a simple nutrient for example, to carry out one of these functions much more efficiently than they normally do or under environmental conditions when these functions might normally be suppressed;
- can be modified or engineered genetically to carry out a completely new function or to carry out a function much more efficiently than they normally would or under conditions when it might normally be suppressed; or
- possess several complimentary pathways for performing identical or closely related functions and select among them for the most useful and efficient depending on environmental conditions.

In each of these cases we need to understand not only the molecular/biochemical pathways directly responsible for these functions but also regulatory mechanisms used to affect the activity levels of specific pathways of interest.

Experimental and computational research is sought that will provide the knowledge and tools needed to predict and reconstruct a microbe's regulatory networks for the control of multi protein complexes, for metabolic pathways, or for the entire organism beginning with knowledge of its DNA sequence. Similarly, research is sought that will provide the knowledge and tools needed to develop computational tools to predict the metabolic, physiologic, and behavioral characteristics of microbial communities from community DNA sequence data. Research is not being sought in this Notice to study the regulation or function of single or small numbers of genes or single metabolic pathways. Researchers should describe a strategy that will, within three to five years:

- enable the construction of a computational model for a microbe or microbial community's central metabolism within a few days or weeks after the genomic sequence has been determined;
- lead to the development of predictive and testable models of regulatory networks for key processes such as environmental sensing, contaminant processing, carbon dioxide fixation, cellulose degradation, or hydrogen or ethanol production for individual microbes or microbial communities.

Researchers should consider the following items when preparing their proposals, though it is not expected that all items will be included in a proposal, that all items will be given equal weight, or that this is an exclusive list of topics for inclusion:

- Methods for developing "simple" connection diagrams to understand dynamic regulatory interactions between different microbial proteins, multi protein complexes, and metabolic pathways.
- Methods for including a stoichiometric component in these "connection diagrams" including, for example, a link to quantitative proteomics or metabolomics.
- Use of traditional molecular tools, such as the generation of deletion mutants and high throughput genetics, in a high throughput format to develop accurate models of key biologic processes.
- Strategies for leveraging genome sequence information from closely related microbes to identify and characterize pathway and regulatory networks.

- Strategies that build and integrate models that represent varying levels of biological or biochemical detail.
- Methods grounded in genomic and/or proteomic analyses to develop predictive capabilities for phenotypic profiling of microbes and microbial communities.
- Strategies for using computational approaches to predict the effects of adding or removing specific components to or from pathways.
- Methods to image metabolites, proteins, protein complexes, community member interactions, and gene expression in microbial communities.
- Methods for coupling data at many scales, e.g., the functional characterization of a microbial community, field studies and characterization of the environment where the community is found.
- Strategies for verifying and validating models and model predictions.
- Strategies for managing data flow, data analysis, data sharing, and sample and process management.

Milestones of annual research progress and success as well as overall project milestones should be included as part of the research plan.

Computational methods and capabilities to advance understanding of complex biological systems and predict their behavior

A central goal of the Genomics:GTL program is to develop computational models that enable an accurate prediction of the behavior of microbes and microbial communities of interest to DOE. An inherent challenge in modeling biological complexity is to make use of the diversity and volume of data that will be available for inclusion in these models. This diversity and volume may soon confront our abilities to efficiently manage, query, and analyze the data. Data types include, but are not limited to, DNA sequence and annotation, gene expression, protein expression and modification, protein interactions, gene regulation, information related to cell and community metabolism, diverse imaging modalities, microbe-microbe interactions, microbe-environment interactions, and multiple environmental conditions all over diverse time scales. High throughput experimental strategies that are essential to the success of Genomics:GTL will also generate very large volumes of both raw and revised data, including DNA sequence, mass spectrometry, imaging, and many others, that will be difficult to manage given current capabilities.

Research is sought that will develop a model, or series of computational models, that captures the biological complexities of the salient functions of a microbial organism of DOE interest. As a part of the model development, a broad range of biological data is expected to be used. It is expected that this effort will be very closely coordinated with other research efforts that provide much of the experimental data to populate the model. Through the application of these diverse data to the development of models and through other means as necessary, the research team will collaborate with data providers to develop data management strategies for the biological data including interfaces, common ontologies, data standards, and other tools to help make the data accessible and useful to the broader biological community. There will be a particular emphasis on nascent sources of data that are likely to grow rapidly in volume and importance.

Development of these new models will require that researchers solve, in parallel, a number of algorithmic, mathematical, and computational challenges that currently impede progress in order to develop models for complex biological systems. As part of their research projects, researchers should consider finding solutions to some of the following challenges, though it is not expected that all items will be included in a proposal, that all items will be given equal weight, or that this is an exclusive list of topics for inclusion:

- New data storage solutions that can accommodate large and diverse data volumes and data types and that can provide rapid data analysis, query, retrieval, and transmission.
- Methods for data representations, standards, and controlled vocabularies for the diverse, bulk data types anticipated in Genomics:GTL, including, but not limited to, gene expression, imaging, mass spectrometry, metabolic profiling, DNA sequence and annotation.
- Development of new types of databases that can accommodate large data volumes, great schema complexity, and rapid query retrieval.
- New data analysis methods and algorithms that can accommodate large and diverse data volumes and data types as they are incorporated into new biological models.
- Strategies for integrating diverse data types, e.g., gene expression, imaging, mass spectrometry, metabolism, into common models and simulations.
- Strategies of incorporating new data, of types not previously integrated, into evolving models of biological processes and functions without starting model development anew.
- Strategies for dealing with incomplete, sparse, and potentially inaccurate data in biological models.
- Methods for visualizing complex and multi-dimensional data.

Proposals for this component of Program Announcement LAB 04-32 will not include a large, independent, laboratory-based research component. It is expected that researchers will interface their proposed modeling research with ongoing laboratory-based research projects, especially those funded by the Genomics:GTL program (http://www.doegenomestolife.org/research/index.shtml#research).

It is expected that some of the computational tools developed here will be executed on existing computer resources with little need for additional computational power. Other tools may require particularly compute-intensive resources. Special consideration will be given to the development of computational tools that can be ported across high- performance computing environments, including computing capabilities that are not yet available but are expected soon.

Appropriate attention should also be paid to attributes such as modularity, interoperability, and scalability.

Milestones of annual research progress and success as well as overall project milestones should be included as part of the research plan.

Program Funding

Up to $10 million of FY 2005 funds will be available, contingent upon availability of appropriated 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. It is anticipated that individual research awards for the first two components of this Notice (multi protein complexes and genetic regulatory network analysis) will be funded at a level of approximately $1-6 million per year (total costs) for 3 to 5 years and that research awards for the third component of this Notice (predictive model development) will be funded at a level of approximately $1-2 million per year (total costs) for 3 to 5 years. Researchers should also describe a scientifically justified scale-up plan to maximize technology development and research productivity.

Proposals

These large, multi investigator proposals will be reviewed as individual research projects consisting of several individual subprojects. The research description (see project description below) for individual subprojects should be no more than 20 pages each, exclusive of attachments. The combined research descriptions for all individual subprojects for each proposal should be no more than 100 pages, exclusive of attachments. In addition, each proposal should contain a project overview, not to exceed 20 pages, that contains an overall project summary, research integration plan, management plan, data and information management plan, and a communication plan. Each research team should identify a single scientific coordinator or point of contact for its proposal.

Each subproject description must contain an abstract or project summary on a separate page with the name of the researcher, mailing address, phone, Fax, and E-mail listed. Each project must include letters of intent from outside collaborators briefly describing the intended contribution of each to the research and short curriculum vitaes, consistent with National Institutes of Health (NIH) guidelines, for all principal investigators and any co-PIs.

Adherence to type size and line spacing requirements is necessary for several reasons. No researcher 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 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). DOE is under no obligation to pay for any costs associated with the preparation or submission of proposals if an award is not made.

Researchers are expected to use the following ordered format to prepare proposals in addition to following instructions listed below in the Guide for Preparation of Scientific/Technical Proposals to be submitted by National Laboratories. Proposals must be written in English, with all budgets in U.S. dollars.

- **Field Work Proposal (FWP) Format** (Reference DOE Order 5700.7C) (DOE ONLY)
- **Proposal Cover Page**
- **Table of Contents**

- **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** (includes goals, background, research plan, preliminary studies and progress, and research design and methodologies)
    - 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.

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 04-32 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

In addition, proposals will be evaluated for the robustness of their organizational framework and coordination plan.

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 a proposal constitutes agreement that this is acceptable to the investigator(s) and the submitting institution.

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 04-32 are to be submitted as 2 paper copies of the proposal and 1 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

Adherence to type size and line spacing requirements is necessary for several reasons. No researcher 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 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).

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 Budget and Budget Explanation

A detailed budget is required for the entire project period 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.

It is anticipated that individual research awards for the first two components of this Notice (multi protein complexes and genetic regulatory network analysis) will be funded at a level of approximately $1-6 million per year (total costs) for 3 to 5 years and that research awards for the third component of this Notice (predictive model development) will be funded at a level of approximately $1-2 million per year (total costs) for 3 to 5 years. Researchers should also describe a scientifically justified scale-up plan to maximize technology development and research productivity.

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

3.6 Project Description

These large, multi investigator proposals will be reviewed as individual research projects consisting of several individual subprojects. The project description for individual subprojects should be no more than 20 pages each, exclusive of attachments. The combined research descriptions for all individual subprojects for each proposal should be no more than 100 pages, exclusive of attachments. In addition, each proposal should contain a project overview, not to exceed 20 pages, that contains an overall project summary, research integration plan, management plan, data and information management plan, and a communication plan. Each research team should identify a single scientific coordinator or point of contact for its proposal.

Each subproject description must contain an abstract or project summary on a separate page with the name of the researcher, mailing address, phone, Fax, and E-mail listed. Each project must include letters of intent from outside collaborators briefly describing the intended contribution of each to the research and short curriculum vitaes, consistent with National Institutes of Health (NIH) guidelines, for all principal investigators and any co-PIs.

The Project Description 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".

3.7 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.

3.8 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.

3.9 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.

3.10 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.

3.11 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.