Biological and Environmental Research

Funding Profile by Subprogram

(dollars in thousands)

	FY 2003 Comparable Appropriation	FY 2004 Original Appropriation	FY 2004 Adjustments	FY 2004 Comparable Appropriation	FY 2005 Request
Biological and Environmental Research					
Life Sciences	181,803	205,913	-1,222[a]	204,691	204,011
Climate Change Research	122,182	142,959	-845[a]	142,114	142,959
Environmental Remediation	101,375	108,930	-622[a]	108,308	105,522
Medical Applications and Measurement Science	89,000	134,198	+52,143[ab]	186,341	44,098
Subtotal, Biological and Environmental Research	494,360	592,000	+49,454[ab]	641,454	496,590
Construction	0	0	0	0	5,000
Subtotal, Biological and Environmental Research	494,360	592,000	+49,454[ab]	641,454	501,590
Use of Prior Year Balances	0	-1,930	0	-1,930	0
Total, Biological and Environmental Research	494,360[cdef]	590,070	+49,454[ab]	639,524	501,590

Public Law Authorization:
Public Law 95-91, “Department of Energy Organization Act”

[a] Excludes $3,795,588 for a rescission in accordance with the Consolidated Appropriations Act, 2004, as reported in conference report H. Rpt. 108-401, dated November 25, 2003, as follows: Life Sciences $-1,221,588; Climate Change Research $-845,000; Environmental Remediation $-622,000; and Medical Applications and Measurement Science $-1,107,000.

[b] Includes $53,250,000 provided by the Consolidated Appropriations Act, 2004.

[c] Excludes $12,139,000 which was transferred to the SBIR program and $728,000 which was transferred to the STTR program.

[d] Excludes $3,424,284 for a rescission in accordance with the Consolidated Appropriation Resolution, FY 2003.

[e] Includes $3,585,770 for the Emergency Wartime Supplemental Appropriations for FY 2003.

[f] Excludes $19,748,000 transferred for Department of Homeland Security activities in FY 2003.

Mission

For over 50 years the Biological and Environmental Research (BER) program has been advancing environmental and biomedical knowledge that promotes national security through improved energy production, development, and use; international scientific leadership that underpins our Nation's technological advances; and research that improves the quality of life for all Americans. BER supports these vital national missions through competitive and peer-reviewed research at national laboratories, universities, and private institutions. In addition, BER develops and delivers the knowledge needed to support the President's National Energy Plan.

Benefits

BER supports DOE's mission of world-class scientific research capacity by providing world-class, peer-reviewed scientific results in biology and environmental science. Basic biological and environmental research has broad impacts on our health, our environment, and our energy future. An ability to predict long-range and regional climate enables effective planning for future needs in energy, agriculture, and land and water use. Biotechnology solutions are possible for DOE energy, environmental, and national security challenges by understanding complex biological systems and developing computational tools to model and predict their behavior. Understanding the global carbon cycle and the associated role and capabilities of microbes and plants can lead to solutions for reducing carbon dioxide concentrations in the atmosphere. Biological solutions can be developed to help clean up metals and radionuclides contaminating former DOE weapons sites. Both normal and abnormal health—from normal human development to cancer to brain function—can be understood using radiotracers and advanced imaging instruments. Understanding the biological effects of low doses of radiation can lead to the development of science-based health risk policy to better protect workers and citizens.

Strategic and Program Goals

The Department's Strategic Plan identifies four strategic goals (one each for defense, energy, science, and environmental aspects) of the mission plus seven general goals that tie to the strategic goals. The BER program supports the following goal:

Science Strategic Goal
General Goal 5, World-Class Scientific Research Capacity: Provide world-class scientific research capacity needed to ensure the success of Department missions in national and energy security, to advance the frontiers of knowledge in physical sciences and areas of biological, medical, environmental, and computational sciences, and to provide world-class research facilities for the Nation's science enterprise.

The BER program has one program goal which contributes to General Goal 5 in the "goal cascade."

Program Goal 05.21.00.00: Harness the Power of Our Living World – Provide the biological and environmental discoveries necessary to clean and protect our environment, offer new energy alternatives, and fundamentally alter the future of medical care and human health.

Contribution to Program Goal 05.21.00.00 (Harness the Power of Our Living World)

Within the Biological and Environmental Research (BER) program, the Life Sciences, Climate Change Research, Environmental Remediation, and Medical Applications and Measurement Science subprograms contribute to Program Goal 05.21.00.00 by advancing fundamental research in climate

change, environmental remediation, genomics, proteomics, radiation biology, and medical applications. BER supports leading research programs that provide world-class, peer-reviewed research results. Discoveries at these frontiers in science will bring revolutionary and unconventional solutions to some of our most pressing and expensive challenges in energy and the environment. We will understand how living organisms interact with and respond to their environments to be able to use biology to produce clean energy, remove excess carbon dioxide from the atmosphere, and help clean up the environment.

Our understanding of global climate change and our ability to predict climate over decades to centuries will enable us to develop science-based solutions to reduce and minimize the impacts of climate change and to better plan for our Nation's future energy needs. Understanding the biological effects of low doses of radiation will lead to the development of science-based health risk policy to better protect workers and citizens. BER will lead the way in discovering innovative approaches along unconventional paths to energy independence and environmental cleanup.

Building on this work, BER develops novel radiopharmaceuticals to image defective genes that cause disease. In addition, research advances the development of a broad range of intelligent biomimetic electronics that can both sense and correctly stimulate the nervous system, e.g., an artificial retina that will enable the blind to read large print and devices that restore neurosensory and motor function to the paralyzed (spinal cord recovery, hearing, bladder control, etc.). This effort builds on leading research programs that provide world-class, peer-reviewed research results. The research capitalizes on the National Laboratories' unique resources and expertise in biological, chemical, physical, and computational sciences for technological advances related to human health. The National Laboratories have highly sophisticated instrumentation (neutron and light sources, mass spectroscopy, and high field magnets), lasers and supercomputers that directly impact research on human health. This research is highly complementary to and coordinated with clinical research at the National Institutes of Health (NIH) and to basic research in the NIH intramural and extramural programs.

In addition, BER plans, constructs, and operates reliable, world-class scientific facilities to serve thousands of researchers at universities, national laboratories, and private institutions from all over the world. Activities include structural biology research beam lines at the synchrotron light sources and neutron sources; the operation of the William R. Wiley Environmental Molecular Sciences Laboratory (EMSL) (including the Molecular Sciences Computing Facility) where research activities underpin long-term environmental remediation and other DOE missions in energy and national security; the Production Genomics Facility and the Laboratory for Comparative and Functional Genomics ("Mouse House"); and the climate change research facilities – the Atmospheric Radiation Measurement (ARM) and the Free-Air Carbon Dioxide Enrichment (FACE) facilities.

The following indicators establish specific long term goals in Scientific Advancement that the BER program is committed to, and progress can be measured against.

- **Life Sciences:** Characterize the multi protein complexes (or the lack thereof) involving a scientifically significant fraction of a microbe's proteins. Develop computational models to direct the use and design of microbial communities to clean up waste, sequester carbon, or produce hydrogen.
- **Climate Change Research:** Deliver improved climate data & models for policy makers to determine safe levels of greenhouse gases for the Earth system. By 2013, substantially reduce differences between observed temperature and model simulations at subcontinental scales using several decades of recent data.

- **Environmental Remediation:** Develop science-based solutions for cleanup and long-term monitoring of DOE contaminated sites. By 2013, a significant fraction of DOE's long-term stewardship sites will employ advanced biology-based clean up solutions and science-based monitors.
- **Medical Applications and Measurement Science:** Develop intelligent biomimetic electronics that can both sense and correctly stimulate the nervous system and new radiopharmaceuticals for disease diagnosis.
- **Facilities:** Manage facilities operations to the highest standards of overall performance using merit evaluation with independent peer review.

Annual Performance Results and Targets

FY 2000 Results	FY 2001 Results	FY 2002 Results	FY 2003 Results	FY 2004 Targets	FY 2005 Targets
Program Goal 05.21.00.00 (World-Class Scientific Research Capacity)					
Life Sciences					
Increase the rate of DNA sequencing: Sequence the genome of 1microbe. [Met Goal]	Increase the rate of DNA sequencing: Produce at least 5.8 billion base pairs of high quality DNA microbial and model organism genome sequence. [Met Goal]	Increase the rate of DNA sequencing; Produce at least 12.7 billion base pairs of high quality DNA microbial and model organism genome sequence. [Met Goal]	Increase the rate of DNA sequencing: Produce at least 14 billion base pairs of high quality DNA microbial and model organism genome sequence. [Met Goal]	Increase the rate of DNA sequencing: Produce at least 20 billion base pairs of high quality DNA microbial and model organism genome sequence.	Increase the rate of DNA sequencing: Produce at least 20 billion base pairs of high quality DNA microbial and model organism genome sequence.
Climate Change Research					
Improve climate models: Demonstrated that a coupled climate model consisting of combined atmospheric and ocean general circulation models more accurately simulates the present climate compared to that simulated by uncoupled atmospheric general circulation models alone. [Met Goal]	Improve climate models: Documented consistency between observed temperature changes in the atmosphere and ocean and model simulated temperature changes using the Parallel Climate Model designed to run on the massively parallel computers at DOE laboratories. [Met Goal]	Improve climate models: Released a new coupled climate model with a horizontal resolution of 2.8 degrees (longitude and latitude) in the atmosphere and 0.7 degrees in the ocean and sea ice components, compared to the previous version with a resolution of 2.8 degrees in the atmosphere and 2.0 degrees in the ocean. Executed an 800-year equilibrium climate simulation with the new model. [Met Goal]	Improve climate models: Constructed a climate model for the next round of IPCC Working Group 1 Assessment simulations. This model increased the realism of the coupled atmosphere-ocean-land surface-sea ice system through improvements in the physical parameterizations, particularly the cloud sub models. The standard model increased the horizontal resolution to 1.4 degrees in the atmosphere and maintained the 0.7 degree resolution in the ocean and sea ice components. More objective and systematic methods to test (evaluate) the performance of both the model components (i.e., atmosphere, ocean, land surface, and sea ice sub models) as well as the fully coupled model were applied. [Met Goal]	Improve climate models: Implement a model test bed system to incorporate climate data rapidly into climate models to allow testing of the performance of sub models (e.g. cloud resolving module) and model parameters by comparing model simulations with real world data from the ARM sites and satellites.	Improve climate models: Develop a coupled climate model with an interactive carbon cycle, a sub model of secondary sulfur aerosols, and an interactive terrestrial biosphere. This capability will enable studies of the interactions between the carbon cycle and climate and between secondary sulfur aerosols and climate. It will also provide a tool to quantify potentially important feedbacks between the climate system and the terrestrial biosphere.

FY 2000 Results	FY 2001 Results	FY 2002 Results	FY 2003 Results	FY 2004 Targets	FY 2005 Targets
Environmental Remediation					
Determine scalability of laboratory results in field environments: Demonstrated that common bacteria can reduce and immobilize contaminants such as uranium, technetium, and chromium in subsurface environments. [Met Goal]	Determine scalability of laboratory results in field environments: Demonstrated that uranium concentrations in groundwater can be significantly decreased using bioremediation at the Field Research Center at ORNL. [Met Goal]	Determine scalability of laboratory results in field environments: Using genomic sequencing data of key bioremediation microbes, such as Geobacter, Deinococcus, and Shewanella, determined that common soil microbes produce organic compounds that interact with radionuclides, such as plutonium, providing the molecular understanding for the detection and transformation of radionuclides in subsurface environments. [Met Goal]	Determine scalability of laboratory results in field environments: Identified naturally occurring microbial populations responsible for transformation of metals and radionuclides at DOE contaminated sites. [Met Goal]	Perform combined field/laboratory/modeling to determine how to interpret data at widely differing scales: Quantify contaminant immobilization and remobilization by different factors: 1. natural microbial mechanisms; 2. chemical reactions with minerals, and 3. colloid formation.	Determine scalability of laboratory results in field environments – Determine actual in-situ rate of metal reduction in subsurface environments and begin to develop a numerical model to describe and predict these rates.
Medical Applications and Measurement Science					
Advance blind patient sight: Developed technology for application of a novel hermetic seal to protect artificial retina device when inserted into the eye of a human patient. [Met Goal]	Advance blind patient sight: Developed an in vitro testing system to test all prototype artificial retina devices for safety before inserting device into a human eye. [Met Goal]	Advance blind patient sight: Developed technology to micromachine new flexible biocompatible material to be used as a platform for multi-electrode array artificial retina. [Met Goal]	Advance blind patient sight: Developed and tested materials for platform and sealants for a prototype artificial retina- a microelectronic array to be used for the treatment of blindness. [Met Goal]	Advance blind patient sight: Complete fabrication of 60 microelectrode array for use as an artificial retina and tested in animal subject.	Advance blind patient sight: Complete testing on a 60 microelectrode array artificial retina and insert prototype device into a blind patient.
All BER Facilities (Efficiency Measure)					
Maintain and operate BER facilities such that achieved operation time is on average greater than 90% of the total scheduled annual operation time. [Met Goal]	Maintain and operate BER facilities such that achieved operation time is on average greater than 90% of the total scheduled annual operation time. [Met Goal]	Maintain and operate BER facilities such that achieved operation time is on average greater than 90% of the total scheduled annual operation time. [Met Goal]	Maintain and operate BER facilities such that achieved operation time is on average greater than 90% of the total scheduled annual operation time. [Met Goal]	Maintain and operate BER facilities such that achieved operation time is on average greater than 90% of the total scheduled annual operation time.	Maintain and operate BER facilities such that achieved operation time is on average greater than 90% of the total scheduled annual operation time.

Means and Strategies

The BER program will use various means and strategies to achieve its program goals. However, various external factors may impact the ability to achieve these goals.

The BER program supports fundamental, innovative, peer-reviewed research to create new knowledge in areas important to the BER mission, i.e., Life Sciences, Climate Change Research, Environmental Remediation, and Medical Applications and Measurement Science. The BER program will continue its investments in core fundamental science and technologies needed to address the interfaces between scientific disciplines such as biology, physics, chemistry, engineering, and information science. Of highest priority will be the development of a new research infrastructure needed to understand fundamental biological principles underlying the function and control of biological systems. A combination of novel, state-of-the-science user facilities coupled with large, well-integrated, interdisciplinary research teams will form the basis of a new approach for studying complex biological systems and for using those systems to solve critical problems in energy and environmental cleanup. Our ability to predict climate on global and regional scales and to develop strategies for the removal of excess carbon dioxide, believed to adversely impact global climate, from the atmosphere will depend on the continued development of novel research tools and a close integration of experimental and computational research. BER also plays a key role in constructing and operating a wide array of biological and environmental user facilities for the Nation's researchers. BER Medical Applications and Measurement Science research capitalizes on the National Laboratories' unique resources and expertise in biological, chemical, physical, and computational sciences for technological advances related to human health. The National Laboratories have highly sophisticated instrumentation that directly impact research on human health. Research is directed to fundamental studies in biological and medical imaging (including construction of the artificial retina), biological and chemical sensors, laser medicine, and informatics.

All BER-supported research projects undergo regular peer review and merit evaluation based on procedures set down in 10 CFR 605 for the extramural grant program, and under a similar process for the laboratory programs and scientific user facilities. All new projects are selected through peer review and merit evaluation.

External factors that affect the programs and performance include: (1) mission needs as described by the DOE and SC mission statements and strategic plans; (2) evolving scientific opportunities, which sometimes emerge in a way that revolutionizes disciplines; (3) results of external program reviews and international benchmarking activities of entire fields or sub fields, such as those performed by the National Academy of Sciences; (4) unanticipated failures, for example, in critical components of scientific user facilities that cannot be mitigated in a timely manner; and (5) strategic and programmatic decisions made by other (non-DOE) Federal agencies and by international entities.

The BER program is closely coordinated with the activities of other federal agencies (e.g., National Institutes of Health, National Science Foundation (NSF), National Aeronautics and Space Administration (NASA), Department of Commerce/National Oceanic and Atmospheric Administration (NOAA), Environmental Protection Administration (EPA), Department of Agriculture, and Department of Defense). BER Climate Change Research is coordinated with the U.S. Global Change Research Program, an interagency program codified by Public Law 101-606 and involving thirteen federal agencies.

BER also promotes the transfer of the results of its basic research to contribute to DOE missions in areas of future energy sources, improved use of fossil fuels (carbon sequestration), and reduced environmental impacts of energy production and use.

Validation and Verification

Progress against established plans is evaluated by periodic internal and external performance reviews. These reviews provide an opportunity to verify and validate performance. Quarterly, semiannual, and annual reviews consistent with specific program management plans are held to ensure technical progress, cost and schedule adherence, and responsiveness to program requirements.

Program Assessment Rating Tool (PART) Assessment

The Department implemented a tool to evaluate selected programs. PART was developed by OMB to provide a standardized way to assess the effectiveness of the Federal Government's portfolio of programs. The structured framework of the PART provides a means through which programs can assess their activities differently than through traditional reviews. The Biological and Environmental Research (BER) program has incorporated feedback from OMB into the FY 2005 Budget Request and has taken, or will take, the necessary steps to continue to improve performance.

In the PART review, OMB gave the Biological and Environmental Research (BER) program a high score of 86% overall which corresponds to a rating of "Effective." OMB found that the program is well coordinated with other federal research agencies, uses targeted grant solicitations that convey the long-term goals of the program, and funds high risk research that regularly delivers important results. Although BER is establishing a Committee of Visitors (COV), to provide outside expert validation of the program's merit-based review processes for impact on quality, relevance, and performance, this committee has not yet met. Once the COV issues a report, BER will develop an action plan to respond to the findings and recommendations within 30 days. The assessment found that BER has developed a limited number of adequate performance measures. However, OMB noted concerns regarding the collection and reporting of performance data. To address these concerns, BER will work with its Advisory Committee to develop research milestones for the long-term performance goals, will work to improve performance reporting by grantees and contractors, and will work with the CFO to improve BER sections of the Department's performance documents. BER's role in providing scientific research facilities is strongly supported by the Administration. Funding is provided in FY 2005 to operate the program's facilities at maximum capacity.

Funding by General and Program Goal

(dollars in thousands)

	FY 2003	FY 2004	FY 2005	$ Change	% Change
General Goal 5, World-Class Scientific Research Capacity					
Program Goal 05.21.00.00 Harness the Power of Our Living World					
Life Sciences	181,803	204,691	204,011	-680	-0.3%
Climate Change Research	122,182	142,114	142,959	+845	+0.6%
Environmental Remediation	101,375	108,308	105,522	-2,786	-2.6%
Medical Applications and Measurement Science	89,000	186,341	44,098	-142,243	-76.3%
Construction (PED)	0	0	5,000	+5,000	+100.0%
Total, Program Goal 05.21.00.00 Harness the Power of Our Living World	494,360	641,454	501,590	-139,864	-21.8%
Use of Prior Year Balances	0	-1,930	0	+1,930	+100.0%
Total, Biological and Environmental Research	494,360	639,524	501,590	-137,934	-21.6%

Overview

The BER program supports fundamental research in climate change, environmental remediation, genomics, proteomics, radiation biology, and medical sciences. BER supports leading edge research facilities used by public and private sector scientists across the range of BER disciplines. BER works with other federal agencies to coordinate research across all of its programs. BER validates its long-range goals through its advisory committee, the Biological and Environmental Research Advisory Committee (BERAC).

The Opportunity

With the 21st Century dawns what many have called the "biological century"–an era when advances in biology, spurred by achievements in genomic research, including the sequencing of the human genome, will bring revolutionary and unconventional solutions to some of our most pressing and expensive challenges in health, energy, the environment, and national security. We will understand how living organisms interact with and respond to their environments so well that we will be able to use biology to produce clean energy, remove excess carbon dioxide from the atmosphere, and help clean up the environment. Our understanding of climate change and our ability to predict climate over decades to centuries will enable us to develop science-based solutions to reduce and minimize the impacts of climate change and to better plan for our Nation's future energy needs. BER will lead the way in discovering innovative approaches along unconventional paths to energy independence and environmental cleanup.

The Challenges

Understanding and predicting climate – Can we understand the factors that determine Earth's climate well enough so that we can predict climate decades to centuries in the future? Advanced climate models are needed to describe and predict the roles of oceans, the atmosphere, sea ice and land masses on climate. So too, the role of clouds in controlling solar and terrestrial radiation onto and away from the Earth needs to be better understood since it is the largest uncertainty in climate prediction. Moreover, the

impacts of excess carbon dioxide in the atmosphere from human sources, including energy use, on Earth's climate and ecosystems need to be determined and possible mitigation strategies developed.

A cleaner environment – Microbes have a remarkable capacity to thrive in almost every environment imaginable, even when heavily contaminated. Can we use nature's own solutions to clean up sites contaminated from years of weapons research? These solutions seem ever closer as we study the molecular details of nature's own cleanup strategies.

Technology for a healthier Nation – At the crossroads of the physical and biological sciences is the promise of remarkable technology for tomorrow's medicine. Developments in imaging technology have the potential to revolutionize all of medical imaging with increases in sensitivity, ease of use, and patient comfort. Technological wonders are on the horizon, like an artificial retina that will give vision to the blind.

A new biology – Can we understand the workings of biological systems well enough so that we can use nature's own principles of design to solve energy and environmental challenges? Understanding nature's array of multi protein molecular machines, each with exquisitely precise and efficient functions and controls, will enable us to use and even redesign these molecular machines to address DOE and national needs.

The Investment Plan

BER will continue its investments in core technologies and fundamental science needed to address these daunting challenges. We believe that the most important scientific advances in the 21st century will occur at the interfaces between scientific disciplines such as biology, physics, chemistry, engineering, and information science. BER investments at these interfaces will enable: (1) the development of a new research infrastructure for understanding the function and control of biological systems that can be used to solve critical problems in energy and the environment; (2) an improved ability to predict climate on global and regional scales; (3) development of strategies to remove excess carbon dioxide from the atmosphere; (4) new science-based strategies for the clean up and long-term monitoring of the environment; and (5) the development of unique devices and technologies for the medical community that improve our Nation's health.

How We Work

BER uses a variety of mechanisms to conduct, coordinate, and fund biological and environmental research. BER is responsible for planning and prioritizing all aspects of supported research, for conducting ongoing assessments to ensure a comprehensive and balanced portfolio that addresses DOE and national science needs, and for coordinating its research programs with those of other federal agencies. BER regularly seeks advice on its research programs from the scientific community and from its diverse stakeholders. BER supports research at national laboratories, universities, research institutes, and in private companies, and maintains a strong research infrastructure across the biological and environmental sciences most relevant to the BER program.

Advisory and Consultative Activities

To ensure that resources are allocated to the most scientifically relevant and promising research, BER actively seeks external input using a variety of advisory bodies. BER regularly compares its programs to the scientific priorities recommended by the BERAC and by the standing committees created by the Office of Science and Technology Policy (OSTP). BER staff and BERAC both interact with and receive feedback from other programs and advisory committees across the Department including Advanced Scientific Computing Research, Basic Energy Sciences, Environmental Management, Energy Efficiency and Renewable Energy, Nuclear Energy, Fossil Energy, and the National Nuclear Security

Administration. BER program coordination across federal agencies also benefits from international and interagency working groups such as those of the International Human Genome Project, the U.S. Global Change Research Program (USGCRP), and the National Institutes of Health Bioengineering Consortium. Finally, BER consults regularly with groups like JASON and The Washington Advisory Group (WAG), involving physicists, mathematicians, engineers, etc., to receive feedback on BER program elements such as the Atmospheric Radiation Measurement (ARM) program, climate change prediction activities, the William R. Wiley Environmental Molecular Sciences Laboratory (EMSL), and the Human Genome program.

Facility Operations Reviews

BER facility operations are monitored by peer reviews and user feedback. BER facility operations have also been reviewed by BERAC and by an OSTP interagency working group evaluating structural biology user facilities. The Office of Science's (SC) Construction Management Support Division has reviewed BER's Joint Genome Institute. BER manages these facilities in a manner that meets user requirements as indicated by achieving performance specifications while protecting the safety of workers and the environment. Facilities are operated reliably and according to planned schedules. Facilities are also maintained and improved to remain at the cutting edge of technology and scientific capability.

Program Reviews

Effective program review, peer review, and user feedback are critical tools for BER to measure performance of research programs, research projects, and user facilities. The quality and scientific relevance of the BER program and its individual research projects are maintained by rigorous peer reviews conducted by internationally recognized scientific experts. The criteria for determining scientific quality and relevance include scientific merit, appropriateness of the proposed approach, requested level of funding, research facilities, and qualifications of the principal investigator. BER expects the highest quality research and, when necessary, takes corrective management actions based on results of the reviews. A measure of the quality of the BER research is the sustained achievement in advancing scientific knowledge. This is demonstrated by the publication of research results in the leading refereed scientific journals pertinent to BER-related research fields, by invited participation at national and international scientific conferences and workshops, and by honors received by BER-supported researchers.

At the highest level, regular reviews of individual BER program elements and of the entire BER research program are conducted by BERAC. As noted above, BER also benefits from interagency and international reviews of programs such as the Human Genome Program, the Global Change Research Program, and the structural biology research program, including reviews by Boards and Committees of the National Academy of Sciences.

BER goes one step further in conducting program reviews. Panels of distinguished scientists are regularly charged with evaluating the quality of individual programs and with exploring ways of entraining new ideas and research performers from different scientific fields. This strategy is based on the conviction that the most important scientific advances of the new century will occur at the interfaces between scientific disciplines, such as biology and information science. The BER program is ideally positioned to facilitate and foster interactions between the physical sciences, the computational sciences, and the life sciences, and aggressively pursues every opportunity to nurture collaborations at the interfaces between these scientific domains.

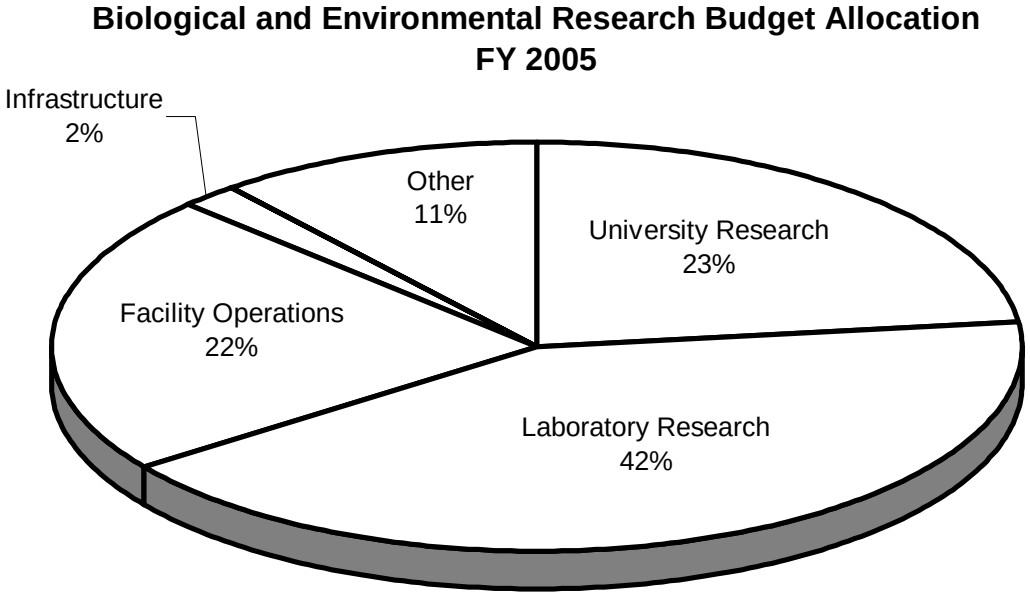
Planning and Priority Setting

BER prides itself on supporting research and developing new research initiatives that lead the way across many fields of science and that effectively bring together many different disciplines, including biology, chemistry, engineering, computing, and the physical sciences. Peer reviews and user feedback are incorporated as BER anticipates and plans for the future needs of DOE research in the life and environmental sciences. This includes: planning for future directions, opportunities, and initiatives within the BER research portfolio; maintaining the flexibility to quickly move into promising new areas; contributing to the health of the educational pipeline in critical subfields and disciplines; planning for upgrades at existing facilities to expand the research capabilities or operational capacity; ensuring the proper balance between facilities and research; and planning for future facilities necessary to advance the science in areas relevant to BER's mission with strong involvement of the research community.

BER planning and priority setting are also key BERAC activities and part of BER's interagency coordination. Individual BER program elements, e.g., human genome, low dose radiation research, Genomics: GTL, bioremediation research, and global climate change develop long-range program plans through coordinated efforts with BERAC and other federal agencies.

How We Spend Our Budget

The BER budget has three major components: basic research at universities (23%); basic research at national laboratories (42%); and user facility support (22%). Research at national laboratories also includes support for high throughput DNA sequencing at the Joint Genome Institute, Atmospheric Radiation Measurement Infrastructure, Free-Air CO_2 Enrichment (FACE) experimental facilities, Unmanned Aerial Vehicles, and other elements that represent a research infrastructure for the scientific community that includes both university and laboratory scientists. BER's user facilities include the infrastructure at synchrotron and neutron sources for structural biology and operation and equipment for the Environmental Molecular Sciences Laboratory (EMSL).



Research

In FY 2005, the BER program will support fundamental research in climate change, environmental remediation, genomics, proteomics, radiation biology, and medical sciences at 220 public and private research institutions in 44 states and at 16 DOE laboratories in 10 states. This research will be conducted in over 1000 different research projects by over 2,275 researchers and students. In addition to the principal investigator for each research project funded by BER, individual projects typically have between 1 and 20 additional PhD-level scientists who are funded collaborators. Information on scientific collaborators is not routinely tracked.

- ***University Research:*** University researchers play a critical role in the BER program, conducting fundamental research and developing the next generation of scientists for the nation's biological and environmental research efforts. BER will continue its commitment to and dependence on scientists at the Nation's universities. In general, BER-supported research at universities and research institutions are single investigator projects. Approximately half of BER basic research funding supports university-based activities directly and indirectly. University scientists are the major scientific users at BER facilities and other enabling research infrastructures such as the ARM program.

  All research projects supported by the BER program undergo regular peer review and evaluation based on the procedures set down in 10 CFR Part 605 for the extramural grant program (http://www.science.doe.gov/grants/merit.html). Peer review of BER projects is performed to provide an independent assessment of the scientific and/or technical merit of the research by peers having knowledge and expertise equal to that of the researchers whose work they review.

- ***National Laboratory Research:*** Research projects at national laboratories are most often multi-investigator team projects that take advantage of unique resources, capabilities, or facilities found at the national laboratories. Researchers at the national laboratories collaborate extensively with academic researchers supported by BER as well as with academic users of the BER facilities and research infrastructure including the EMSL, ARM, FACE, AmeriFlux sites, Natural and Accelerated Bioremediation Research (NABIR) Field Research Center, the Joint Genome Institute (JGI), and the structural biology user facilities at the synchrotron and neutron sources.

All DOE laboratory research projects supported by the BER program undergo regular peer review and evaluation. BER research at the DOE Laboratories and scientific user facilities undergoes peer review and evaluation in a similar procedure to that used for university-based research.

BER Leadership and Unique Roles

The BER program has a broad range of unique roles for the Department and the national and international scientific communities including:

- Manage research on microbes for energy and the environment, and work with the Advanced Scientific Computing Research program to develop the computational methods and capabilities needed to advance understanding of complex biological systems, predict their behavior, and use that information to address DOE needs.
- Provide the facilities, instrumentation, and technology needed to (1) characterize the multi-protein complexes that result in microbial products and processes of use to DOE, and (2) determine the functional repertoire of complex microbial communities that can be used to address DOE needs.
- Develop cutting edge technologies, facilities, and resources, including animal models, for the Human Genome Project.

- Provide world leadership in low dose radiation research.
- Provide world-class structural biology user facilities and unique computational and experimental structural biology research emphasizing protein complexes involved in recognition and repair of DNA damage and remediation of metals and radionuclides.
- Provide world leadership in ground-based measurement of clouds and atmospheric properties to resolve key uncertainties in climate change, through the ARM program.
- Develop advanced predictive capabilities using coupled climate models on the Nation's premier computers for decade-to-century long simulations of climate change.
- Support fundamental research on carbon sequestration to develop technologies that enhance the uptake of carbon in terrestrial and ocean ecosystems.
- Provide the scientific knowledge and enabling discoveries to reduce the risks and costs associated with the cleanup of the DOE weapons complex.
- Provide world-class scientific user facilities for environmental and climate change research.
- Provide world leadership in radiopharmaceutical development for wide use in the medical and research communities.
- Maintain world leadership in instrumentation development for medical and biological imaging.
- Enable interdisciplinary teams of scientists to use the unique resources in physics, chemistry, material sciences, and biology at the National Laboratories to develop novel medical applications.
- Provide world leadership in the development of intelligent micro machines that interface with the brain and spinal cord to overcome disabilities.
- Ensure that the rights and welfare of human research subjects at the Department are protected while advances in biomedical, environmental, nuclear, and other research lead to discoveries that benefit humanity.

Significant Program Shifts

For FY 2005, BER will focus on:

- Project Engineering and Design (PED) of a Genomics: GTL facility for the Production and Characterization of Proteins and Molecular Tags. This facility will incorporate a new generation of sophisticated high-throughput technologies that are required for translating the new biology, making them widely and readily available, and using them effectively to serve the community of national laboratories, academic, and industrial researchers. Research underpinning the development and design of the technologies to be incorporated into this facility is currently being funded as part of the GTL program.
- Changing the Atmospheric Science Program from air quality research on tropospheric ozone and particulates to the direct and indirect effects of aerosols on the atmospheric radiation balance and climate. New field measurement campaigns and modeling studies of the formation, transport, and transformation of aerosols and their radiative properties will be initiated in conjunction with the ARM program. The research will focus on key uncertainties that currently limit our ability to accurately simulate and predict the direct and indirect effect of aerosols on climate.
- Integration of Environmental Remediation research from EMSP, NABIR, EMSL, and SREL to perform "comprehensive" field studies.

Genomics: GTL Research

The FY 2005 budget includes funds for the continued expansion of the Genomics: GTL program—a program at the forefront of the biological revolution. This program employs a systems approach to biology at the interface of the biological, physical, and computational sciences to address DOE's energy, environment, and national security mission needs. This research will continue to more fully characterize the inventory of multi protein molecular machines found in selected DOE-relevant microbes and higher organisms. It will determine the diverse biochemical capabilities of microbes and microbial communities, especially as they relate to potential biological solutions to DOE needs, found in populations of microbes isolated from DOE-relevant sites. In FY 2005, PED for a facility for the Production and Characterization of Proteins and Molecular Tags will be initiated. This facility will be a high throughput user facility that will use highly automated processes to mass-produce and characterize proteins directly from microbial DNA sequence data and create affinity reagents or "tags" to identify, capture, and monitor the proteins from living systems.

Climate Change Science Program

In 2003, the Administration launched a new Climate Change Research Initiative (CCRI) to focus research on areas where substantial progress in understanding and predicting climate change, including its causes and consequences, is possible over the next five years. The CCRI was then combined with the existing U.S. Global Change Research Program (USGCRP) to form a combined USGCRP/CCRI managed as the Climate Change Science Program (CCSP) by the cabinet-level Committee on Climate Change Science and Technology Integration (BER request for CCSP for FY 2005 is $134,169,000). DOE, in conjunction with its interagency partners, including NSF, NASA, NOAA, USDA, Interior, and EPA, will continue to focus its Climate Change Research in CCSP priority areas. These areas include advanced climate modeling, critical climate processes (including effects of clouds and water vapor on the atmospheric radiation balance), carbon cycling, atmospheric composition (with a focus on both greenhouse gas concentrations and effects of various aerosols on climate), effects of climate change on important terrestrial ecosystems, and the development and evaluation of tools for assessing the costs and benefits of climate change mitigation options. The deliverables from this BER research will be highlighted by information useful to policy makers.

In FY 2005, BER will contribute to the CCRI from four programs: Terrestrial Carbon Processes, Climate Change Prediction, ARM, and Integrated Assessment. Activities will be focused on (1) helping to resolve the North American carbon sink question (i.e., the magnitude and location of the North American carbon sink); (2) development and operation of a mobile ARM Cloud and Radiation Testbed facility to provide data on the effects of clouds and aerosols on the atmospheric radiation budget in regions and locations of opportunity where data is lacking or sparse; (3) using advanced climate models to simulate potential effects of natural and human-induced climate forcing on global and regional climate and the potential effects on climate of alternative options for mitigating increases in human forcing of climate; and (4) developing and evaluating assessment tools needed to study costs and benefits of potential strategies for reducing net carbon dioxide emissions.

Scientific Discovery through Advanced Computing (SciDAC)

The Scientific Discovery through Advanced Computing (SciDAC) program is a set of coordinated investments across all Office of Science mission areas with the goal of achieving breakthrough scientific advances via computer simulation that are impossible using theoretical or laboratory studies alone. The power of computers and networks is increasing exponentially. Advances in high-end computing technology, together with innovative algorithms and software, are being exploited as intrinsic tools for scientific discovery. SciDAC has also pioneered an effective new model of multidisciplinary collaboration among discipline-specific scientists, computer scientists, computational scientists, and

mathematicians. The product of this collaborative approach is a new generation of scientific simulation codes that can productively exploit terascale computing and networking resources. The program is bringing computation and simulation to parity with experiments and theory in the scientific research enterprise as demonstrated by major advances in climate modeling and prediction, plasma physics, particle physics, accelerator design, astrophysics, chemically reacting flows, and computational nanoscience.

In FY 2005, BER will continue to advance the science of climate modeling by coupling models of different components of the Earth system related to climate and by significantly increasing the spatial resolution of global climate models. These SciDAC-enabled activities will allow climate scientists to gain unprecedented insights into potential effects of energy production and use on the global climate system.

Scientific Facilities Utilization

The BER request includes funds to maintain support of the Department's major scientific user facilities. BER has expanded the definition of a scientific user facility to include facilities such as structural biology research beam lines at the synchrotron light sources and neutron sources; the operation of the William R. Wiley Environmental Molecular Sciences Laboratory where research activities underpin long-term environmental remediation and other DOE missions in energy and national security; the Production Genomics Facility and the Laboratory for Comparative and Functional Genomics ("Mouse House"); and the ARM and FACE facilities. With this funding, BER will provide for the operation of the facilities, assuring access for scientists in universities, federal laboratories, and industry. BER will also leverage both federally and privately sponsored research to maintain support for and operation of these facilities.

BER will maintain and operate EMSL and the structural biology user facilities so that the achieved operation time will be greater than 90%, on average, of total scheduled annual operation.

User Statistics

	FY 2000	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005
	Achieved				Planned	
EMSL[a]						
Maximum hours	4,365	4,365	4,365	4,365	4,365	4,365
Scheduled hours	3,130	3,130	4,275	4,365	4,365	4,365
Operation Time	95%	95%	95%	95%	95%	95%
Production Genomics Facility						
Maximum hours	3,600	3,600	3,600	3,600	3,600	3,600
Scheduled hours	3,600	3,600	3,600	3,600	3,600	3,600
Operation Time	>99%	>99%	>99%	>98%	>98%	>98%
Center for Comparative Genomics ("Mouse House")						
Maximum hours	0	0	0	0	8,760	8,760
Scheduled hours	0	0	0	0	8,760	8,760
Operation Time	N/A	N/A	N/A	N/A	>99%	>99%
Atmospheric Radiation Measurement (ARM)						
Maximum hours	6,290	6,290	6,290	6,290	6,290	6,290
Scheduled hours[b]	6,290	6,290	6,290	6,290	6,290	6,290
Operation Time	>98%	>98%	>98%	>98%	>98%	>98%
Free Air Carbon Dioxide Enrichment (FACE)						
Maximum hours	15,865	15,865	15,865	15,865	15,865	15,865
Scheduled hours	15,865	15,865	15,865	15,865	15,865	15,865
Operation Time	93%	93%	94%	>94%	>95%	>95%

User statistics for BER structural biology user facilities at DOE neutron and light sources are included as part of the user statistics collected and reported by the Basic Energy Sciences (BES) program and are not repeated here.

Construction and Infrastructure

BER will meet the cost and schedule milestones for construction of facilities and major items of equipment within 10% of baseline estimates.

Funding for capital equipment is decreased in FY 2005 after a one-time increase in FY 2004 for instrument modifications at EMSL. For all other BER activities the capital equipment is held approximately at the FY 2004 level.

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[a] Scientists use, or remotely access, some of the more than 100 instrumentation/computer systems in the EMSL 24 hours/day while other instruments are used only 10-12 hours/day. Maximum hours identified above are therefore based on a 12-hour day average estimate. Scheduled hours and downtime for each of the 100 instrument systems are also unique. As a result, the scheduled hours identified above are based on a 10-hour day average estimate. None of the major instrument systems within the EMSL have experienced any significant unscheduled downtimes.

[b] Allows for weather related downtime based on climatology (e.g., lightning strikes, hail, extreme winds, and cold events).

The BER program, as part of its responsibilities as landlord for the Pacific Northwest National Laboratory (PNNL) and the Oak Ridge Institute for Science and Education (ORISE), provides funding for the general plant projects (GPP) and general plant equipment (GPE). In addition to the general-purpose line item projects funded out of the Science Laboratories Infrastructure program, GPP and GPE represent the capital investment funding provided by the Department for the general laboratory infrastructure. This ensures that the PNNL and ORISE infrastructures will continue to enable the Department's mission activities at these sites.

Workforce Development

Workforce development is an integral and essential element of the BER mission to help ensure a science-trained workforce, including researchers, engineers, science educators, and technicians. The research programs and projects at the National Laboratories, universities, and research institutes actively integrate undergraduate and graduate students and post-doctoral investigators into their work. This "hands-on" approach is essential for the development of the next generation of scientists, engineers, and science educators. Specific fellowship programs are also sponsored by BER to target emerging areas of need. Over 1,500 graduate students and post-doctoral investigators will be supported at universities and at National Laboratories in FY 2005. BER will continue its support for graduate students and post-doctoral investigators in FY 2005. The number of graduate students and post-doctoral investigators will remain approximately at the FY 2004 level.

Graduate students and postdoctoral investigators use Office of Science user facilities. For example, they use the structural biology experimental stations on the beam lines at the synchrotron light sources and the instruments at the EMSL. Using these unique research tools enables the graduate students and post-doctoral investigators to participate in and conduct leading edge research. Approximately half of all of the facility users are graduate students and post-doctoral investigators; some 600 graduate students and post-doctoral investigators will conduct their research at the EMSL in FY 2005. The graduate students and post-doctoral investigators are supported by resources from a wide variety of sponsors, including BER, other Departmental research programs, other federal agencies, and U.S. and international private institutions. Graduate students and post-doctoral investigators at the synchrotron light sources are included in the BES user facility statistics and are thus not included here.

BER will continue its commitment to and dependence on research scientists at the Nation's universities. Approximately half of BER basic research funding directly or indirectly supports university-based activities. University scientists are the major users at BER facilities and other enabling research infrastructure. University-based scientists are an integral part of research programs across the entire range of the BER portfolio. These scientists are funded through individual peer-reviewed grants and as members of peer-reviewed research teams involving both national laboratory and university scientists.

University-based scientists are the principal users of BER user facilities for structural biology at the synchrotron and neutron sources. They are also users of the EMSL, and the NABIR program's Field Research Center. University scientists also form the core of the science teams in the Climate Change Research Programs that network with the broader academic community as well as with scientists at DOE laboratories and other agencies, such as the National Aeronautics and Space Administration and the National Oceanic and Atmospheric Administration. In addition, university-based scientists are funded through Requests for Applications across the entire BER program including genomics, structural biology, low dose radiation research, climate change research, bioremediation research, medical imaging, and radiopharmaceutical development. Furthermore, university scientists work in close partnership with scientists at National Laboratories in many other BER programs including genomics, and carbon sequestration research.

DOE-BER Human Capital

	FY 2000	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005
# University Grants	532	579	628	630[a]	630[a]	630[a]
Size / Duration	$302,000/yr	$287,000/yr	$309,000/yr	$300,000/yr[a]	$300,000/yr[a]	$300,000/yr[a]
	3 years	3 years	3 years	3 years	3 years	3 years
# Lab Projects.....	379	397	392	395[a]	400[a]	400[a]
# Permanent PhDs[b]	1310	1370	1427	1491[a]	1489[a]	1490[a]
# Postdocs[c]	251	274	357	373[a]	372[a]	375[a]
# Graduate Students[c]..	438	443	491	481[a]	488[a]	490[a]
# PhDs awarded[d]	NA[d]	NA[d]	NA[d]	NA[d]	NA[d]	NA[d]

[a] Estimated. Information on the number of research projects funded, the size of those projects, or the number of personnel involved cannot be known prior to the receipt of research applications or proposals, their peer review, and the completion of funding decisions.

[b] Estimated. Information is not readily available on the total number of permanent PhD scientists associated with each research project. In addition to the principal investigator for each research project funded by BER, individual projects typically have between 1 and 20 additional PhD-level scientists who are funded collaborators. Information on scientific collaborators is not routinely tracked.

[c] Estimated for national laboratory projects.

[d] Information is not available on the number of PhDs awarded as a result of BER funded research at universities or national laboratories. Such data will be collected for FY 2005.

Life Sciences

Funding Schedule by Activity

(dollars in thousands)

	FY 2003	FY 2004	FY 2005	$ Change	% Change
Life Sciences					
Structural Biology	26,689	27,036	21,871	-5,165	-19.1%
Molecular and Cellular Biology	71,384	97,794	101,954	+4,160	+4.2%
Human Genome	73,217	64,230	64,572	+342	+0.5%
Health Effects	10,513	10,175	10,237	+62	+0.6%
SBIR/STTR	0	5,456	5,377	-79	-1.4%
Total, Life Sciences	181,803	204,691	204,011	-680	-0.3%

Description

The mission of the Life Sciences subprogram is to foster fundamental research in the biological and life sciences that will provide new insights and advance knowledge of the life sciences to underpin the Department of Energy's mission needs. Biotechnology offers the promise of revolutionary solutions to energy and environmental challenges facing DOE and the Nation. Fundamental research in the Life Sciences subprogram will deliver a new knowledge base for cost effective cleanup of environmental contamination, design of new strategies for enhanced capture of atmospheric carbon dioxide, and increased bio-based sources of fuel or electricity. The program will also deliver new knowledge underpinning rigorous, cost-effective standards to protect the health of DOE cleanup workers and the public, and for science-based decisions on DOE site cleanup.

Benefits

Fundamental research is supported in structural biology, genomics, and the health effects of low dose radiation. DNA sequencing is used to understand the genetic and environmental basis of normal and abnormal biological function, from human genes that make some people more sensitive to the adverse effects of low doses of radiation to the biochemical capabilities of complex microbial communities that could be used to produce clean energy, clean up or stabilize wastes *in situ* to minimize risks to humans and the environment, or sequester excess atmospheric carbon dioxide. Scientific tools and resources are developed and made widely available for determining protein structures at DOE synchrotron and neutron sources and for high throughput genomic DNA sequencing. New capabilities are developed in the Genomics: GTL program for understanding the structure, function, and regulation of multi protein complexes from DOE-relevant organisms and of complex, DOE-relevant microbial communities – information that can then be used to develop biotechnological solutions for DOE needs.

Supporting Information

BER Life Sciences supports research in the following areas:

- biological effects of low doses of ionizing radiation. The program works closely with scientists, regulators, and the public to ensure that the research results are available to develop a better scientific basis for adequately protecting people from the adverse effects of ionizing radiation.
- Genomics: GTL research, developing, together with the Advanced Scientific Computing Research program, experimental and computational resources, tools, and technologies to understand the complex behavior of biological systems – from single microbes to communities of multiple microbial species. This information can be used to develop innovative biotechnology solutions for energy production, waste cleanup, and carbon management.
- a high throughput DNA sequencing user resource to meet DNA sequencing needs of the scientific community.
- resources, tools, and technologies to understand the function of human genes that it identified as part of the International Human Genome Project using model organisms such as the mouse, *Fugu* (the puffer fish), and *Ciona* (the sea squirt).

Periodic retrospective analysis will be employed to evaluate the accumulation of knowledge and validate specific outcomes. This subprogram was reviewed as part of a BERAC review of the entire BER program in FY 2001. The next scheduled comprehensive review of the Life Sciences subprogram by BERAC will be in FY 2004.

Accomplishments:

- *Sequencing Leap-Frogs to another Milestone.* The genome of the West African clawed frog, *Xenopus tropicalis*, was sequenced as part of an international collaboration led by the DOE Joint Genome Institute (JGI), with participation by the U.S. Environmental Protection Agency (EPA) and the National Institutes of Health (NIH). This 1.7 billion base pair genome is the first amphibian sequenced. The frog is scientifically important for a number of reasons. It marks an evolutionary milestone coinciding with the appearance of four-legged animals. It serves an "environmental sentinel" for environmental contamination and clean-up since its development is exquisitely sensitive to chemical contaminants. It is also a model organism for studying embryonic development, growth, and maturation and will help scientists decipher gene regulatory and morphogenetic events in early vertebrate development leading to greater understanding of human biology.
- *A New Window on the Microbial World - Studying the Other 99%.* Microbes play a major role in the health of our planet; but fewer than 1% of the Earth's microbes can be cultured in the laboratory. These unculturable bacteria and archaea live in every imaginable environment on Earth, thriving under remarkably harsh conditions and possessing metabolic capabilities that enable them to detoxify contaminants and use unique sources of energy. They live in our oceans and terrestrial environments, playing critical roles in the maintenance and regulation of water and atmospheric composition. In several pioneering projects, JGI scientists and their collaborators have opened a new window on microbial diversity, using DNA sequencing of environmental samples to reveal the genomic underpinnings and biochemical capabilities of the resident microbes. These new analyses are illuminating the diversity of unculturable microbial life on Earth, revealing a wide range of

biochemical capabilities that suggest new approaches for environmental cleanup, energy production, and carbon sequestration.

- *Victory Declared - Human Genome Sequence Finished.* In April 2003, the International Human Genome Consortium announced the formal completion of the sequencing of the human genome. This announcement, two years ahead of original projections, represents the achievement of the quality and completeness milestones for the human DNA sequence – a sequence accuracy of less than one error in ten thousand bases and the closure of all sequence gaps within the limits of current technology. For its role in this international project, the JGI produced nearly 12% of the finished human genome sequence, human chromosomes 5, 16, and 19, which include the most gene-rich human chromosome (number 19) and one of the most internally duplicated chromosomes (number16). Computational and biological analyses of these three chromosomes to date have revealed nearly 4,000 genes impacting human health. Deciphering our genomic "text" will be a major focus of future biology, relying in part on extensive comparisons with other related genome sequences such as the frog, Fugu fish, and sea squirt all sequenced by the JGI.
- *Revealing the genomes of "Sudden Oak Death" and other plant pathogens.* Genome sequencing of pathogens provides direct insight into the working of these agents that informs the diagnosis, treatment, and ultimately prevention of disease in both plants and animals. In collaboration with the U.S. Department of Agriculture, the JGI determined and analyzed the genome sequences of two members of the genus *Phytophthora*, including the organism causing "Sudden Oak Death" in California, as well as two species of the fungal genus *Phakopsora*, the cause of soybean blight and a potential agricultural bioterror agent. By sequencing pairs of related organisms simultaneously, similarities and differences between the genomes can be used to identify genes that determine the host specificity of a pathogen and its ability to evade the host immune response.
- *Primate Genomes Help Understanding of Human Gene Function.* While comparisons between DNA sequences of the human and of the rat and mouse can illuminate characteristics shared by mammals; not surprisingly many human-specific molecular traits cannot be understood by studying these evolutionarily distant DNA sequences. DOE scientists developed a new approach that uses DNA sequence information from close primate relatives to decipher functional elements in the human genome. Human and primate DNA sequences are quite similar. New methods to identify these differences across a range of primates provide a novel tool for identifying the presence and functionality of genes that are unique to the human genome.
- *First Tree Genome is Sequenced.* The genome of the black cottonwood tree (*Populus balsamifera ssp. trichocarpa*), a member of the poplar family, is the first tree genome to be sequenced. Scientists working on tree genetics, productivity, and forest product utilization are enthusiastic about the sequencing of this tree species because it represents an important first step in understanding the genome of a common, commercially important tree species with potential impacts including improved carbon sequestration and biomass for energy. This effort was led by a consortium of scientists from the JGI, Oak Ridge National Laboratory, the University of Washington, the British Columbia Genome Sequence Center, the Swedish University of Agricultural Sciences, Oregon State University, Pennsylvania State University, the National Center for Genome Research, and other institutions. The sequencing, assembly, and initial analysis were carried out at DOE's high throughput DNA sequencing facility, the Production Genomics Facility.
- *Beginning to Decipher Poplar's Genome.* Molecular markers derived from the Poplar DNA sequence have been used to create the most complete genetic map ever assembled for a forest tree

species. Research was begun to identify regions of the Poplar genome responsible for above- and below-ground carbon allocation/chemistry in the Poplar that could lead to innovative plantation strategies for bioenergy and carbon sequestration. This included an extensive carbon inventory conducted for stems, branches, leaves, coarse roots, and fine roots, as well as chemical composition of selected tissues from more than 1000 progeny of a unique hybrid poplar family growing in the Pacific Northwest and use of the newly created Poplar genetic map. Preliminary model analyses indicate that increasing the allocation of carbon to Poplar's roots and altering Poplar's tissue chemistry to favor longer-lived pools of soil organic matter, i.e., lignin, would together enhance global carbon sequestration in terrestrial ecosystems by 0.56 Gigatons of carbon per year (approximately 8.6% of annual global carbon emissions), assuming that 222 million hectacres of land was available globally for the establishment of fast-growing poplar forest plantations (an area the size of Texas and Alaska combined).

- *First DNA sequence of a green algae*. The genome of a unicellular green algae has been determined by the JGI - the first algae to be sequenced. *Chlamydomonas reinhardtii* - known as the "green yeast" for its ease of study and manipulation - is a model organism for the study of various fundamental biological processes, including photosynthetic carbon fixation, important for carbon sequestration in the ocean, and flagellar structure and function. Unicellular green algae are found nearly everywhere - in soil, fresh water, oceans, and even in snow on mountaintops. DOE is interested in *Chlamydomonas* because of its widespread global distribution and its ability to carry out photosynthesis, the most powerful biological technology for carbon dioxide capture from the atmosphere. An international consortium of scientists is participating in the analysis and interpretation of the genome of this model alga.
- *First DNA sequence of a diatom*. The genome of a marine diatom, *Thalassiosira pseudonana*, has been determined by the JGI and analyzed in collaboration with an international consortium of marine biologists. Diatoms, a type of marine phytoplankton, are important model organisms for carbon sequestration and are found in all of Earth's oceans. They display an incredible and intriguing variety of shapes and are major players in the Earth's carbon cycle. They are responsible for much of the ocean's ability to move carbon dioxide captured in the near surface regions by photosynthesis to the deep ocean. The shapes, growth rates, and carbon fixation processes of diatoms are all under genetic control and could be exploited to enhance their carbon processing capabilities as one strategy towards mitigation of global warming. Additionally, the silicate shells of many diatoms are engineering and material science marvels and could provide important insights for nanoscience research.
- *Sea Squirt Genome Gives New Clues to Origins of Chordates and Vertebrates.* Humans are members of the chordate phylum, an ancient group of animals that first appears in the fossil record over 540 million years ago. Our most distant living relatives in this group are the sea squirts, humble filter-feeding marine creatures whose tadpole larvae represent plausible modern approximations to the ancestral chordates. To understand the origins of chordates and vertebrates, the JGI previously sequenced the genome of the most studied sea squirt, *Ciona intestinalis*. Ciona has approximately 16,000 protein-coding genes, similar to the number in other invertebrates, but only half that found in vertebrates. Vertebrate gene families are typically found in simplified forms in Ciona, suggesting that these primitive organisms have the basic ancestral complement of genes involved in cell signaling and development. The Ciona genome also has a number of lineage-specific biochemical pathways such as a group of genes for cellulose metabolism related to those found in bacteria and fungi. This international project includes scientists from the US, Japan, Italy,

France, Canada, and Australia, and provides a foundation for genome-scale analysis of gene regulatory networks.

- *Another Record-Breaking Year of Microbial DNA Sequencing.* The JGI has again surpassed expectations in microbial DNA sequencing in FY 2003 by determining high quality draft sequences of 41 microbes important to DOE needs in energy, environmental cleanup, and counter-terrorism. Twelve of these organisms are pathogens or their close genetic relatives that were sequenced as part of a coordinated interagency effort to quickly characterize as many potential threat agents as possible.
- *Rapid Detection of DNA Sequence Variants.* The mouse continues to be a valuable research tool for helping scientists understand the function of the human genome. DOE's long history of leading mouse genetics research continues to provide scientists with new tools that take advantage of current capabilities in genomics. A strength of mouse genetics research has always been the ability to isolate mouse mutants that provide insights on the homologous human genes. A new method for rapid detection of mutants has been developed that combines gradient capillary electrophoresis (TGCE) for mutation and single-nucleotide polymorphism (SNP) detection, DNA sequencing to identify the exact location in the DNA sequence of the identified variants, and multiplexed single-base extension to survey the mutations and SNPs at the known sites of the mutation within the DNA sequence. This combined approach offers scientists a fast and cost-effective method for high-throughput mutation/SNP detection. This new method was enabled by the DOE investments in DNA sequencing technology that contributed to the successful completion of the Human Genome Project.
- *Protein X-ray Crystallography Upgraded.* The National Synchrotron Light Source (NSLS) at Brookhaven National Laboratory (BNL) serves a large community of structural biologists in the northeastern United States. However, its X-ray beams are not as bright as those at the newest light sources, limiting its usefulness for determining the structures of larger, more complicated proteins and protein complexes. A beam line has now been assembled at the NSLS using new technology in which the X-rays are produced by a mini-gap undulator device, resulting in beam brightness close to the best at the other American light sources. This beam line was developed by BNL in collaboration with the Albert Einstein College of Medicine.
- *Robots Enhance Protein Crystallography Throughput.* Obtaining protein structures using X-ray crystallography involves screening a hundred or more crystals of the protein one at a time to find the one that gives the best data. A new robotic crystal handling system at the Stanford Synchrotron Radiation Laboratory (SSRL) was installed early in FY 2003. This system enabled a user group to test 130 crystals of a protein complex in less than eight hours. The previous experiment by this group with manual handling of the samples required 24 hours to screen 100 crystals of a similar complex, with several of the samples being damaged or lost. All of the Department of Energy synchrotron light sources are implementing automated systems for this process, which will enable a substantial increase in the number of users that can be accommodated.
- *A Step Closer to Automated Protein Structure Prediction.* Being able to predict the three dimensional structure of a protein from its amino acid sequence is one of the grand challenges in structural biology. A new threading-based protein structure prediction system, PROSPECT, is the latest addition to the structural biologist's tool kit. PROSPECT consists of a dozen tools for identification of protein domains and signal peptide, protein triage to determine the protein type (membrane or globular), protein fold recognition, generation of atomic structural models, prediction

result validation, etc. Different processing and prediction branches are determined automatically by a prediction pipeline manager based on identified characteristics of the protein. The pipeline has been implemented to run in a heterogeneous computational environment as a client/server system with a web interface. PROSPECT placed fifth in a field of 150 in the Fifth Critical Assessment of Techniques for Protein Structure Prediction Experiment (CASP5) in the fold recognition category.

- *Responses to Low Dose Rates of Radiation Not All the Same.* Sensitive genetic assays (microarrays) have been used to identify genes whose expression is induced by radiation delivered at low dose rates. Two classes of genes exhibiting different responses to low dose rates of radiation were identified in cultured human myeloid cells. One group of genes induced in a dose rate-dependent fashion included a preponderance of genes with known roles in the regulation of apoptosis, a form of terminal differentiation. A second group of genes induced in a dose rate-independent manner included a preponderance of genes involved in cell cycle regulation. If these results hold true *in vivo*, there may be important implications for carcinogenesis and risk assessment. For example, cells damaged by exposure to very low doses and dose rates of radiation may escape apoptosis, but undergo normal cell cycle arrest. This increases the likelihood that some critically damaged cells may misrepair their damage and continue proliferating. Under this scenario, low doses of radiation delivered at low dose rates could pose a greater carcinogenic risk than radiation delivered at a higher dose rate.

Detailed Justification

(dollars in thousands)

	FY 2003	FY 2004	FY 2005
Structural Biology	**26,689**	**27,036**	**21,871**
▪ **Basic Research**	**11,389**	**11,736**	**6,571**

Understanding the workings of the multi-protein molecular machines that enable microbes to cleanup metals and radionuclides or to sequester carbon dioxide will help us to design biotechnology solutions for environmental cleanup and for reducing atmospheric levels of carbon dioxide. Multi-protein complexes, or molecular machines, carry out most of the biochemical functions within cells. Understanding how molecular machines form and work requires that we observe dynamic changes in protein structure, modification, translocation, and subcellular concentration. Research is supported to understand the structures of microbial molecular machines, the regulatory networks that they are part of, and the structures and regulation of their component proteins.

The research activities in this subprogram are carried out at National Laboratories, universities, and private institutions and selected through competitive and peer-reviewed processes.

Structural biology research is reduced and the funds are redirected to the PED construction project for the Genomics: GTL Facility for Production and Characterization of Proteins and Molecular Tags. The research being reduced is more than offset by large National Institutes of Health increases in investments in the Protein Structure Initiative to determine the structures of a large number of individual proteins and multiprotein complexes.

(dollars in thousands)

FY 2003	FY 2004	FY 2005

- **Infrastructure Development** **15,300** **15,300** **15,300**

BER develops and supports access to beam lines and instrumentation at DOE's national user facilities for the Nation's structural biologists. BER coordinates, with the NIH and the NSF, the management of experimental stations at DOE synchrotrons (Advanced Photon Source, Advanced Light Source, Stanford Synchrotron Radiation Laboratory (SSRL) and National Synchrotron Light Source) and neutron beam sources (the Los Alamos Neutron Science Center (LANSCE) and High Flux Isotope Reactor (HFIR) at ORNL). User statistics for all BER structural biology user facilities are included in the BES facility user reports. BER also supports access to unique high performance mass spectrometry and nuclear magnetic resonance spectrometry user facilities at the EMSL that are used for both proteomic and structural biology research. DOE investment in structural biology facilities has a large impact on basic research investments made by other agencies. DOE investments in structural biology user facilities at synchrotron light sources and at the EMSL enabled the National Institute of General Medical Sciences at the NIH to make a large investment (over $30,000,000 per year from FY 2001 to FY 2005) in pilot projects for NIH's Protein Structure Initiative to develop high throughput methods for determining protein structure. Six of the nine pilot projects funded by NIH include partners from DOE Laboratories and nearly all make substantial use of DOE user facilities. BER also continually assesses the quality of the instrumentation at its experimental stations and supports upgrades to install the most effective instrumentation for taking full advantage of the facility capabilities as they are improved by DOE.

Molecular and Cellular Biology **71,384** **97,794** **101,954**

- **Microbial Genomics** **9,906** **9,932** **9,838**

Microbial genomics research underpins DOE research programs - Fundamental microbiology research will continue to underpin DOE's need to exploit the capabilities of microbes to address mission needs from clean up of the environment to sequestration of atmospheric carbon dioxide to new sources of bio-fuels. Microbial genomics research strengthens the foundation that underpins other BER and DOE programs, including Genomics: GTL, bioremediation research, and carbon sequestration. The underlying scientific justification remains a central principle of the BER genome programs – knowing the complete DNA sequence of a microbe provides important keys to its biological capabilities and is the first step in developing strategies to more efficiently use, or reengineer it to address DOE needs. The complete sequence is also an extraordinarily powerful engine for developing new and testable hypotheses about microbial functions thus advancing fundamental science.

Microbial genomics research includes:

Development of bioinformatics tools for analyzing microbial DNA sequence information. More than a third of the several hundred publicly available genomic sequences of archaea and bacteria are a result of DOE funding. Novel computational tools are being developed to increase the value of microbial genomic information, such as identifying distant relationships of genes, understanding microbial evolution, predicting gene function, identifying and modeling gene expression networks, and extracting longer stretches of useable DNA sequence from raw sequence data.

Microbial Systems and Functional Analysis. Even simple microbes are constituted from thousands of genome-derived proteins that often do no act alone but are parts of protein complexes that carry out functions not mediated by the individual gene products themselves. Research is being conducted to improve and develop high-throughput approaches to the functional characterization (e.g., transporters, environmental sensors, redox enzymes, cytoskeletal components, DNA repair systems, metal reductases, biodegradative enzymes, etc.) of the multi-protein complexes within microbes whose DNA sequences are known and that play a role in bioremediation, carbon sequestration, or energy production.

Consortia and Hard-to-Culture Microbes. Most of our knowledge of microbes is derived from individual species that either cause diseases or can be grown in laboratory conditions. However, most microbes in the environment do neither. In fact, many microbes are part of interdependent consortia in which one species supplies a nutrient necessary for the growth of another. Virtually nothing is known of the organization, membership, or functioning of these microbial consortia. Research is conducted to develop technologies and approaches that will enable genomic analyses of microbial consortia as well as analyses of the genomic information content and diversity of those species that have proven refractory to laboratory culture but are plentiful in environments challenged with metal and radionuclide wastes, or involved in carbon sequestration.

The research activities in this subprogram are carried out at National Laboratories, universities, and at private institutions and are selected through competitive and peer-reviewed processes.

- **Carbon Sequestration Research** **6,028** **7,063** **7,127**

Microbes and plants play substantial roles in the global cycling of carbon through the environment. Carbon sequestration research seeks to understand how plants, and the microbes that enable them to grow, work together to sequester atmospheric carbon dioxide. In FY 2005 the program continues to leverage the genomic DNA sequence of the poplar tree, completed in FY 2003, by developing high throughput experimental and computational methods for understanding the poplar genome and proteome, especially related to carbon utilization. Research will also focus on microbes that live in the poplar rhizosphere (root zone) with the intent of understanding the role that these microbes play in the transfer of carbon between the roots and the soil. The program will emphasize organisms and pathways that serve to increase long-term carbon storage over organisms and pathways that decrease carbon storage. A goal is to identify strategies that would lead to increased carbon storage in the poplar rhizosphere and surrounding soil, such as manipulation of the soil chemical environment to promote certain microorganisms or particular metabolic pathways. In FY 2005, the program also completes the DNA sequencing and preliminary annotation (DNA sequence analysis) of another plant, such as switch grass. This new information will enable scientists to develop new strategies for carbon sequestration and for generating energy from biomass.

The research activities in this subprogram are carried out at National Laboratories, universities, and private institutions and selected through competitive and peer-reviewed processes.

- **Genomics: GTL** **35,321** **63,460** **67,493**

Genomics: GTL is a microbe-based program at the forefront of the biological revolution - a systems approach to biology at the interface of the biological, physical, and computational sciences. It will

take advantage of solutions that nature has already devised to solve many of DOE's most pressing and expensive problems. Genomics: GTL offers the possibility of biotechnology solutions that can give us abundant sources of clean energy yet control greenhouse gases such as carbon dioxide, a key factor in global climate change, and that can help us clean up past contamination of the environment.

Genomics: GTL is a comprehensive, systems-level, interdisciplinary research program that will require development of novel capabilities for new high-throughput biological research, e.g., for protein production, molecular imaging, small molecule production, and proteomics. It will involve a well integrated mix of experimental and computational science that will, in the end, enable us to predict responses of biological systems to their environments and to use that capability to address DOE and National challenges.

Over the long-term, Genomics: GTL will support a combination of:

- fundamental research and technology development;
- development and use of scientific user facilities that will implement much of this new research and technology in high throughput biological research "factories" much like DNA sequencing was moved from the research laboratory to sequencing factories in the human genome project; and
- demonstration projects developed in partnership with other DOE offices such as Energy Efficiency and Renewable Energy, Fossil Energy, and Environmental Management to "field test" potential biotechnology solutions for clean energy production, reducing carbon dioxide in the atmosphere, and cleanup of the environment.

Anticipated outcomes of Genomics: GTL include, within 10 years, advances in systems biology, computation, and technology to address challenges in:

- *Clean Energy* — that will contribute to increased biology-based energy sources. In the long-term, they could contribute to energy security through a major new bioenergy industry;
- *Reduced Carbon Dioxide in the Atmosphere* — that will help us understand Earth's carbon cycle and design ways to enhance carbon dioxide (CO_2) capture. In the long-term, these advances could help us stabilize atmospheric carbon dioxide to counter global warming; and
- *Cleanup of the Environment* — that will lead to cost-effective ways for environmental cleanup. In the long-term, new technology could save billions in waste cleanup/disposal.

Nature has created a remarkable array of multi-protein molecular machines and complex microbial community structures with exquisitely diverse, precise, and efficient functions and controls. The goal of Genomics: GTL is to understand the nature and control of these molecular machines and of complex microbial communities so well that we can use and even redesign them to address DOE and

National needs. Success in Genomics: GTL will be measured by scientific breakthroughs that lead to predictive computational models for –

- molecular machines and other molecules that work together in microbes,

- complex networks that control the assembly and operation of these machines, and
- the structure and biochemical capabilities of complex microbial communities.

The overriding goal of this long-term research program is to understand biology well enough to be able to predict the behavior and responses of biological systems – from cells to organisms so that they can best be used to develop biotechnology solutions that address DOE mission needs in energy, the environment, and national security. This research will lead to greatly improved computational strategies, tools and resources that are central to the success of Genomics: GTL and, indeed, to all of biology, and that will be developed in partnership with the Advanced Scientific Computing Research program.

The broad goals of this research are shared with other agencies, such as the National Institutes of Health, the National Science Foundation, the Department of Agriculture, the Environmental Protection Agency, and private sector companies and will require coordination exceeding that of the Human Genome Project. The program focuses on scientific challenges that can be uniquely addressed by DOE and its National Laboratories in partnership with scientists at universities and in the private sector and will focus on high throughput genomic-scale activities (e.g., DNA sequencing, complex computational analysis, imaging, and genomic protein-expression experimentation and analysis) that are beyond the reach of individual investigators or even small teams.

In FY 2005, the program continues to support a mix of large multidisciplinary research teams and smaller individual investigator projects to:

- characterize and develop computational models to describe the biochemical capabilities of microbial communities;
- develop high throughput approaches for isolating and characterizing microbial molecular machines;
- develop computational models that accurately describe and predict the behavior of genetic regulatory networks;
- develop new technologies and strategies for imaging individual proteins and molecular machines inside microbes;
- develop new technologies for producing large numbers of microbial proteins and molecular tags to identify those proteins; and
- determine the societal and legal implications of GTL research and technology.

In FY 2005, research will also continue on the high-throughput DNA sequencing of microbes and microbial communities. This DNA sequence information will continue to serve as the core of biological information needed to understand the control and function of molecular machines and complex microbial communities.

In FY 2005, the program will also initiate the engineering and design of a Facility for the Production and Characterization of Proteins and Molecular Tags. This facility will be a high-throughput user facility that will use highly automated processes to mass-produce and characterize proteins directly from microbial DNA sequence data and create affinity reagents or “tags” to identify, capture, and

monitor the proteins from living systems. This facility will greatly accelerate the rate of scientific discovery in the GTL program.

The research activities in this subprogram are carried out at National Laboratories, universities, and private institutions and selected through competitive and peer-reviewed processes.

- **Human Frontiers Science** **500** **0** **0**

BER has completed its funding of the Human Frontiers Science program, an international program of collaborative research to understand brain function and biological function at the molecular level.

- **Low Dose Radiation Research** **19,629** **17,339** **17,496**

The goal of the Low Dose Radiation Research program is to support research that will help determine health risks from exposures to low levels of ionizing radiation, information critical to adequately, and appropriately, protect people and to make the most effective use of our national resources. Information developed in this program will provide a better scientific basis for making decisions with regard to remediating contaminated DOE sites and for determining acceptable levels of human health protection, both for cleanup workers and the public, in the most cost-effective manner.

BER will continue to emphasize research that leads to a molecular level understanding of the biological effects of low doses of radiation exposure and the characterization of individual genetic susceptibility to radiation.

In FY 2005, BER will continue to increase its emphasis on the development and use of experimental systems that enable scientists to make a transition from the use of highly quantifiable but less relevant *in vitro* systems for studying low doses of radiation to *in vivo* systems that are more relevant to human risk from exposure to low doses of radiation but in which it has been very difficult to quantify results. Only by understanding the effects of low doses of radiation in intact tissues or organisms can we hope to determine the health risks from those exposures.

BER will also increase its emphasis on research that results from productive linkages between experimentalists and risk modelers, a relationship that lies at the critical interface between experimental science, risk analysis, and development of better risk management policies.

In particular, research will focus on:

- *Bystander effects* – are the responses of cells that are not directly traversed by radiation but that respond with gene induction and/or production of potential genetic and carcinogenic changes. It is important to know if bystander effects can be induced by exposure to low LET (linear energy transfer) radiation delivered at low total doses or dose-rates. This bystander effect potentially "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. Scientists will be challenged to determine if bystander effects to low doses of ionizing radiation occur *in vivo*.
- *Genomic instability* – is the loss of genetic stability, a key event in the development of cancer, induced by radiation and expressed as genetic damage that occurs many cell divisions after the insult is administered. Current evidence indicates 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, but there is virtually no information on the underlying mechanisms. Its role in radiation-induced cancer remains to be determined experimentally. It is also important to determine if genomic instability occurs at low total doses (<10 rads) or low dose rates. Scientists will be challenged to determine the extent to which low doses of radiation induce genomic instability *in vivo*.

- *Adaptive response* – is the ability of a low dose of radiation to induce cellular changes that reduce 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 needs to be further in *in vivo* systems.
- *Genetic factors that affect individual susceptibility to low dose radiation* – Research is also focused on determining whether genetic differences make some individuals more sensitive to radiation-induced damage since these differences could result in individuals or sub-populations that are at increased risk for radiation-induced cancer.
- *Mechanistic and risk models* – Novel research is supported that involves innovative collaborations between experimenters and modelers to model the mechanisms of key radiation-induced biological responses and to describe or identify strategies for developing biologically based risk models that incorporate information on mechanisms of radiation-induced biological responses. This has been the most difficult and challenging component of the program. A comprehensive effort is underway to identify innovative new research strategies that will determine the extent to which the development of biologically based risk models for low dose radiation is possible. This will involve interactions between experimental and computational scientists and with scientists at regulatory agencies responsible for developing risk policy.

The research activities in this subprogram are carried out at National Laboratories, universities, and private institutions and selected through competitive and peer-reviewed processes. University scientists, competing for funds in response to requests for applications, conduct a substantial fraction of the research in this program.

Human Genome	**73,217**	**64,230**	**64,572**
▪ **Joint Genome Institute**	**53,405**	**51,480**	**51,480**

In April 2003, the scientific community celebrated the completion of the high quality DNA sequence of the human genome and announced the official end of the International Human Genome Project (HGP). Although research to understand the genes identified in the HGP continues, the Joint Genome Institute's (JGI) high-throughput DNA sequencing factory, the Production Genomics Facility, has transitioned away from human sequencing to help meet the growing demand for DNA sequencing in the broader scientific community. The JGI is devoting 60% of its sequencing capacity to peer reviewed sequencing needs of the broader scientific community, including the needs of other agencies. DNA sequencing targets are being chosen using a process of peer review of requests for

sequencing submitted by individual scientists and other federal agencies. Forty percent of the JGI's DNA sequencing capacity are being used to address DOE sequencing needs, including BER programs such as carbon sequestration research and bioremediation research, and other DOE and national needs. The substantial high throughput DNA sequencing needs of the GTL program are supported directly by the Genomics: GTL program and are not included in funds for the JGI.

The JGI is a virtual research institute principally comprised of research programs at DOE national laboratories (LLNL, LANL, LBNL, PNNL, ORNL) and a significant partnership with Stanford University. The JGI's DNA sequencing factory is located in Walnut Creek, California.

- **Tools for DNA Sequencing and Sequence Analysis** **17,823** **11,045** **11,245**

BER continues to develop the tools and resources needed by the scientific, medical, and private sector communities to fully exploit the information contained in complete DNA sequences, including the first human sequence. Unimaginable amounts of DNA sequencing, at dramatically increased speed and reduced cost, will still be required in the future for medical and commercial purposes and to understand the information in the DNA sequence that has already been determined. BER continues to further improve the efficiency and cost effectiveness of its own DNA sequencing factory at the JGI by improving the reagents used in DNA sequencing and analysis (including genome assembly and annotation); decreasing the costs of sequencing; increasing the speed of DNA sequencing; and developing more robust computational tools for genome-wide data analysis.

Use of sequence information to understand human biology and disease will also require new strategies and tools capable of high-throughput, genome-wide experimental and analytic approaches. BER will continue efforts to develop high-throughput approaches for analyzing gene regulation and function.

The research activities in this subprogram are carried out at the JGI, national laboratories, universities, and private institutions and selected through competitive and peer-reviewed processes.

- **Ethical, Legal, and Societal Issues (ELSI)** **1,989** **1,705** **1,847**

The completion of the International Human Genome Project does not end the need to understand the ethical, legal, and societal issues associated with genomics research and information. The DOE ELSI program continues to support research focused on issues of: (1) the use and collection of genetic information in the workplace especially as it relates to genetic privacy; (2) the storage of genetic information and tissue samples especially as it relates to privacy and intellectual property; (3) genetics and ELSI education; and (4) the ELSI implications of advances in the scientific understanding of complex or multigenic characteristics and conditions.

The research activities in this subprogram are carried out at National Laboratories, universities, and private institutions and selected through competitive and peer-reviewed processes.

A table follows displaying both DOE and NIH Human Genome Project funding through the project's completion in FY 2003.

U.S. Human Genome Project Funding

(dollars in millions)

	Prior Years	FY 2003	FY 2004	FY 2005
DOE Funding (FY 87-03)	954.6	73.2	0.0	0.0
NIH Funding (FY 88-03)	2,674.6	467.0	0.0	0.0
Total U.S. Funding	3,629.2	540.2	0.0	0.0

(dollars in thousands)

	FY 2003	FY 2004	FY 2005
Health Effects	**10,513**	**10,175**	**10,237**
▪ **Functional Genomics Research**	**10,513**	**10,175**	**10,237**

Understanding the structure and function of the human genome. – Many individual genes and the regulatory networks that control them have been conserved during evolution in organisms as diverse as yeast and humans. Thus, model organisms including *Fugu* (puffer fish), *Ciona* (sea squirt), frog, and mouse can be used to efficiently understand the organization, regulation, and function of much of the human genome. Functional genomics research is a key link between human genomic sequencing, that provides a complete parts list for the human genome, and the development of information (a high-tech owner's manual) that is useful in understanding normal human development and disease processes. The mouse continues to be a major focus of our efforts and is an integral part of our functional genomics research program. This effort is greatly enhanced by the completion of the Center for Comparative and Functional Genomics at Oak Ridge National Laboratory that will serve as a national focal point for high throughput genetic studies using mice. BER creates and genetically characterizes new mutant strains of mice that serve as important models of human genetic diseases and for understanding gene function especially as they relate to the genetic information found on human chromosomes 5, 16, and 19 (DOE's chromosomes in the International Human Genome Project). It also develops high-throughput tools and strategies to characterize these mutant strains of mice. This mouse genetics research provides tools useful to the entire scientific community for decoding the functionality of the human genome as human DNA sequence becomes available. Research to develop new high-throughput strategies for using model organisms such as the mouse, *Fugu*, and *Ciona* to understand the function of human genes continues.

The research activities in this subprogram are carried out at National Laboratories, universities, and private institutions and selected through competitive and peer-reviewed processes.

(dollars in thousands)

	FY 2003	FY 2004	FY 2005
SBIR/STTR	**0**	**5,456**	**5,377**

In FY 2003 $4,375,000 and $256,000 were transferred to the SBIR and STTR programs, respectively. FY 2004 and FY 2005 amounts are the estimated requirements for continuation of these programs.

Total, Life Sciences	**181,803**	**204,691**	**204,011**

Explanation of Funding Changes

	FY 2005 vs. FY 2004 ($000)
Structural Biology	
▪ Structural Biology basic research is reduced by $5,000,000 and the funds are redirected to the PED construction project for the Genomics: GTL Facility for Production and Characterization of Proteins and Molecular Tags.	-5,165
Molecular and Cellular Biology	
▪ Microbial genomics research maintained at near FY 2004 level	-94
▪ Carbon sequestration research maintained at near FY 2004 level	+64
▪ Increase for "Genomics: GTL" supports additional research to develop high-throughput methods for the production of microbial proteins and molecular tags that will be implemented in the first GTL facility.	+4,033
▪ Low dose radiation research maintained at near FY 2004 level.	+157
Total Molecular and Cellular Biology	+4,160
Human Genome	
▪ Tools for DNA sequencing and sequence analysis maintained at near FY 2004 level	+200
▪ Ethical, Legal and Societal Issues (ELSI) support slightly increased due to rescission in FY 2004.	+142
Total Human Genome	+342
Health Effects	
▪ Functional genomics research maintained at near FY 2004 level.	+62
SBIR/STTR	
▪ Decrease in SBIR/STTR due to decrease in research funding for the Genomics: GTL program.	-79
Total Funding Change, Life Sciences	-680

Climate Change Research

Funding Schedule by Activity

(dollars in thousands)

	FY 2003	FY 2004	FY 2005	$ Change	% Change
Climate Change Research					
Climate and Hydrology	68,956	74,107	74,559	+452	+0.6%
Atmospheric Chemistry and Carbon Cycle	34,546	37,477	37,707	+230	+0.6%
Ecological Processes	11,678	18,612	18,726	+114	+0.6%
Human Interaction	7,002	8,022	8,071	+49	+0.6%
SBIR/STTR	0	3,896	3,896	0	0.0%
Total, Climate Change Research	122,182	142,114	142,959	+845	+0.6%

Description

The mission of the Climate Change Research subprogram is to deliver relevant scientific knowledge that will enable scientifically based predictions and assessments of the potential effects of greenhouse gas and aerosol emissions on climate and the environment.

Benefits

This subprogram's research will reduce and resolve key uncertainties and provide the scientific foundation needed to predict, assess, and mitigate adverse effects of energy production and use on the environment through research in climate modeling and simulation, climate processes, carbon cycle and carbon sequestration, atmospheric chemistry, and ecological science.

Supporting Information

The Climate Change Research subprogram supports four contributing areas of research: Climate and Hydrology; Atmospheric Chemistry and Carbon Cycle; Ecological Processes; and Human Interactions. The research is focused on understanding the physical, chemical, and biological processes affecting the Earth's atmosphere, land, and oceans and how these processes may be affected, either directly or indirectly, by energy production and use, primarily the emission of carbon dioxide from fossil fuel combustion. BER has designed and planned the research program to provide the data that will enable objective assessments of the potential for, and consequences of, global warming. It is intended to provide a scientific basis that will enable decision makers to determine a "safe level" of greenhouse gases in the Earth's atmosphere to avoid a disruptive, human-induced, climate change. The BER Climate Change Research subprogram (excluding the carbon sequestration element) represents DOE's contribution to the interagency U.S. Global Change Research Program (USGCRP) proposed by

President Bush in 1989 and codified by Congress in the Global Change Research Act of 1990 (P.L. 101-606). It also contributes to the Administration's Climate Change Research Initiative (CCRI) initiated in FY 2003.

The CCRI is a set of cross-agency programs in areas of climate change research of high priority and where substantial progress is anticipated over the next three to five years. The specific focus areas of the research are climate forcing (atmospheric concentrations of greenhouse gases and aerosols); climate feedbacks and sensitivity; climate modeling, including enabling research; regional impacts of climate change, including environment-society interactions; and climate observations. FY 2005 funding allows DOE to participate in one of the specific research areas: climate forcing, which includes modeling carbon sources and sinks, especially those in North America. In FY 2005 BER will continue to support research to quantify the magnitude and location of the North American carbon sink, a high priority need in the interagency Carbon Cycle Science Plan and expand its CCRI research to include climate modeling, ARM, and Integrated Assessment activities (FY 2005 request is $25,335,000).

The National Institute for Global Environmental Change (NIGEC) is integrated throughout the subprogram (FY 2005 request is $8,495,000). NIGEC regional centers are located at Harvard University (Northeast Region); the University of California, Davis (Western Region); the University of Nebraska, Lincoln (Great Plains Region); Indiana University, Bloomington (Midwest Region); Tulane University, New Orleans (South central Region); and the University of Alabama, Tuscaloosa (Southeastern Region). The national office of NIGEC center is located at the University of California, Davis.

A major emphasis of the Climate Change Research subprogram is on understanding the radiation balance from the surface of the Earth to the top of the atmosphere and how changes in this balance due to increases in the concentration of greenhouse gases in the atmosphere may alter climate. Much of the research is focused on improving the quantitative models necessary to predict possible climate change at global and regional scales. Research in the ARM program will continue to focus on resolving the greatest scientific uncertainty in climate change prediction – the role of clouds and their interactions with solar radiation. ARM seeks to develop a better quantitative understanding of how atmospheric properties, including the extent and type of cloud cover and changes in aerosols and greenhouse gas concentrations, affect the solar and infrared radiation balance that drives the climate system.

BER's Climate Modeling program develops advanced, fully coupled, atmosphere-ocean-sea ice-land surface, climate models and uses premier supercomputers to simulate and predict climate and climate change, including evaluating uncertainties in climate models due to changes in atmospheric levels of greenhouse gases on decade-to-century time scales.

The Atmospheric Science program is focused on acquiring the data to understand the atmospheric processes that control the transport, transformation, and fate of energy-related chemicals and particulate matter emitted to the atmosphere. In FY 2005, the program will shift to studies of the direct and indirect effects of aerosols on climate.

Research on the carbon cycle explores the movement of carbon on a global scale starting from natural and anthropogenic emissions to ultimate sinks in the terrestrial biosphere and the oceans. Experimental and modeling efforts primarily address the net exchange of carbon between major types of terrestrial ecosystems and the atmosphere. This research includes DOE's contribution to the CCRI.

The BER carbon sequestration element funds basic research that seeks to exploit the biosphere's natural processes to enhance the sequestration of atmospheric carbon dioxide in terrestrial and marine ecosystems. It also seeks the understanding needed to assess the potential environmental implications of purposeful enhancement and/or disposal of carbon in the terrestrial biosphere and at the surface or in the deep ocean. The carbon sequestration activities include research to identify and understand the environmental and biological factors or processes that limit carbon sequestration in these systems and to develop approaches for overcoming such limitations to enhance sequestration. The research includes

studies on the role of ocean and terrestrial microorganisms and terrestrial higher plants in carbon sequestration.

The Ecological Processes research is focused on experimental and modeling studies to understand and be able to predict the effects of climate and atmospheric changes on the biological structure and functioning of terrestrial ecosystems. The research also seeks to identify the potential feedbacks from ecosystems to climate and atmospheric composition. The research emphasizes major field studies of intact ecosystems using experimental manipulations of, for example, carbon dioxide and ozone concentrations and precipitation, and using data from these experiments to develop, test, and improve models for simulating and predicting ecosystem responses to environmental changes associated with energy production and use. The research also focuses on the causal mechanisms and pathways of biological and ecological responses ranging from the proteome of individual species to the whole ecosystem and will develop advanced computational models to establish how changes in the proteomes of single species or whole systems can explain the responses and behavior of complex ecosystems.

The Human Interactions research is focused on improving methods and models that can be used to assess the economic and societal costs and benefits of both human-induced climate change and possible response options or strategies for mitigating or adapting to climate change. It also includes support to archive and analyze climate change data and make it available for use by the broader climate change research community.

Periodic retrospective analysis will be employed to evaluate the accumulation of knowledge and validate specific outcomes. This program was examined as part of a BERAC review of the entire BER program in FY 2001. The next scheduled comprehensive review of the Climate Change Research subprogram by BERAC will be in FY 2005.

Accomplishments:

- *New analysis demonstrates better agreement between model simulations and satellite observations of tropospheric warming.* Scientists from BER's Climate Change Prediction Program found a strong agreement between observed three dimensional tropospheric temperature changes and simulations of the 20th Century climate that included anthropogenic forcing. There has been considerable debate over the last few years about the lack of agreement between the upper tropospheric temperatures recorded by satellite measurements, which show little or no warming, and climate model results, which show warming. Recently, the satellite data have been reanalyzed and the temperature trend in the observations is consistent with that produced by the models. Although this result (published in *Science*) does not end the debate, it does set a new standard for the quantitative comparison of model results to observational data.
- *First-of-a-kind measurements help provide better understanding of aerosol effects on climate.* Using new ARM measurements from the ARM Southern Great Plains site, scientists provided new insights into the effect of pollution on clouds, and, in turn, the heating and cooling of the earth's atmosphere. This question, known as the aerosol indirect effect, has been studied by scientists for thirty years. One of the fundamental theories is that by increasing the number of particles in the atmosphere upon which cloud droplets can form, clouds will have more, but smaller, droplets. Since smaller droplets are more reflective, clouds affected by pollution may cool the earth more than clouds unaffected by pollution. Researchers recently presented the first simultaneous measurements of cloud droplet size and aerosol amount to provide a direct link between the properties of the measured aerosol particles and their effect on the cloud droplets. Seven cases were studied in which the aerosol amount changed significantly over a day. The aerosol indirect effect was calculated by

quantifying how much the cloud droplet size changed in response to the changing aerosol amount. The new measurement strategy provides important data for the development of new cloud model parameterizations within climate models.

- *Effects of emissions from urban areas show that air quality management strategies will require tailoring different strategies for different cities.* Research findings from the air quality studies in the southeast Texas/Houston area and Atlanta show that the primary cause of exceedence of ozone standards in these two urban areas is due to different factors that will have to be considered in developing strategies for reducing tropospheric ozone levels to meet air quality standards in a particular region. In the Houston area, for example, elevated ozone is primarily a result of emissions of non-methane hydrocarbons (the fuel that drives ozone formation) from petrochemical facilities, whereas in Atlanta, it is due to both naturally occurring terpenes emitted by vegetation and elevated nitrogen oxide (the catalyst that controls ozone formation) from fossil fuel combustion. The results indicate that controlling ozone levels in Houston will require a different strategy from that in Atlanta because in the case of Atlanta, the primary source of hydrocarbon emissions are natural and can not be easily controlled, whereas hydrocarbon emissions in the Houston region are primarily from human sources that can be reduced. The results of the study have been incorporated into a new east Texas air quality management strategy.
- *First discovery that carbon allocation in plants is genetically controlled.* Carbon allocation and partitioning among woody plant tissues affects various growth processes, and influences pathways and mechanisms of carbon sequestration by terrestrial ecosystems. Research supported by BER showed that the amount of carbon partitioned to stems, roots, branches, leaves and fine roots is genetically controlled. While genetic factors or environmental variation can theoretically affect carbon partitioning, it has now been determined that for *Populus* trees, a small number of genes control cell wall chemistry and carbon partitioning to substances that have long residence times. More detailed studies of biochemistry have found that plant lignin content is also controlled genetically, and since lignin is relatively resistant to microbial degradation, plant tissues enriched in this substance lead to enhanced carbon sequestration in soil organic matter. These studies point toward plant properties and biophysical mechanisms that may be selected for enhanced carbon sequestration. Studies of genetic variability and understanding the functional relationships will further accelerate research on the application of genome sequence data for manipulating plant carbon partitioning when the *Populus* genome sequence maps are provided by JGI. The research contributes unique information to forest geneticists to use in accelerating development and testing of new *Populus* varieties for enhancing intrinsic productivity and carbon sequestration in terrestrial ecosystems.
- *Deep sea experiments using autonomous undersea vehicles (AUV) assess direct injection as a strategy for ocean carbon sequestration.* Using sophisticated AUV's, experiments supported by BER's ocean carbon sequestration program were conducted in marine sediments at a depth of 3600m to determine the potential impact on deep sea organisms of the direct injection of liquid carbon dioxide (CO_2). The research, which was co-funded by BER and the Office of Fossil Energy, showed for the first time the potential effects of a plume of CO_2 on deep sea animals. Mortality and metabolic effects (such as acidosis and decline in respiratory rate) were a direct function of the distance from the CO_2 plume with immotile animals, but varied among different deep sea fish species. Results from these and other experiments will be essential in assessing the potential environmental consequences of deep ocean injection of CO_2 as a potential purposeful strategy for

sequestering carbon that would have been otherwise emitted to the atmosphere from facilities that burn fossil fuels.

- *First-ever 10-year-long soil warming experiment produces surprises.* BER's Ecological Processes program, some of which is funded through NIGEC, completed the first ever decade-long soil warming experiment. The study documented changes in soil carbon and nitrogen cycling caused by long-term warming in a Massachusetts hardwood forest. Soil warming accelerated soil organic matter decay and carbon dioxide release from the soil to the atmosphere, but that response was small and short-lived (being mostly dissipated by the eighth year of the experiment) because of the limited size of the soil carbon pool in that forest. Soil warming also increased the availability of soil nitrogen to plants in the experimental area. This effect of warming has the potential to stimulate tree growth because many of the forests in the mid latitudes are nitrogen-limited. The increase in nitrogen availability has the potential to stimulate enough carbon storage in trees to compensate for carbon losses from the soil in such forests, at least for a time. These results challenge assumptions made in some coupled climate-carbon cycle models that lead to projections of large and long-term releases of soil carbon to the atmosphere in response to warming of forest ecosystems.
- *Unique field experiments document potential impacts of climatic change*. BER's Ecological Processes research program tested effects of increased variability in rainfall, a prediction of climate models, on the structure and functioning of native grasslands in Kansas. During a 4-year period, rainstorm frequency was reduced and rainfall amount during each storm was increased, without a change in total annual rainfall, in experimental plots. The rainfall manipulations increased temporal variability in soil moisture and plant species diversity. Carbon cycling processes (such as carbon dioxide release from the soil and carbon dioxide assimilation by the dominant prairie grasses) was slowed by increased rainfall variability. The results show that projected increases in rainfall variability might rapidly alter key carbon cycling processes and plant community composition in Midwestern grasslands.

Detailed Justification

(dollars in thousands)

	FY 2003	FY 2004	FY 2005
Climate and Hydrology	**68,956**	**74,107**	**74,559**
▪ **Climate Modeling**	**26,025**	**26,973**	**27,138**

Model-based climate prediction provides the most scientifically valid way of predicting the impact of human activities on climate for decades to centuries in the future. BER will continue to develop, improve, evaluate, and apply the best coupled atmosphere-ocean general circulation models (GCMs) that simulate climate variability and climate change over these time scales. The goal is to achieve statistically accurate forecasts of future climate over regions as small as river basins using ensembles of model simulations. The ensembles will accurately incorporate the dynamic and thermodynamic feedback processes that influence climate, including clouds, aerosols, and greenhouse gas forcing. Current predictions are limited by computational resources and uncertainties in the model representations of key small-scale physical processes, especially those involving clouds, evaporation, precipitation, and surface energy exchange. BER will address both the computational and scientific shortcomings through an integrated effort. Support will continue to provide climate modelers access to the high-end computational resources needed to complete ensembles of climate simulations using present and future models. BER will

emphasize research to develop and employ information technologies that can quickly and efficiently work with large and distributed data sets of both observations and model predictions to produce quantitative information suitable for the study of regional climate changes. BER will continue to fund the multi-institutional research consortia established in FY 2001 to further the development of comprehensive coupled GCMs for climate prediction that are of higher resolution and contain accurate and verified representations of clouds and other important climate processes. In FY 2005 BER will continue the partnership with the Advanced Scientific Computing Research program. This includes applying the computing resources for climate simulation and continuing climate model development and application through the use of collaboratory technologies. Additionally, BER will emphasize data assimilation methods so as to quickly make use of the high-quality observational data streams provided by ARM, satellite, and other USGCRP climate data programs to evaluate model performance.

For CCRI the research will provide ensemble projections of multi-century climate change using the Community Climate System Model through the Climate Change and Assessment Working Group. Additionally, the program will provide the infrastructure for major model evaluation and model improvement research through the coordination of model intercomparisons and the maintenance of model test beds for parameterization testing. In FY 2005 climate model experiments ($15,347,000) will provide scenarios, such as CO_2 stabilization scenarios.

In FY 2005 BER's SciDAC program ($7,776,000) will focus on improving the models used for climate simulation and prediction. A major effort will be dedicated to providing a robust and extensible software engineering framework for the Community Climate System Model, a code used by hundreds of researchers on many different high-end computing platforms. Additional research will provide the prototype climate model of the future that will explore approaches to climate simulation and prediction for the next ten years.

In FY 2005, NIGEC will continue to support research needed to understand how changes in terrestrial ecosystems brought about by climatic changes may, in turn, affect climatic changes through various feedback processes (FY 2005 request is $1,933,000).

The research activities in this subprogram are carried out at National Laboratories, universities, and at private institutions and are selected through competitive and peer-reviewed processes.

High performance computing resources are provided for development and implementation of advanced climate models.

- **Atmospheric Radiation Measurement (ARM) Research** **11,238** **12,960** **13,247**

In FY 2005, the principal goal of the ARM scientific enterprise continues to be the development of an improved understanding of the radiative transfer processes in the atmosphere and to formulate better parameterizations of these processes in climate prediction models, referred to as General Circulation Models (GCMs). ARM research supports about 50 principal investigators involved in studies of cloud physics and the interactions of solar and infrared radiation with water vapor and aerosols (including black soot). University scientists form the core of the ARM science team that networks with the broader academic community as well as with the scientists at the

DOE National Laboratories and with federal scientists at NASA, NOAA, and DOD. ARM scientists pursue research as individuals and as members of teams and contribute both to the production of ARM data, e.g., as designers of cutting-edge remote sensing instrumentation, as well as consumers of the data produced at the three ARM sites. To facilitate the knowledge transfer from the ARM program to the premier modeling centers, the ARM program supports scientific "Fellows" at the NSF's National Center for Atmospheric Research, the NOAA's National Center for Environmental Prediction, and the European Center for Medium-Range Weather Forecasting in the U.K. In addition, a model parameterization test bed initiated in FY 2003 will be continued to enable the testing and improvement of submodels by rapidly incorporating data from the ARM sites into the models to enable diagnostic tests and intercomparisons of model simulations with real world data.

- **Atmospheric Radiation Measurement (ARM) Infrastructure**..... **28,965** **31,441** **31,441**

In FY 2005, the ARM infrastructure program will continue to develop, support, and maintain the three ARM sites and associated instrumentation. BER will continue to operate over two hundred instruments (e.g., multifilter shadowband radiometers for aerosol measurements; Raman Lidar for aerosol and cloud measurements; radar wind profiler systems; radar cloud measurement systems; sky imaging systems; arrays of pyranometers, pyrgeometers, and pyrheliometers for atmospheric and solar radiation measurements; and standard meteorological measurement systems for characterization of the atmosphere) at the Southern Great Plains site and will continue operations at the Tropical Western Pacific station and at the North Slope site in Alaska. The ARM program will continue to provide data to the scientific community through the ARM Archive.

The ARM data streams will continue to be enhanced periodically by additional measurements at the ARM sites during intensive field campaigns referred to as Intensive Operation Periods (IOPs). Ranging from two weeks to two months, the campaigns bring together teams of scientists testing cutting edge remote sensing instruments and coordinate measurements with airborne and satellite observations. The ARM sites have become major testbeds of research in atmospheric processes serving as scientific user facilities for hundreds of scientists from universities and government laboratories. For example, both DOD and NASA have used the ARM sites to "ground truth" their satellite instruments.

The UAV program will conduct a major field campaign in conjunction with the ARM program to measure the effect of cirrus clouds on the absorption and scattering of downwelling radiation over the Western Tropical Pacific ARM-CART site.

The CCRI ARM program will deploy a mobile climate observatory to provide new atmospheric measurements needed to fill data gaps and will develop the corresponding data products needed for evaluating and modeling the effects of atmospheric processes and properties on the radiation balance and for developing and evaluating the models. In FY 2005 a mobile Cloud and Radiation Testbed (CART) ($4,100,000), consisting of a variety of meteorological and atmospheric sensors, will be deployed in a selected data-poor region (e.g., tropics) or a region that represents a location of opportunity for measuring the effects of atmospheric conditions on the radiation balance that are currently poorly understood (e.g., direct and indirect effects of aerosols). The mobile climate

observatory will be instrumented for cloud and radiation measurements. The primary siting criterion is to provide those measurements needed to address specific modeling needs that presently cannot be addressed by the permanent ARM sites. Activities will be coordinated with other U.S. agencies and international partners, such as Australia, Japan, China, and European countries. Data products will be developed through collaborations with model developers. In FY 2005 the criteria for data products for evaluating precipitation processes will be established.

The research activities in this subprogram are carried out at National Laboratories, universities, and at private institutions and are selected through competitive and peer-reviewed processes.

- **Atmospheric Radiation Measurement (ARM)/Unmanned Aerial Vehicles (UAV)** **2,728** **2,733** **2,733**

The UAV program will conduct one major field campaign in conjunction with the ARM program to provide high altitude measurements of cloud properties and radiation balance.

Atmospheric Chemistry and Carbon Cycle **34,546** **37,477** **37,707**

- **Atmospheric Science** **11,546** **12,475** **12,551**

The CCSP strategic plan has raised the priority of research dealing with the climate effects of atmospheric aerosols. As a result BER is restructuring the Atmospheric Science program to focus entirely on the aerosol-climate connection.

In FY 2005 the Atmospheric Chemistry Program will, in effect, become the Tropospheric Aerosol Program (TAP) to quantify the impacts of energy-related aerosols on climate. It will be closely coupled with other components of DOE's climate change research, especially the ARM program. TAP will also be broadly coordinated with the air quality and global change research communities, including collaborations with the EPA, NASA, and NOAA and with the DOE Office of Fossil Energy's Airborne Fine Particulate Matter (PM) Research program. Regional patterns of aerosol distribution will be related to sources and sinks and the information will feed the models that simulate the impacts of aerosols on climate.

The Atmospheric Science program will acquire data to understand the atmospheric processes that control the transport, transformation, and fate of energy-related aerosols. Emphasis will be on processes relating to particulate matter and climate change. Field and laboratory studies will continue to be conducted in atmospheric chemistry and acquired data will be used to develop and validate predictive models of atmospheric processes. The research will include studies of chemical and physical processes affecting sulfur and nitrogen oxides, gas-to-particle conversion processes, and the deposition and resuspension of associated aerosols. It will also include studies to improve understanding of the meteorological processes that control the dispersion of energy-related chemicals and particulates in the atmosphere. Much of this effort will involve multi-agency collaboration, and university scientists will play key roles. The information is essential for assessing the effects of energy production on climate and will contribute to the evaluation of science-based options for minimizing the impact of energy production on climate change.

In FY 2005, NIGEC will support research to quantify the effects of natural processes on atmospheric composition, focusing on the exchange of carbon dioxide between the atmosphere and the terrestrial biosphere (FY 2005 request is $2,187,000).

(dollars in thousands)

FY 2003	FY 2004	FY 2005

The research activities in this subprogram are carried out at National Laboratories, universities, and private institutions and selected through competitive and peer-reviewed processes.

- **Terrestrial Carbon Processes and Ocean Sciences** **15,776** **16,410** **16,613**

In FY 2005, BER will continue supporting the AmeriFlux program, a network of approximately 25 research sites that measure the net exchange of CO_2, energy, and water between the atmosphere and major terrestrial ecosystems in North America. These measurements are linked to field measurement campaigns across North America that will test how well point measurements represent larger areas and allow the estimation of carbon sources and sinks on a regional basis. This research supports the interagency Carbon Cycle Science Plan. The fluxes of other greenhouse gases, e.g., methane and nitrous oxide, will also be measured at 5 to 10 AmeriFlux sites.

BER will also continue research to refine and test terrestrial carbon cycle models (based on mechanistic representations and carbon accounting). The models will be used to estimate potential carbon sinks and sources in response to changes in environmental factors, including climate.

The continuing focus of the ocean science element is on using microbiological tools to determine the linkages between the carbon and nitrogen cycles involving marine microbes. This research is conducted through partnerships between institutions with a tradition of research in oceanography (such as Skidaway Institute of Oceanography, U. of Washington, U. of Delaware, Rutgers U., U. of South Florida, Princeton U.), and institutions traditionally serving minority students (such as Lincoln U., Howard U., Savannah State U., U. of Puerto Rico, and San Francisco State).

In FY 2005 BER CCRI activities on the carbon cycle will continue to explore the movement of carbon starting from natural and human-induced emissions to the atmosphere to ultimate sinks in the terrestrial biosphere and the oceans. The AmeriFlux sites supported by BER are essential to quantifying the net exchange of carbon between the atmosphere and major terrestrial ecosystems in North America. Hence, they are essential to documenting the magnitude and variation in the North American carbon sink and how it is affected by variation and changes in environmental factors such as climate. BER will continue measurements and process studies at the network of AmeriFlux sites across North America. This information, along with data from extensive measurements around the sites, will provide a sound scientific basis for extrapolating carbon flux measurements at AmeriFlux sites to landscape and regional scales. Hence, it will improve estimates of the magnitude of the North American carbon sink and identify the regions and ecosystem types that account for the sink. In FY 2005 the research will deliver an intercomparison of AmeriFlux-based estimates of the net annual exchange of CO_2 between terrestrial ecosystems and the atmosphere for a region of the U.S. with independent estimates using atmospheric sampling and inverse modeling.

The research activities in this subprogram are carried out at National Laboratories, universities, and private institutions and selected through competitive and peer-reviewed processes.

- **Carbon Sequestration Research** **7,224** **8,592** **8,543**

In FY 2005, BER will continue support for one carbon sequestration research consortium, led by ORNL, PNNL, and ANL, and involving six collaboratory universities, that focuses on terrestrial

sequestration, consortium for research on enhancing Carbon Sequestration in Terrestrial Ecosystems (CSiTE) ($3,000,000). The consortium develops information to enhance the natural sequestration of carbon in terrestrial soils and vegetation. BER will also continue the support of research at universities and DOE laboratories on ocean carbon sequestration ($2,000,000). The focus of the research on terrestrial and ocean sequestration will continue to be on cellular and biogeochemical processes that control the rate and magnitude of carbon sequestration in terrestrial and oceanic systems, including the identification of pathways and processes that could be modified to enhance the net flow of carbon from the atmosphere to terrestrial plants and soils, and to the ocean surface and, ultimately, to the deep ocean. Also, BER will support the research needed to assess the environmental implications of enhancing carbon sequestration and storage in the ocean and in terrestrial systems. BER research on carbon sequestration in terrestrial ecosystems will improve the scientific understanding of mechanisms of sequestration and how to alter them to enhance sequestration. The CSiTE activity will conduct research that specifically examines those plant and soil processes that capture and retain carbon in chemical and physical forms that are resistant to decay. The data will inform new models for estimating carbon sequestration in terrestrial ecosystems. New technologies will be developed by the BER-supported ocean carbon sequestration research to facilitate the export of carbon to the deep ocean and for re-mineralization of organic carbon at depth. Such technologies are vital to assessing accurately the potential of enhancing ocean carbon sequestration. Initial *in situ* experiments will be designed to determine the feasibility and potential environmental impacts of deep ocean injection of CO_2. Associated research will include determination of chemical reactions at depth, stability of products, and effects of those products on marine organisms.

In FY 2005, university scientists will continue the analyses of research results on the effects of iron fertilization on plankton communities in the Southern Ocean. The ocean surrounding Antarctica is the largest high-nutrient, low-chlorophyll region in the world. The joint DOE-NSF Southern Ocean Iron Enrichment Experiment (SOFeX) will help scientists understand the potential to enhance ocean carbon sequestration through iron enrichment.

Ecological Processes	**11,678**	**18,612**	**18,726**

In FY 2005, new ecological research will continue to develop a more mechanistic understanding of the scales of response of complex ecosystems to environmental changes, including identifying the underlying causal mechanisms and pathways and how they are linked, ranging from the proteomes of individual species to the whole ecosystem. The focus will be on understanding the linkages of scales in model terrestrial ecosystems containing simplified but hierarchical communities (higher plants, consumers of plant production, and soil microorganisms). A key environmental factor such as temperature that is known to affect ecosystem functioning (e.g., carbon and nutrient cycling) will be experimentally manipulated and proteomic responses of individual species and the whole ecosystem will be measured. Advanced biologically based computational algorithms and ecosystem models will be developed to establish whether and how proteomic changes (in either single species or whole systems) explain the responses and behavior of complex ecosystems. Tools and principles developed from this research should have broad generality and eventual application to problems in carbon sequestration, ecological risk assessment, environmental restoration and cleanup, and early detection of ecological responses to climate change and other environmental factors.

(dollars in thousands)

FY 2003	FY 2004	FY 2005

BER will continue four Free-Air Carbon Dioxide Enrichment (FACE) experiments. They are located at Duke University (North Carolina), Rhinelander (Wisconsin), Oak Ridge (Tennessee), and Mercury (Nevada) on the Nevada Test Site. The experiments will improve understanding of the direct effects of elevated carbon dioxide and other atmospheric changes (such as elevated ozone) on the structure and functioning of various terrestrial ecosystems. Emphasis will be on understanding the cause of differential responses of plant species that may impact plant competition, succession, and productivity in terrestrial ecosystems. Research will explore changes, over time, in the effects of elevated atmospheric carbon dioxide concentrations on net primary productivity.

The long-term experimental investigation of altered precipitation at the Walker Branch Watershed in Tennessee will continue to improve the understanding of the direct and indirect effects of changes in the annual average precipitation amount on the functioning and structure of a southeastern deciduous forest ecosystem.

Both the FACE network and the Walker Branch Watershed represent scientific user facilities that have attracted scientists from both the academic community and government laboratories who use the facilities to test scientific hypotheses related to ecosystem responses, including carbon sequestration, to climatic and atmospheric changes.

In FY 2005, NIGEC will support experimental studies to understand how climate change and increasing CO_2 levels in the atmosphere affect structure and functioning of terrestrial ecosystems (FY 2005 request is $2,625,000).

The research activities in this subprogram are carried out at National Laboratories, universities, and private institutions and selected through competitive and peer-reviewed processes.

Human Interactions **7,002** **8,022** **8,071**

The Integrated Assessment program, with a strong academic involvement, will continue to support research that will lead to better estimates of the costs and benefits of possible actions to mitigate global climate change. The goal is to improve the integrated assessment models to include several greenhouse gases, carbon sequestration, and international trading of emission permits. The models will better represent the efficiency gains and losses of alternative emission reduction plans, including market adjustments to inter-regional differences among relative energy prices, regulations, and production possibilities in the international arena. Integrated assessment models will be modified to include carbon sequestration as an alternative mitigation option. This representation will include both options to enhance natural carbon storage in the terrestrial biosphere, as well as engineering options, such as the capture of carbon dioxide and storage in geologic formations.

The research will include integrating a new land and ocean carbon sub-model in a large integrated assessment model. The submodel includes a detailed representation of direct human influence (mainly agriculture and forestry) on the terrestrial biosphere. In addition to providing a more accurate representation of the global carbon cycle, the improvement will ensure consistent accounting of carbon-sink projects and the carbon uptake that occurs as a result of other land-use change and the effects of climate change and carbon fertilization. A second integrated assessment model will be used to simulate the effect of (1) climate on crop yields and (2) the amount of crop and pasture land necessary to provide (a) a sufficient diet in developing countries under climate change and (b) the

(dollars in thousands)

likely increase in dietary requirements as developing countries become richer.

The Integrated Assessment research program will fund research to develop internally consistent sets of scenarios that can be used for national-scale decision-making. The scenarios will be evaluated in selected integrated assessment models, also funded by the Integrated Assessment program. In FY 2005 the Integrated Assessment program will produce at least four scenarios to provide alternatives to the scenarios that were published by the Intergovernmental Panel on Climate Change (IPCC) since the published IPCC scenarios have received significant criticism. These scenarios will include forecasts of such items as economic productivity, population, and energy use by global region. They will serve as input to the Integrated Assessment Models and will be used as input to decision support analysis in the CCRI ($2,972,000).

In FY 2005, NIGEC will support research to develop and test ecological models and coupled models of climatic ecologic-economic systems that would be required to conduct integrated assessments of the effects of climate change on regionally important natural resources in the U.S. (FY 2005 request is $1,750,000).

The Information and Integration element stores, evaluates, and quality-assures a broad range of global environmental change data, and disseminates those data to the broad research community. BER will continue the Quality Systems Science Center for the tri-lateral (Mexico, United States, and Canada) NARSTO (formally known as the North American Strategy for Tropospheric Ozone), a public partnership for atmospheric research in support of air quality management. The Center serves a diverse set of users, including academic and laboratory scientists and policy makers across North America.

The Global Change Education program supports DOE-related research in global environmental change for both undergraduate and graduate students, through the DOE Summer Undergraduate Research Experience (SURE), the DOE Graduate Research Environmental Fellowships (GREF), and collaboration with the NSF Significant Opportunities in Atmospheric Research and Science (SOARS) program.

The research activities in this subprogram are carried out at National Laboratories, universities, and private institutions and selected through competitive and peer-reviewed processes.

SBIR/STTR	**0**	**3,896**	**3,896**

In FY 2003 $3,108,000 and $186,000 were transferred to the SBIR and STTR programs, respectively. FY 2004 and FY 2005 amounts are the estimated requirements for continuation of these programs.

Total, Climate Change Research	**122,182**	**142,114**	**142,959**

Explanation of Funding Changes

	FY 2005 vs. FY 2004 ($000)
Climate and Hydrology	
▪ Climate Modeling funding restored to FY 2004 level prior to rescission.	+165
▪ Atmospheric Radiation Measurement (ARM) research funding restored to FY 2004 level prior to rescission.	+287
Total, Climate and Hydrology	+452
Atmospheric Chemistry and Carbon Cycle	
▪ Atmospheric Science funding restored to FY 2004 level prior to rescission.	+76
▪ Terrestrial Carbon Processes and Ocean Sciences restored to near FY 2004 level prior to rescission.	+203
▪ Carbon Sequestration maintained at near FY 2004 level.	-49
Total, Atmospheric Chemistry and Carbon Cycle	+230
Ecological Processes	
▪ Ecological Processes funding restored to FY 2004 level prior to rescission.	+114
Human Interactions	
▪ Human interactions funding restored to FY 2004 level prior to rescission.	+49
Total Funding Change, Climate Change Research	+845

Environmental Remediation

Funding Schedule by Activity

(dollars in thousands)

	FY 2003	FY 2004	FY 2005	$ Change	% Change
Environmental Remediation					
Bioremediation Research	29,063	27,359	30,640	+3,281	+12.0%
Clean Up Research	33,094	39,013	35,027	-3,986	-10.2%
Facility Operations	39,218	39,158	37,138	-2,020	-5.2%
SBIR/STTR	0	2,778	2,717	-61	-2.2%
Total, Environmental Remediation	101,375	108,308	105,522	-2,786	-2.6%

Description

The mission of the Environmental Remediation subprogram is to deliver the scientific knowledge, technology, and enabling the discoveries in biological and environmental research needed to underpin the Department of Energy's mission for environmental quality.

Benefits

The fundamental research supported in this subprogram will reduce the costs, risks, and schedules associated with the cleanup of the DOE nuclear weapons complex; extend the frontiers of biological and chemical methods for remediation; to discover the fundamental mechanisms of contaminant transport in the environment; develop cutting edge molecular tools for investigating environmental processes; and develop an understanding of the ecological impacts of remediation activities. In addition much of the work performed for the cleanup program will provide fundamental knowledge that applies to a broad range of remediation problems, as well to the development of advanced nuclear waste management approaches, and the prediction and avoidance of environmental hazards for future nuclear energy options.

Supporting Information

Research priorities include bioremediation, contaminant fate and transport, nuclear waste chemistry and advanced treatment options, and the operation of the William R. Wiley Environmental Molecular Sciences Laboratory (EMSL) and the Savannah River Ecology Laboratory (SREL). These activities provide complementary knowledge and capabilities, which will be integrated to optimize the research.

Bioremediation activities are centered on the Natural and Accelerated Bioremediation Research (NABIR) program, a basic research program focused on determining how and where bioremediation may be applicable as a reliable, efficient, and cost-effective technique for cleaning up or containing metals and radionuclides in contaminated subsurface environments. In the NABIR program, research advances will continue to be made from molecular to field scales in the Biogeochemical Dynamics element; on genes and proteins used in bioremediation and in overcoming physicochemical impediments to bacterial activity through the Biomolecular Science and Engineering element; in non-destructive,

real-time measurement techniques in the Assessment element; on species interaction and response of microbial ecology to contamination in the Community Dynamics and Microbial Ecology element; and in understanding microbial processes for altering the chemical state of metallic and radionuclide contaminants through the Biotransformation element. In analogy with the Ethical, Legal, and Social Implications component of the Human Genome program, the Bioremediation and its Societal Implications and Concerns component of NABIR is exploring societal issues surrounding bioremediation research and promoting open and interactive communication with stakeholders to help ensure understanding and acceptance of bioremediation as a potential solution to remediating contaminants. All NABIR elements and EMSL activities have a substantial involvement of academic scientists.

The Clean Up Research and Environmental Management Science Programs (EMSP) focus on a variety of solutions for the DOE weapons complex cleanup effort. Three primary elements include: contaminant fate and transport in the subsurface, nuclear waste chemistry and advanced treatment options, and novel characterization and sensor tools. This program works closely with related programs in the Basic Energy Sciences program and with related programs of other agencies. The SREL is managed through a cooperative agreement with the University of Georgia and performs ecological research aimed at understanding bioavailability of contaminants and ensuring that environmental cleanup operations do not disturb the biodiversity at the restored environment.

Within Facility Operations, support of the EMSL national user facility operations is focused on providing advanced molecular tools to the scientific community in such areas as environmental remediation sciences, biology and genomics, and atmospheric science. In FY 2005, unique EMSL facilities, such as the newly upgraded Molecular Science Computing Facility, 900 MHz nuclear magnetic resonance (NMR) spectrometers, and the High-Field Mass Spectrometry Facility will expand both their scientific scope and their user base.

Periodic retrospective analysis will be employed to evaluate the accumulation of knowledge and validate specific outcomes. The next scheduled comprehensive review of the Environmental Remediation Sciences subprogram by BERAC will be in FY 2004.

Accomplishments:

- *Diverse microorganisms reduce metal and radionuclide contaminants and are common in subsurface environments.* Studies funded by the NABIR Program have found that a wide diversity of naturally occurring microorganisms have the capability of reducing metals and radionuclides to an insoluble state. These microorganisms include many different genera from within the family Geobacteraceae as well as unrelated microbes from genera such as *Clostridium* and *Anaeromyxobacter.* Metal reducing microbes were found at six DOE sites as well as at industrial and pristine sites. This finding is important because it means that it will not be necessary to genetically engineer microorganisms for this important function. Rather, we can take advantage of the natural catalytic power of *in situ* microorganisms to remediate metals and radionuclides.
- *Field studies confirm the potential of natural communities of microorganisms to reduce and immobilize uranium and technetium*. "Push-pull" tests are a means to interrogate subsurface microbial communities to assess their ability to perform different metabolic activities. A series of tests (>60) performed at the NABIR Field Research Center at the Oak Ridge Reservation confirmed that naturally occurring subsurface microorganisms can reduce technetium (Tc) and uranium (U) *in situ*. When these microbial communities were fed carbon sources such as ethanol, a sharp reduction occurred in the concentrations of soluble Tc and U at moderate pH's and low nitrate. However, the

presence of high nitrate or low pH inhibited the removal of Tc and U *in situ*. These findings are of critical importance to the development of new *in situ* bioremediation and monitored natural attenuation strategies and technologies.

- *Solve foaming problems in treatment of radioactive wastes*. Foaming during treatment of high level wastes is a major cause of delays and processing problems. Commercial antifoaming agents are not effective because of the complex physicochemical behavior of these wastes. An Environmental Management Science Program (EMSP) project "Foaming and Antifoaming in Waste Pretreatment and Immobilization Processes," studied the detailed mechanisms of foaming in processes for treating high and low level radioactive wastes, and developed plans for preventing this foaming. The project is based at the Illinois Institute of Technology (IIT) in Chicago, with collaborators at the DOE Hanford and Savannah River sites, where the largest quantities of high level radioactive wastes await treatment. Using this knowledge, they designed a combination of antifoam agents that have been deployed successfully to bring the foaming problem under control.
- *Test x-ray analyzer for measuring radioactive elements in waste streams.* Scientists carrying out an EMSP project at Los Alamos National Laboratory entitled "Radiochemical Analysis by High Sensitivity Dual-Optic Micro X-ray Fluorescence," are providing a new and reliable means for measuring small amounts of radioactive species in radioactive wastes. Measurement of the particles emitted when a radioactive atom decays requires preliminary treatment of test samples when the emissions are non-penetrating alpha or low-energy beta particles, as for example with the major fission product technetium-99. The new technique makes use of the characteristic X-rays given off by this element when excited by an X-ray beam, enabling measurements without removal of samples from the waste stream being treated. The new instrumentation has been developed in collaboration with X-ray Optical Systems, Inc.
- *Experimental and computational research by EMSL scientists and users eliminates need for multi-million dollar corrective action at Hanford*. Understanding the extent and potential for migration of radioactive contaminants in the subsurface beneath the high level waste tanks at the Hanford Site are difficult challenges for DOE. Key to understanding the potential for migration is the solubility of contaminants such as cesium, as well as the potential for cesium interactions with mineral surfaces. Using spectroscopic techniques, computational modeling, and other techniques, a group of scientists from the EMSL collaborated with a number of users to demonstrate that cesium leaking from tanks in the S-SX tank farm would interact with mineral surfaces, and would not migrate in ground water. These results provided the scientific basis for an agreement made between DOE-RL and the regulators to avoid such costly cleanup effort at the S-SX Hanford tank farm.
- *EMSL instrumentation used to determine the structure of breast cancer tumor suppressor protein interactions.* The availability of high-end (750 MHz and 800 MHz) NMR spectrometers within the EMSL makes possible studies of the molecular structures of proteins and enzymes. Using these high end NMR's, EMSL users from the University of Washington were able to determine the structure and interactions of proteins and protein complexes involved in breast cancer. These researchers were able to determine structural changes that predispose the protein complexes to lead to breast cancer tumors.

Detailed Justification

(dollars in thousands)

	FY 2003	FY 2004	FY 2005
Bioremediation Research	**29,063**	**27,359**	**30,640**
▪ **NABIR and Bioremediation Research**	**23,145**	**21,589**	**24,097**

In FY 2005, NABIR will continue to increase the understanding of the intrinsic bioremediation (natural attenuation) of DOE-relevant metal and radionuclide contaminants, as well as of manipulated, accelerated bioremediation using chemical amendments. Laboratory and field experiments will be conducted to explore the fundamental mechanisms underlying chemical processes and complexation/transformation of contaminants. The NABIR Field Research Center (FRC) is operated by the Oak Ridge National Laboratory. Field site characterization of this FRC and distribution of research samples to investigators will continue. In FY 2005, science elements in the NABIR program continue fundamental research on the following subjects: (1) Biotransformation (microbiology to elucidate the mechanisms of biotransformation of metals and radionuclides); (2) Community Dynamics and Microbial Ecology (structure and activity of subsurface microbial communities); (3) Biomolecular Science and Engineering (molecular and structural biology to enhance the understanding of bioremediation and identify novel remedial genes); (4) Biogeochemical Dynamics (dynamic relationships among *in situ* geochemical, geological, hydrological, and microbial processes); and (5) Assessment (measuring and validating the biological and geochemical processes of bioremediation). University scientists continue to form the core of the NABIR science team that networks with the broader academic community as well as with scientists at the National Laboratories and at other agencies.

The NABIR FRC is located near the Y-12 area at the Oak Ridge Reservation and is the site of field-scale, hypothesis-driven research on the bioremediation of metals and radionuclides. Researchers are characterizing and modeling the subsurface water flow, contaminant transport, and biogeochemical processes at the FRC. These experiments will be completed and prepared for peer-reviewed publication in FY 2003. In FY 2005, field experiments will continue. They will combine both microbiological and chemical treatment of uranium and the common co-contaminant, nitrate.

Additional funds will support new field experiments and will support development of a second FRC, with different geophysical characteristics than the current FRC, as recommended by BERAC.

The NABIR program will continue to take advantage of recently completed genome sequences of important metal and radionuclide-reducing microorganisms to study the regulation and expression of genes that are important to bioremediation.

The research activities in this subprogram are carried out at National Laboratories, universities, and private institutions and selected through competitive and peer-reviewed processes.

▪ **General Plant Projects (GPP)**	**4,749**	**4,811**	**5,584**

The General Plant Projects (GPP) funding is continued for minor new construction, other capital alterations and additions, and for buildings and utility systems such as replacing piping in 30- to 40-year old buildings, modifying and replacing roofs, and HVAC upgrades and replacements. Funding of this type is essential for maintaining the productivity and usefulness of Department-owned facilities and in meeting the requirements for safe and reliable facilities operation. This subprogram

(dollars in thousands)

FY 2003	FY 2004	FY 2005

includes stewardship GPP funding for Pacific Northwest National Laboratory (PNNL) and for Oak Ridge Institute for Science and Education (ORISE). The total estimated cost of each GPP project will not exceed $5,000,000.

- **General Purpose Equipment (GPE)**..... **1,169** **959** **959**

The General Purpose Equipment (GPE) funding will continue to provide general purpose equipment for PNNL and ORISE such as information system computers and networks, and instrumentation that supports multi-purpose research.

Clean Up Research **33,094** **39,013** **35,027**

- **Clean Up Research**..... **1,823** **2,362** **0**

The activities in clean up research that were directly related to Environmental Management clean up operations have concluded and will be incorporated into the EMSP program.

- **Environmental Management Science Program** **24,471** **29,052** **27,251**

The goal of the Environmental Management Science Program (EMSP), transferred in FY 2003 from Environmental Management to the BER program, is to support basic research that improves the science base underpinning the clean up of DOE sites. Traditional clean up strategies may not work or be cost effective for many of the challenges that could prevent the successful closure of DOE sites. The EMSP, through its support of basic research aims to develop and validate technical solutions to complex problems, providing innovative new technologies to overcome major obstacles that lead to future risk reduction and cost and time savings. It is the intent or the expectation of the EMSP that the basic research projects funded are directed toward specific issues and uncertainties at the DOE cleanup sites. EMSP research will focus on contaminant fate and transport in the subsurface, nuclear waste chemistry and advanced treatment options, and novel characterization and sensor tools. In addition, studies on bioremediation of organic contaminants are conducted in EMSP, complementing the NABIR program, which focuses on metals and radionuclides.

EMSP projects will continue to be funded through a competitive peer review process. The most scientifically meritorious research proposals and applications will be funded based on availability of funds and programmatic relevance to ensure a complete and balanced research portfolio that addresses DOE needs. Research will be funded at universities, national laboratories, and at private research institutes and industries. This research will be conducted in collaboration with the Office of Environmental Management. Funding is reduced to increase research at and development of Field Research Centers through the NABIR program.

(dollars in thousands)

FY 2003	FY 2004	FY 2005

- **Savannah River Ecology Laboratory**..... **6,800** **7,599** **7,776**

  This activity supports, through a cooperative agreement with the University of Georgia, a long-term (40+ years) ecological research activity aimed at reducing the cost of clean up and remediation while ensuring biodiversity at the restored environment. Peer-reviewed research will be supported to assess the ecological risks of environmental contaminants and remediation activities. Characterizing and understanding the impacts of environmental contamination on intact, living ecosystems is a complex and long-term process since the research is dependent on natural cycles of growth, reproduction, and normal environmental variation. .

  In FY 2005, new ecological research will be focused around the Environmental Remediation Science Division Field Research Centers so that it can be integrated with the flow and transport and characterization studies. This will continue a broad educational component at the site including opportunities for K-12, undergraduate, and graduate students, and post doctoral fellows

Facility Operations: William R. Wiley Environmental Molecular Sciences Laboratory (EMSL)..... **39,218** **39,158** **37,138**

- **Operating Expenses** **38,579** **35,169** **35,149**

  The EMSL is a scientific user facility located at the Pacific Northwest National Laboratory focused on conducting interdisciplinary, collaborative research in molecular-level environmental science. Operating funds are essential and will continue to allow the EMSL to operate as a user facility, and are used for maintenance of buildings and instruments, utilities, staff support for users, environment, safety and health compliance activities, and communications. With over 55 leading-edge instruments and a supercomputer system, the EMSL annually supports approximately 1400 users. University scientists form the core of the EMSL science team that networks with the broader academic community as well as with scientists at DOE National Laboratories and at other agencies. EMSL users have access to unique instrumentation for environmental research, including a new Linux-based supercomputer, a 900 MHz NMR spectrometer that adds to the suite of NMRs in EMSL, a suite of mass spectrometers, including an 11.5 Tesla high performance mass spectrometer, laser desorption and ablation instrumentation, ultra-high vacuum scanning tunneling and atomic force microscopes, and controlled atmosphere environmental chambers.

- **Capital Equipment**..... **639** **3,989** **1,989**

  Capital equipment support for the EMSL enables instrument modifications needed by collaborators and external users of the facility as well as the purchase of state-of-the-art instrumentation to keep EMSL capabilities at the leading edge of molecular-level scientific research. Funding is reduced due to completion, in FY 2004, of capital purchases associated with the EMSL computer upgrade and installation of the 900 MHz NMR.

	(dollars in thousands)		
	FY 2003	FY 2004	FY 2005
SBIR/STTR	**0**	**2,778**	**2,717**

In FY 2003 $2,385,000 and $149,000 were transferred to the SBIR and STTR programs, respectively. FY 2004 and FY 2005 amounts are the estimated requirements for continuation of these programs.

Total, Environmental Remediation	**101,375**	**108,308**	**105,522**

Explanation of Funding Changes

	FY 2005 vs. FY 2004 ($000)
Bioremediation Research	
▪ NABIR and Bioremediation increase will be used for additional integrated Field Research Centers, which are needed to address the complexity, scaling issues, and coupled interactions between microbes and environmental entities.	+2,508
▪ GPP funding increased to reduce maintenance backlog at PNNL	+773
Total, Bioremediation Research	+3,281
Clean Up Research	
▪ Clean Up Research activities are concluded and program objectives incorporated into EMSP.	-2,362
▪ Environmental Management Science Program funding is redirected to enhance NABIR and bioremediation research at the Field Research Centers.	-1,801
▪ Savannah River Ecology Laboratory is maintained at near FY 2004 level.	+177
Total, Clean Up Research	-3,986
Facility Operations	
▪ EMSL operating expenses are maintained at near FY 2004 level.	-20
▪ EMSL capital equipment reduced with completion of congressionally-directed instrument modifications.	-2,000
Total Facility Operations	-2,020
SBIR/STTR	
▪ SBIR/STTR decreases with reduction in research	-61
Total Funding Change, Environmental Remediation	-2,786

Medical Applications and Measurement Science

Funding Schedule by Activity

(dollars in thousands)

	FY 2003	FY 2004	FY 2005	$ Change	% Change
Medical Applications and Measurement Science					
Medical Applications	86,704	175,206	36,942	-138,264	-78.9%
Measurement Science	2,296	5,917	5,952	+35	+0.6%
SBIR/STTR	0	5,218	1,204	-4,014	-76.9%
Total, Medical Applications and Measurement Science	89,000	186,341	44,098	-142,243	-76.3%

Description

The mission of the Medical Applications and Measurement Science subprogram is to deliver the scientific knowledge and discoveries that will lead to innovative diagnostic and treatment technologies for human health, supporting Department of Energy's Medical Science mission.

Benefits

The basic research supported by this program builds on unique DOE capabilities in physics, chemistry, engineering, biology, and computational science. The developed technologies will improve the diagnosis and treatment of psycho-neurological diseases and cancer and lead to improvement in the function of patients with neurological disabilities, such as blindness and paralysis. The research will lead to new metabolic labels and imaging detectors for medical diagnosis; tailor-made radiopharmaceutical agents and beam delivery systems for treatment of inoperable cancers; and the ability to predict structure and behavior of cells and tissues to better engineer targeted drugs, biosensors, and medical implants. The basic research technologies growing out of this program offer applications for study, detection, diagnosis and early intervention of biochemical, bacterial, and viral health risks of biological, and/or gross environmental insults.

Supporting Information

The modern era of nuclear medicine is an outgrowth of the original charge of the Atomic Energy Commission (AEC), "to exploit nuclear energy to promote human health." From the production of a few medically important radioisotopes in 1947, to the development of production methods for radiopharmaceuticals used in standard diagnostic tests for millions of patients throughout the world, to the development of ultra-sensitive diagnostic instruments, e.g. the PET (positron emission tomography) scanner, the Medical Applications program has led and continues to lead the field of nuclear medicine.

Today the subprogram seeks to develop new applications of radiotracers in diagnosis and treatment driven by the latest concepts and developments in genomic sciences, structural and molecular biology, computational biology, and instrumentation. Using non-invasive technologies and highly specific radiopharmaceuticals, BER is ushering in a new era of brain mapping detection of stem cell turnover and trafficking, and highly specific disease diagnostics. New tools will enable the real-time imaging of gene expression in a developing organism.

Research capitalizes on the National Laboratories' unique resources and expertise in biological, chemical, physical, and computational sciences for technological advances related to human health. The National Laboratories have highly sophisticated instrumentation (neutron and light sources, mass spectroscopy, high field magnets), lasers, and supercomputers that directly impact research on human health. Research is directed to fundamental studies in biological and medical imaging, biological and chemical sensors, laser medicine, and informatics. The expertise of the National Laboratories in micro-fabrication micro-electronics, material sciences, and computer modeling provides the capability to develop intelligent micro-machines (e.g., the artificial retina) that interface with the brain to overcome disabilities. This research is highly complementary to and coordinated with clinical research at the National Institutes of Health (NIH) and to basic research in the NIH intramural and extramural programs.

Coordination is provided through joint participation of senior NIH research staff and management as BERAC Committee and Subcommittee members. NIH technical staff participates in merit review panels to reduce the possibility of undesirable duplications in research funding. DOE and NIH organize and sponsor workshops in common areas of interest, for example: A joint workshop Optical Imaging of Soft Tissue will be held early in 2004. Members of the Medical Sciences Division staff are formal members of the National Cancer Advisory Board and the BioEngineering Consortium (BECON) of NIH Institutes. Furthermore, a DOE National Laboratory scientist provides technical liaison between the Medical Applications and Measurement Science subprogram and the recently established National Institute of Bioimaging and Bioengineering (NIBIB).

DOE supports cutting edge, high-risk, proof-of-concept research that develops research tools with broad applications in clinical medicine and in biological research. NIH supports cutting edge, disease-specific research that uses those tools, along with many others, to determine fundamental mechanisms of human disease for better diagnosis and treatment. For example, NIH supports clinical imaging research but not the research to develop radiotracers or imaging instruments, whereas DOE is the only government agency that supports research to develop imaging instruments and the radiotracers needed to carry out imaging procedures.

The different focus, roles, and strengths of the DOE and NIH medical sciences research programs are clear:

- DOE medical sciences research is built on a base of chemistry, physics, engineering, computation, and biology. NIH medical sciences research is built on a complementary base of biology and medicine. DOE research leverages the unique combination of multidisciplinary competencies available at the DOE national laboratories.
- DOE develops research tools for medicine by supporting high-risk research often based on theoretical predictions of success rather than preliminary studies that demonstrate a promise of success. As in other fields of science, high risk research often leads to spectacular advances, e.g., the human genome project and genetics. NIH develops disease-specific applications for these research tools by supporting research that is generally based on substantive preliminary studies that demonstrate a promise of success.
- These differences increase opportunities for success in medical sciences research.

Measurement Science research emphasizes development of novel biomedical sensors, including cantilever sensors, with a broad range of biomedical applications including neural prostheses, such as the artificial retina, and detection of carcinogen damage to DNA.

The Medical Applications and Measurement Science subprogram continues a substantial involvement of academic scientists along with the scientists in the National Laboratories.

Periodic retrospective analysis will be employed to evaluate the accumulation of knowledge and validate specific outcomes. This program was examined as part of a BERAC review of the entire BER program in FY 2001. The next scheduled comprehensive review of the Medical Applications and Measurement Science subprogram by BERAC will be in FY 2006.

Accomplishments:

- *New radiotracer developed to diagnose Parkinson's disease.* BER investigators at the University of Pennsylvania have developed a new technetium labeled pharmaceutical (TRODAT-1) that specifically localizes in the regions of the brain that are affected by Parkinson's disease. Technetium brain scans of Parkinson's patients show a dramatic decrease in the uptake of the radiopharmaceutical as compared to normal individuals. The radiotracer is in clinical testing to diagnose and monitor treatment of patients with Parkinson's disease.
- *New technologies for diagnosing early Alzheimer's disease.* BER investigators at the University of Pennsylvania, Pittsburgh, and the University of California, Irvine, developed three unique radiopharmaceutical agents that can pinpoint the brain plaque that is the cause of the mental deterioration in Alzheimer's disease. The radiotracers can be detected by Single Photon Emission Tomography (SPECT) and PET clinical imaging. Brain imaging to detect early lesions in Alzheimer's disease has become critically important with the advent of new drugs that can delay the onset of symptoms if the disease is diagnosed in the early stages.
- *New cancer treatment using radiopharmaceuticals.* BER investigators at Duke University have coupled astatine-211 to an antibody to deliver the radionuclide to cancer cells. This technology which utilizes specific radioisotope targeting of tumors with minimal effects on normal cells is presently being tested in a clinical trial at Duke.
- *NIH cancer treatment study initiated at DOE supported reactor at MIT.* The NIH has entered its first patients in a clinical trial to test the efficacy of boron neutron capture therapy in the treatment of malignant melanoma. The neutron beam development and clinical protocols were developed by research supported by BER. The MIT medical nuclear reactor is the best neutron source in the world for clinical studies and is being supported by BER for these NIH funded studies.
- *Sensitive chip to detect carcinogen effects.* BER investigators at Ames National Laboratory have developed a sensitive chip to detect the adducts which form when a carcinogen attaches to DNA. Adducts are the first step in the development of a cancerous cell. Fluorescent antibodies on the chip specifically bind to the adducts and may give investigators an early warning sign that the affected cell may transform into a cancer cell.
- *Using plant proteins to restore human vision.* BER-supported investigators at ORNL, in collaboration with investigators from the Doheny Eye Institute of the University of Southern California, have constructed a hybrid photosynthetic-mammalian system using the spinach photosystem I protein. The investigators successfully inserted the photosystem I protein into a human nerve cell, resulting in the cell becoming light sensitive. This technology has the potential to restore light sensitivity to defective photoreceptive cells in the eye.
- *Artificial retina research project established at USC.* BER has established a research project at the Doheny Eye Institute of USC for the preclinical testing of artificial retina prototypes developed in the DOE artificial retina project. The Doheny Eye Institute successfully inserted the third artificial

retina into the eye of a blind patient with retinitis pigmentosa and that patient is undergoing clinical testing.

- *Progress in helping the blind to see.* The collaborative project between five National Laboratories (Oak Ridge National Laboratory, Lawrence Livermore National Laboratory, Argonne National Laboratory, Los Alamos National Laboratory, and Sandia National Laboratory) and the Doheny Eye Institute, University of California at Santa Cruz, North Carolina State, and Second Sight Corporation to develop an artificial retina achieved a number of notable technical successes. A new material, rubberized silicon, was micro machined and performed well in pre-clinical testing and will be used to support the multielectrode array. A novel technology using finely powdered diamond crystals was developed to hermetically seal the device to protect it in the eye for the lifetime of the patient.

Detailed Justification

(dollars in thousands)

	FY 2003	FY 2004	FY 2005
Medical Applications	**86,704**	**175,206**	**36,942**
▪ **Novel cell-directed cancer therapies**	**4,366**	**4,833**	**3,162**

In FY 2005, BER continues to support fundamental research on the therapeutic use of ionizing radiation that may be achieved with radionuclide therapy and novel methods of tumor targeting. Recent therapeutic successes employing antibodies or ligands linked to radionuclides has grown out of fundamental combinatorial radiochemistry supported by BER. The specific goals include the development of novel therapeutic agents and delivery techniques to target and treat cancer at the cellular level. Research will address such complex challenges as chemical ligand synthesis, tumor-targeting, and dosimetry.

Overall program objectives include: (1) techniques to ensure highly selective tumor-targeting by the proposed therapeutic agents; (2) efficient screening techniques for selecting candidate therapeutic agents for *in vivo* testing; (3) research suggesting a reasonable likelihood of success for *in vivo* targeting of primary tumors and their metastases in pre-clinical animal trials; (4) reliable approaches for dosimetry calculations to normal tissues and to tumor sites based on 3-dimensional modeling; (5) measurement techniques for accurately assessing the success of tumor-targeting *in vivo*; and (6) measurement techniques for assessing therapy effects *in vivo* at the molecular, cellular and metabolic levels.

FY 2004 was intended to be the final year of BER support for BNCT-related medical research reactors. BER's current role in BNCT is to complete the orderly transfer of the clinical BNCT programs to the National Cancer Institute (NCI). This primarily involves facility support for the two research reactors that were upgraded for BNCT applications with DOE funds. The MIT medical reactor is used to conduct the NCI-funded clinical trials, whereas the Washington State University reactor is designed for pre-clinical studies in animals. FY 2005 now provides the final year of BER support for these two reactors. BER will transfer this activity to NIH/NCI. BER also supports the BNCT dosimetry and support programs at INEEL and the core programs at Cornell University and INEEL to determine boron concentrations in biologic specimens.

(dollars in thousands)

FY 2003	FY 2004	FY 2005

The research activities in this subprogram are carried out at National Laboratories, universities, and private institutions and selected through competitive and peer-reviewed processes.

- **Radiopharmaceutical Design and Synthesis**... **22,844** **24,266** **24,407**

In FY 2005, BER will continue to support research on radiopharmaceutical design and synthesis using concepts from genomics as well as computational biology and structural biology. BER will continue research into radiolabeling of monoclonal antibodies for cancer diagnosis and new radiotracers for the study of brain and heart function. Molecules directing or affected by homeostatic controls always interact with each other and, thus, are targets for specific molecular substrates. The substrate molecules can be tailored to fulfill a specific need and labeled with appropriate radioisotopes to become measurable in real time in the body on their way to, and during interaction with their targets, allowing the analysis of molecular functions in the homeostatic control in health and disease. The function of radiopharmaceuticals at various sites in the body is imaged by nuclear medical instruments, such as, gamma ray cameras and positron emission tomographs (PET). This type of imaging refines diagnostic differentiation between health and disease at the molecular/metabolic levels leading to more effective therapy. If labeled with high-energy-emitting radioisotopes, the substrate molecules, carrying the radiation dose may be powerful tools for targeted molecular therapy especially of cancer. The program will continue to support development of new radiotracer and radiopharmaceutical molecules for PET imaging applications in normal and abnormal brain function cancer and to monitor stem cell trafficking in animals.

BER will also develop nuclear medicine driven technologies to image mRNA transcripts in real time in tissue culture and whole animals. Currently the expression of endogenous genes in animals (including humans) cannot be imaged, at least not directly. However, given the astounding pace of biotechnology development, such imaging is an attainable goal. This research includes an emphasis on nucleic acid biochemistry, radioactive ligand synthesis and macromolecular interactions. It addresses the functional consequences of gene expression by targeting and perturbing the activity of a particular gene in living cells or animals. It also develops new biological applications using optical and radionuclide imaging devices for imaging specific gene expression in real time in both animals and humans. Methods such as combinatorial chemistry techniques will be used to develop antisense radiopharmaceuticals that hybridize DNA probes to RNA transcripts in highly specific ways to block their activity or function. Molecular signal amplification methods that work *in vivo* at the mRNA level will be developed. Drug-targeting technology will be developed to such an extent that the various biological barriers can be safely surmounted *in vivo*. The research will evaluate the clinical potential of real-time imaging of genes at work in cells, tissues, and whole organisms, including humans. This information will have applications ranging from understanding the development of a disease to the efficacy of treatments for the disease. This new technology will strongly impact developmental biology, genome research, and medical sciences.

The research activities in this subprogram are carried out at National Laboratories, universities, and private institutions and selected through competitive and peer-reviewed processes.

(dollars in thousands)

FY 2003	FY 2004	FY 2005

- **Imaging Sciences Instrumentation and Research** **11,409** **9,309** **9,373**

In FY 2005, BER will emphasize support in fundamental research to facilitate the development of imaging systems relevant to solving critical problems related to human health in the Nation. This program capitalizes on the unique resources at the National Laboratories in the fields of computational modeling, detector development, multimodal spectroscopy, high-field magnet development, and microelectronics. Imaging instrumentation and technology being developed includes: **(**1) the development of a high-density microelectronic array (the artificial retina) that can be packaged into a tiny device to be implanted in to the back of the eye, which will be used for the treatment of the major causes of blindness in the United States, retinitis pigmentosa and age-related macular degeneration; (2) PET and MRI instruments that will be used to study brain function in the awake individual, which will obviate the necessity of anesthetizing animals (inducing coma) to acquire brain images and may also have great potential for use with infants; (3) a range of image detector systems that will be more sensitive and cost effective than current instrumentation used in the diagnosis of human disease; and (4) novel biosensor devices that can detect specific molecules or biological processes important in human biology and disease and convert this information into a measurable signal. These devices can be adapted to rapidly diagnose microorganisms in the field.

BER's imaging technology program works closely with other Federal Agencies, especially the NIH, to help coordinate and focus the research efforts at the National Laboratories. Federal Agency partners include BECON and NIBIB at the National Institutes of Health.

The research activities in this subprogram are principally carried out at National Laboratories.

- **Congressional Direction** **48,085** **136,798** **0**

Congressional direction was provided in FY 2003 for University of South Alabama Cancer Center; Institute for Biomedical Science and Biotechnology, University of Arizona; Vocational Education Programs at the Los Angeles Trade Technical College; Fuel Cell Advanced Materials and Demonstration Project at Humboldt State University; National Center for Neurogenetic Research and Computational Genomics at the University of Southern California; Magnetic Resonance Microscope at the Children's Hospital of Los Angeles; PET/CT Scanner at Christiana Care Health System; University of Southern Florida Center for Biological Defense; Barry University Minority Science Center; Natural Energy Laboratory in Hawaii; Riverside Hospital Regional Cancer Center; Bioengineering Research Program at the University of Illinois, Chicago; CT Scanner at Edward Hospital; Purdue University Technology Incubator in Northwest Indiana; University of Notre Dame College of Engineering Multidisciplinary Research Facility; Indiana Genomics Initiative at Indiana University; University of Northern Iowa Existing Business Enhancement Program; Stanley Scott Cancer Center; University of Louisiana-LaFayette National Wetlands Research Center; University of Southern Maine School of Applied Sciences, Engineering, and Technology; Morgan State University Center for Environmental Toxicology; Pioneer Valley Life Sciences Initiative between the University of Massachusetts and the Baystate Medical Center; Hampshire College National Center for Science Education; University of Massachusetts at Boston Multidisciplinary Research Facility and Library; Boston University Photonics Center; Michigan Western Michigan University Nanoscience Research and Computational Institute; Nanotechnology Applications at Western

(dollars in thousands)

FY 2003	FY 2004	FY 2005

Michigan University in Partnership with Altair; North Mississippi Health Services Positron Emission Tomography Cancer Center; University of Missouri-Columbia Nuclear Medicine and Cancer Research Program; Nevada Cancer Institute; Linear Accelerator at the University Medical Center of Southern Nevada; Nevada Space Grant Consortium at the Desert Research Institute; Drew University Hall of Science; Public Health Research Institute Rapid Detection for Bioterrorism Program in New Jersey; Operations and Capital Investments at the Mental Illness and Neuroscience Discovery Institute (MIND); Environmental Systems Center at Syracuse University; Audubon Biomedical Science and Technology Park at Columbia University ; Center for Sustainable Energy at the Bronx Community College; New York University Genomics Project; Wittenberg University Science Center, Infrastructure and Equipment; Legume Genome Initiative at the University of Oklahoma; Green Chemistry Project at Carnegie Mellow University; Medical University of South Carolina; Center for Environmental Radiation Studies at Texas Tech University; Inland Northwest Natural Resources Research Center at Gonzaga University; and International Water Institute.

Congressional direction was provided in FY 2004 for University of Alabama-Huntsville Climate Action Project; University of South Alabama Cancer Center; Judson College library, academic and service center; Functional genomics research by the University of Kentucky and the University of Alabama; St. Joseph Hospital in Arizona; University of Arizona Institute for Biomedical Science and Biotechnology; Derby Center for Science and Mathematics at Lyon College; Southern California Water Education Center; St. Joseph Hospital technologyupgrade in California; University of Southern California Center for Excellence in Neurogenetics; Vanguard University Science Center; National Childhood Cancer Foundation; Tahoe Center for Environmental Sciences; Christiana Comprehensive Cancer Initiative; Clean Energy Research at the University of Delaware; Eckerd College Science Center; Jacksonville University Environmental Science Center; Earth University Foundation in Georgia; Georgia State University Science Research & Teaching Lab; Mercer University Critical Personnel Development Program; Material research for energy security in Idaho; Cancer Center at Edward Hospital; Illinois Museum of Science and Industry; Northwestern University Institute of Bioengineering and Nanoscience in Medicine; Rush-Presbyterian-St. Luke's Medical Center; St. Francis Medical Center Rapid Treatment Unit in Illinois; St. Francis Hospital Emergency Services Department; Genomics research at Indiana University; Notre Dame Multi-Discipline Engineering Center; Tri-State University Technology Center; University of Dubuque Environmental Science Center; University of Northern Iowa building design and engineering; Biomedical Engineering Laboratory at the Center for Biomedical Engineering in Louisiana; Mary Bird Perkins Cancer Center; Morgan State University Center for Environmental Toxicology; Experimental Medicine Program at the Dana Farber Cancer Institute; Nuclear Resonance Mass Spectrometer at the University of Massachusetts Medical School; University of Massachusetts at Boston Multidisciplinary Research Facility and Library; Green power technology development at Grand Valley State University; Michigan Research Institute life sciences research; Michigan Technology Center for Nanostructure and Light Weight Materials; Augsburg College; CHP project at Mississippi State University; University of Missouri Cancer Center; Advanced bioreactor technology development in Montana; Boulder City Hospital Emergency Room Expansion; Digitalization of the Cardiac Cath Lab at the University Medical Center of Southern Nevada; Mega Voltage Cargo Imaging Development Applications for the Nevada Test Site; Nevada Cancer Institute; Research Foundation at the University of Nevada-Las Vegas to assess earthquake hazards and seismic risk in

(dollars in thousands)

FY 2003	FY 2004	FY 2005

Southern Nevada; Research Foundation at the University of Nevada-Las Vegas to conduct safety and risk analyses, simulation and modeling, systems planning, and operations and management to support radioactive and hazardous materials transportation; Space Grant Consortium at the Desert Research Institute; University of Nevada-Reno to conduct nuclear waste repository research in the areas of materials evaluation, fundamental studies on degradation mechanisms, alternate materials and design, and computational and analytical modeling; University of Nevada-Reno to expand the earthquake engineering and simulation facility; Upgrade the Grover C. Dils Medical Center; Upgrade the Pahrump Medical Center; Hackensack medical building in New Jersey; Hackensack University Medical Center; Robert Wood Johnson University Hospital; Upgrade the Drew University Hall of Science in New Jersey; Mental Illness and Neuroscience Discovery Institute; University of New Mexico medical building; Bronx Community Center for Sustainable Energy; College of Mount St. Vincent Science Hall; Comparative Functional Genomics at New York University; Genomics Laboratory at SUNY-Oneonta; University of Buffalo Center of Excellence in Bioinformatics; Rensselaer Polytech Center for Quantitative Bioscience; Structural Biology Research Center at the Hauptman-Woodward Medical Research Institute; Syracuse University Environmental Systems Center; Carolinas Medical Center; Western Carolinas Biotechnology Initiative; Community Improvement Corporation of Springfield-Clark County for a computing and data management center; Middletown Regional Hospital in Ohio; Ohio State University for environmental research in cooperation with Earth University; Carnegie Mellon University Green Chemistry Project; Urban Education Research Center in Pennsylvania; Clafin University Science Center; Coastal Research Center at the Medical University of South Carolina; University of South Carolina study of groundwater contamination; Life Sciences Facility, Tennessee State University; T3 MRI for St. Jude's Children Research Hospital in Tennessee; University of Tennessee Climate Change Research Initiative; Center for Advanced Research in Texas; San Antonio Cancer Therapy and Research Center; Surgical robotics research at the Keck Cancer Center with the Cleveland Clinic; Huntsman Cancer Institute; Swedish American Regional Cancer Center; Adventist Health Care; Environmental Control and Life Support Project; UCLA - New Molecular Imaging Probes; Cedars Sinai Gene Therapy Research; Hartford Hospital Interventional Electro-Physiology Project; De Paul University – Biological Sciences; Coralville-Iowa Project on Alternative Renewable Energy Resources; and Western Michigan University – Nanotechnology Research and Computation Center.

Measurement Science	**2,296**	**5,917**	**5,952**

In FY 2005 BER will continue research and development of biomedical sensors, including micromechanical and microelectronic sensors and devices, with a broad range of biomedical applications including neural prostheses, such as the artificial retina, and detection of carcinogen damage to DNA. Fundamental research in the biomedical application of microelectronics, particularly with reference to neural prostheses, including the artificial retina, will continue. This research will include biocompatible chip design, dual band telemetry (for receiving and sending signals), and development of human interface software and design of multiplex electronics that can be directly applied to devices interfacing with the nervous system.

The research activities in this subprogram are carried out at National Laboratories, universities, and private institutions and selected through competitive and peer-reviewed processes.

	(dollars in thousands)		
	FY 2003	FY 2004	FY 2005
SBIR/STTR	**0**	**5,218**	**1,204**

In FY 2003 $2,271,000 and $137,000 were transferred to the SBIR and STTR programs, respectively. FY 2004 and FY 2005 amounts are the estimated requirements for continuation of these programs.

Total, Medical Applications and Measurement Science	**89,000**	**186,341**	**44,098**

Explanation of Funding Changes

	FY 2005 vs. FY 2004 ($000)
Medical Applications & Measurement Science	
▪ FY 2004 was intended to be the final year of BER support for medical reactor operations. To facilitate an orderly transition of these reactors to NIH/NCI, novel cell-directed cancer therapies research decreases to provide one final year of support for medical reactor operations in FY 2005.	-1,671
▪ Radiopharmaceutical Design and Synthesis funding restored to FY 2004 level prior to rescission.	+141
▪ Imaging Sciences Instrumentation and Research funding restored to FY 2004 level prior to rescission.	+64
▪ Congressionally-directed projects completed.	-136,798
▪ Measurement Science funding restored to FY 2004 level prior to rescission.	+35
▪ SBIR/STTR decreases as research program decreases	-4,014
Total Funding Change, Medical Applications and Measurement Science	-142,243

Construction

Funding Schedule by Activity

(dollars in thousands)

	FY 2003	FY 2004	FY 2005	$ Change	% Change
Construction (PED)	0	0	5,000	+5,000	+100.0%

Description

Construction is needed to support the research under the Biological and Environmental Research (BER) program. Cutting-edge basic research requires that state-of-the-art facilities be built or existing facilities modified to meet unique BER requirements.

Benefits

The first Genomics: GTL facility, the Facility for the Production and Characterization of Proteins and Molecular Tags, will surmount a principal roadblock to whole-system analysis by implementing high-throughput production and characterization of microbial proteins. It also will generate protein-tagging reagents for identifying, tracking, quantifying, controlling, capturing, and imaging individual proteins and molecular machines in living systems. Over the next 10 years, our goal is to produce 250,000 proteins in milligram quantities; around 1 million molecular tags for those proteins; and multiple biophysical characterizations of each, beginning with an organism's genomic sequence.

Detailed Justification

(dollars in thousands)

	FY 2003	FY 2004	FY 2005
Construction	**0**	**0**	**5,000**

- Initiate Project Engineering and Design (PED) for the Genomics: GTL Facility for the Production and Characterization of Proteins and Molecular Tags. This will be a cost-effective, high throughput facility for the production of proteins, along with molecular tags for their identification. The proteins will mostly be from microbes and will be produced directly from the DNA sequences of microbes previously determined by BER. These proteins and molecular tags are necessary for the high throughput characterization of molecular machines in DOE-relevant microbes with applications to DOE energy and environmental needs.

Explanation of Funding Changes

	FY 2005 vs. FY 2004 ($000)
Construction	
▪ Funding is initiated for the Project Engineering and Design for the Genomics: GTL Facility for the Production and Characterization of Proteins and Molecular Tags.	+5,000
Total Funding Change, Construction	**+5,000**

Capital Operating Expenses & Construction Summary

Capital Operating Expenses

(dollars in thousands)

	FY 2003	FY 2004	FY 2005	$ Change	% Change
General Plant Projects	4,749	4,811	5,584	+773	+16.1%
Capital Equipment	24,257	21,788	19,625	-2,163	-9.9%
Total Capital Operating Expenses	29,006	26,599	25,209	-1,390	-5.2%

Construction Projects

(dollars in thousands)

	Total Estimated Cost (TEC)	Prior Year Approp.	FY 2003	FY 2004	FY 2005	Unappro-priated Balance
PED, 05-SC-004 Production and Characterization of Proteins and Molecular Tags	5,000	0	0	0	5,000	0
Total, Construction		0	0	0	5,000	0

05-SC-004, Project Engineering Design (PED), Facility for the Production and Characterization of Proteins and Molecular Tags

1. Construction Schedule History

	Fiscal Quarter				Total Estimated Cost ($000)
	A-E Work Initiated	Completed A-E Work	Physical Construction Start	Physical Construction Complete	
FY 2005 Budget Request *(Current Estimate)*.....	1Q 2005	2Q 2006	N/A	N/A	5,000[a]

2. Financial Schedule

(dollars in thousands)

Fiscal Year	Appropriations	Obligations	Costs
2005	5,000	5,000	3,000
2006	0	0	2,000

3. Project Description, Justification and Scope

This PED request provides for Title I and Title II Architect-Engineering (A-E) services for the first Genomics: GTL facility - the Facility for Production and Characterization of Proteins and Molecular Tags. The design effort will be sufficient to assure project feasibility, define the scope, provide detailed estimates of construction costs based on the approved design, working drawings and specifications, and provide construction schedules including procurements. The design effort will ensure that construction can physically start or long-lead procurement items can be procured in the fiscal year in which Title III construction activities are funded.

Genomics: GTL User Facilities

Genomic information is providing the starting point for understanding the instructions for the manufacture of all of life's molecular machines and the systems needed to control and operate them. Understanding, not "simply" decoding, the operation, function, and coordination of genome information will be the next transforming phase in biology. From experience gained in sequencing genomes and conducting large scale biology projects, we have learned that the combined capabilities and imagination of biological, physical, and computational scientists will be needed to organize creative new venues for discovery.

[a] The full Total Estimated Cost (design and construction) ranges between $170,000,000 and $200,000,000. This estimate was based on preliminary data and should not be construed as a project baseline.

The central goal of the Genomics: GTL program is to understand the microbes and communities of microbes, and their molecular machines at the molecular level to address DOE and national needs. The DOE Office of Science has the ability and institutional traditions to bring the biological, physical, and computing sciences together at the scale and complexity required for Genomics: GTL success.

The Facility for the Production and Characterization of Proteins and Molecular Tags will implement high-throughput production of and characterization of microbial proteins.

This resource will help build a bridge between large and small laboratories by making the most sophisticated and comprehensive technologies, materials, and information equally available to all scientists. Using combinations of new equipment and technologies, automation, data management, and data analysis tools, this user facility will provide the Genomics: GTL program and the scientific community with an unprecedented resource for systems biology.

SC has determined that the site selection strategy for this facility will be based upon a competition within the DOE laboratory system. This facility will be a high throughput production facility that will produce or isolate hundreds of proteins or molecular tags. It will likely require a close working relationship with other facilities and resources such as synchrotron light sources and neutron sources that will provide some of the many resources that will be needed to characterize the products of this facility. This facility will also be highly dependent on the development and use of robotics for many aspects of the protein and molecular tag production lines. Finally, high performance computational resources will be required to plan, monitor, and characterize both the production, characterization, and inventory aspects of this facility. All of these features are necessary to ensure that this facility provide high quality, reproducible products to the scientific community and users of this facility. The National Laboratory setting will be essential for this facility, for the National Laboratories provide both the necessary experience in developing and operating large multi-disciplinary high-throughput facilities, and the close proximity to the associated specialized technological resources cited above.

Key performance criteria under consideration for selecting a contract and for inclusion in the resultant contract include maximizing the involvement of the full scientific community in the design, construction, and use of this facility and ensuring broad public notice to universities and other potential users of the need for input in the design, construction, and use of this facility. A tentative schedule for the Facility for the Production and Characterization of Proteins and Molecular Tags includes a solicitation for site selection in February 2004, followed by an information workshop approximately one month after the solicitation, and review and site selection in the summer of 2004. The Project Engineering and Design datasheet will then be updated to identify the project site.

FY 2005 Proposed Design Projects

05-01: Facility for the Production and Characterization of Proteins and Molecular Tags

Fiscal Quarter				Total Estimated Cost (Design Only) ($000)	Full Total Estimated Cost Projection ($000)
A-E Work Initiated	A-E Work Completed	Physical Construction Start	Physical Construction Complete		
1Q 2005	2Q 2006	N/A	N/A	5,000 [a]	N/A[a]

(dollars in thousands)

Fiscal Year	Appropriations	Obligations	Costs
2005	5,000	5,000	3,000
2006	0	0	2,000

The Facility for the Production and Characterization of Proteins and Molecular Tags, will surmount a principal roadblock to whole-system analysis by implementing high-throughput production and characterization of microbial proteins. It also will generate protein-tagging reagents for identifying, tracking, quantifying, controlling, capturing, and imaging individual proteins and molecular machines in living systems. Over the next 10 years, our goal is to produce 250,000 proteins in milligram quantities; around 1 million molecular tags for those proteins; and multiple biophysical characterizations of each, beginning with an organism's genomic sequence.

Research is being conducted in the Genomics: GTL program to develop the core technologies that will underpin the high throughput capabilities of this facility including the development of technologies for the high-throughput synthesis of proteins and their biophysical characterization and for the production of molecular tags to identify individual proteins and to characterize multi-protein complexes in microbial cells.

It is recognized that no satisfactory general approach currently exists for the production of proteins in the laboratory from DNA sequences and that not all proteins will likely yield to the same techniques. It is expected that a variety of both cell-free and cell-based systems will be required, as well as multiple characterization methods. Production and characterization technologies should be scalable, economic, and sufficiently robust to work in a production environment. Another early need is the development of improved techniques for predicting from sequence what production and purification approaches are most likely to succeed with each protein. Thus, informatics is an integral component. Algorithms based on data from successful and failed protein expressions are expected to substantially inform and improve future protein production efficiency. Informatics coupled with biophysical characterizations are expected to provide functional insights that may also explain why such a large number of biologically important, full-length proteins either can not be expressed in soluble form, or have structures that cannot

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be determined once expressed. These proteins may include substantial disordered regions that adopt structures only after interaction with appropriate protein binding partners. Reliable predictive algorithms based on expression and characterization databases are therefore needed to predict disorder and binding partners.

Research is being and will be supported to:

- Optimize cloning and clone validation techniques to support the protein production process.
- Optimize cell-free and cellular expression methods.
- Optimize protein purification protocols.
- Improve strategies for increasing the fraction of proteins that can be synthesized by automated methods. This may include sequence-based predictions of methods most likely to succeed and insights for optimization of expression protocols.
- Optimize high-throughput, economical approaches for characterizing synthesized protein to assess product quality and to predict protein function such that each protein produced will be characterized biophysically under several conditions.

Research is also being supported to advance the technology needed to mass-produce molecular tags for proteins and protein complexes as tools to be used for determining function. As a top priority, technologies are being developed for mass-producing specific protein recognition tags capable of functioning as capture reagents in affinity extraction and purification protocols and as labeling reagents for intracellular and *'in situ'* localization and mapping studies. As for protein production strategies, these technologies must also be scalable to permit large numbers of useable molecular tags to be produced and characterized per year at affordable costs. None of the many approaches under development to address this problem have yet demonstrated sufficient scalability. It is assumed that purified protein 'targets' will be provided to the researchers in micro-gram to milligram quantities so that tags can be optimized and characterized. Tags that interfere with function as well as those that do not interfere with protein function are both needed to help better define the biological roles of proteins.

Research is being and will be supported to:

- Develop scalable methods for producing 'epitope-directed' affinity reagents of high specificity and affinity for proteins capable of functioning either as affinity extraction and capture reagents or as intra-cellular labeling reagents. High success ratios (fraction of protein epitopes yielding useful reagents) are essential.
- Improve protein-directed affinity tag design to improve tag utility, e.g., to facilitate subsequent purification and or/imaging, to facilitate release of the tagged protein, to image with and without disrupting activity, etc.
- Improve methods for developing tags directed specifically to protein complexes as distinct from their component proteins. Labeling complexes with and without disrupting interactions amongst protein components will provide important functional insights.

- Improve strategies for predicting, from sequence data, what potential protein epitopes are likely to be successful targets for tagging with and without interfering with function, and for predicting what tag development methods are likely to work for a particular protein/epitope.
- Develop imaging and labeling methods for multiplex mapping of proteins within cells. Simultaneously monitoring multiple labeled proteins will provide more comprehensive views of multi-protein complexes and their activities.
- Optimize informatics tools both for managing tag production processes and for managing the data resulting from their use

The Facility for the Production and Characterization of Proteins and Molecular Tags will be a user facility that integrates the necessary basic research, technology and automation to enable (1) the production and characterization of all proteins expressed by a genome and (2) the generation of affinity reagents to each protein. The goal of the facility will be to make possible rapid experimental characterization of the function of gene products on the scale of whole genomes.

Protein production will utilize multiple bacterial expression systems; cell free expression; and chemical synthesis methods. Protocols for automated expression, purification and characterization of proteins will be optimized for multiple classes of soluble proteins; membrane proteins; periplasmic proteins; and very small or very large proteins. Cloning, expression, purification, quality assurance (QA) and characterization will be carried out by automated systems directly linked to the Laboratory Information Management System (LIMS). Clones, proteins and affinity tags will be shipped to collaborators at other DOE laboratories, universities and corporate partners for further functional characterization.

Comprehensive protein characterization will include a QA suite to demonstrate that the proper proteins have been produced and to determine the physical state of the proteins. This suite will include mass spectrometry and DNA sequencing for protein identification; dynamic light scattering to assess solubility and ultra violet spectrometry.

Bioinformatics will be used to make an initial assignment of protein function where possible. Further characterization will be designed to elaborate on this assignment and identify additional biophysical and biochemical clues as to protein function. Biophysical characterization techniques to be used include circular dichroism to assess secondary structure; small angle x-ray scattering to determine quaternary structure; x-ray absorption fine structure to determine metal content and the environment of metal ions; wide-angle x-ray scattering to determine the quaternary structure as well as assignment of a structural fold. Biochemical characterizations will include mass spectrometry to identify co-factors and bound ligands; binding assays to the most common small molecule ligands; and high-throughput enzymatic assays for the most common biochemical activities.

The facility will be run by an advanced Laboratory Information Management System (LIMS) that will be capable of predicting the optimum method for production and purification of any protein based on its amino acid sequence and past experimental outcomes. The LIMS will collect experimental data from automated systems as well as manual input from handheld computers in a completely wireless environment. The results of expression, purification, quality assurance and characterization experiments will be automatically fed into a database of protein properties accessible through web-based servers. Results of experiments that are both successes and failures will be available to guide future work.

At least 50% of all proteins are anticipated to pose significant problems for any current production

method. Consequently a significant component of the protein production and characterization facility will be research into new methods of protein production and into automation of existing methods of expression, purification and characterization. Proteins that cannot at present be readily produced include most membrane proteins, high molecular weight proteins, toxic and unstable proteins, proteins with unknown co-factors and proteins that are integral parts of complexes. Consequently a significant research effort will be needed to (i) address the 50% of all proteins that currently cannot be produced in milligram quantities in soluble, native conformations (ii) automate all portions of the multiple synthetic routes needed (iii) automate the purification and characterization of all proteins (iv) devise informatic methods to predict optimal strategies for each protein to be produced (v) develop novel libraries of affinity tags, advanced methods of library production and methods for screening these libraries.

The primary production facility will include approximately 125,000 to 175,000 sq. ft. consisting of laboratory space for production, as well as research, office and administrative space. A protein characterization network including researchers from multiple national laboratories and universities will utilize the proteins and affinity tags produced in the facility and feed the results of characterization experiments into the central facility database.

4. Details of Cost Estimate [a]

(dollars in thousands)

	Current Estimate	Previous Estimate
Design Phase		
Preliminary and Final Design costs (Design Drawings and Specifications)	3,600	N/A
Design Management costs (13.9% of TEC)	700	N/A
Project Management costs (13.9% of TEC)	700	N/A
Total Design Costs (100% of TEC)	5,000	N/A
Total, Line Item Costs (TEC)	5,000	N/A

5. Method of Performance

Site selection will be made based on a complete scientific, technical, and project management review of offers received. Conceptual design of the facility and technical equipment will be completed by the fourth quarter of FY 2005 to establish an appropriate cost range and conceptual scope. PED will be utilized to perform preliminary and final design of the building; and engineering, design, and development of the technical equipment. Design services will be obtained through competitive and/or negotiated contracts. Site staff may be utilized in areas involving security, production, proliferation, etc.

[a] These costs reflect only those associated with design phase activities only.

6. Schedule of Project Funding

(dollars in thousands)

	Prior Year Costs	FY 2003	FY 2004	FY 2005	Outyears	Total
Facility Cost						
PED	0	0	0	3,000	2,000	5,000
Other Project Costs						
Conceptual Design Costs	0	0	850	150	0	1,000
NEPA Documentation	0	0	150	50	0	200
Total, Other Project Costs	0	0	1,000	200	0	1,200
Total Project Cost (TPC)	0	0	1,000	3,200	2,000	6,200