BER Response to the Report of the BERAC Committee of Visitors Review of the Life and Medical Sciences Division

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Introduction

The Committee of Visitors (COV) has provided a wealth of informative comments and helpful recommendations for the management of the programs in the Biological Systems Science Division (BSSD or 'division')[*] in the Office of Biological and Environmental Research (BER). The division staff appreciate the care with which the members of the COV prepared for the site visit, interacted with the staff during the meeting at Department of Energy Headquarters in Germantown, Maryland, and prepared the final report. The time and thought devoted to the responsibilities of the COV was substantial for every one of its members, and we wish at the outset to acknowledge our gratitude for this.

The division includes a wide range of scientific programs and research projects, as well as a major national user facility and several larger research centers, including three Bioenergy Research Centers established at the very end of the period reviewed by the COV. The management of BER places a high priority on cooperative teaming of the program staff to manage these programs, so that in the division's activities there is a focus on the overall vision of the division and a sharing of expertise across the programs. It is hoped that this response reflects not just the necessary discussions of the individual program recommendations in isolation, but also how they relate to the division as a whole.

Finally, we note that the COV reviewed BSSD program management for the period October 1, 2004, through September 30, 2007 (Fiscal Years 2005, 2006, and 2007). Yet the programs are continuing ones, most of them initiated before the start of this period and all of them continuing beyond its end. It is hoped that occasional mention of actions and activities that extend outside the official period of review will be excused, as they are in many cases necessary to provide accurate responses to the COV recommendations.

[*] Note that the name was Life and Medical Sciences Division until June 2008. This name and the acronym LMSD appear throughout the report of the COV, and the extracts included in this response, as their meeting occurred prior to the name change. However, the new name and its acronym BSSD are used in the Program Response and Action Plan as it will be under this name that the division will carry out the plans developed in response to the report.

Responses to comments and recommendations

COV Recommendation	Program Response	Action Plan
General Division issues		
COV recommendations for continued good program management and documentation.	Program staff appreciates the comments of the COV on management of the solicitation, review, award, and post-award aspects of the research programs. It is recognized that careful resource allocation and management are required to carry out these responsibilities for the long run in an optimal way.	1. The needs for additional staff that are pointed out by the COV will be brought to DOE management with emphasis on the urgency of meeting these needs if the programs funded by the Division are to make their essential contributions to the national needs they are addressing. 2. BER will seek ways to improve the use of staff time and reduce the time needed for less essential activities. 3. The travel budget was increased substantially in Fiscal Year 2008. The allocation of the travel funds for different types of activities will be reassessed regularly to maximize the ability of staff to carry out program responsibilities.
COV recommendations for scientific advisory committees for specific program elements within the division (BRCs, Structural Biology, and ELSI specifically mentioned)	BER recognizes that input from the scientific community is an essential component in the Division's decision making. Several mechanisms are used to obtain this input, including BER-organized workshops, attendance by Division staff members at meetings organized by other agencies, at meetings of professional societies and at Gordon Conferences and similar specialized meetings, and periodic BERAC reviews. Additionally, all larger program projects funded by the Division have external advisory committees that meet regularly with BER program managers present. This is generally true where annual funding level is $2	1. No new advisory committees will be organized by the Division at this time. 2. Division program managers will monitor the effectiveness of the existing mechanisms of obtaining external scientific input, and revisit this question prior to the next COV. 3. BER will continue to hold annual meetings of ELSI PIs (in association with the annual GTL PI meeting); additional input will be solicited with workshops. 4. BRC members will continue to be active participants in the annual GTL PI meeting.

	million and higher. It is not clear that adding BER scientific advisory committees for program elements such as the BRCs, structural biology or ELSI would provide significant additional value given the mechanisms already noted.	
COV recommendations for levels of funding (Computational Biology and Carbon Sequestration Programs specifically mentioned).	It is clear that computational biology is an integral part of the Genomics:GTL program and plays a significant role in essentially all of the research programs funded by the Division. BER strives to maintain a balance between computational infrastructure, data management, and biological modeling and experimental validation. Therefore, as integrated programs such as Genomics:GTL mature and develop a robust knowledgebase and computational biology framework, we will work to allocate sufficient program funds to address all our programmatic needs.	BER does not believe that this is the appropriate forum for specifying budget allocations to targeted programs such as computational biology or carbon sequestration. Division program managers will continue to assess this question periodically to determine the appropriate resource allocation for all programmatic priorities.
Genomics:GTL		
The COV recommends that the PMs include in the "Summary of the review and selection process for proposals submitted…" a copy of the spreadsheet used by the PMs to cull pre-proposals, which would make the process even more transparent.	BER agrees that improved transparency of the review and selection process reflecting the key reasons for funding decisions is important.	BER will review the appropriate format to implement this recommendation and will implement with new solicitations in Fiscal Year 2009.
The COV urges the PMs to continue to seek such a broad mix of high to low risk and small to large research projects in its portfolio.	BER agrees with the desirability of maintaining a mixed portfolio.	No specific action needed. Continue current strategy.
The COV recommends that the LMSD require a more appropriate manner of review, even if it is in addition to the format formally required by the National Laboratories. It is	BER agrees that a better annual reporting format and mechanism is needed for national laboratories.	BER is implementing Science Focus Areas at the national laboratories participating in its programs. As part of this change at the labs, a formal annual reporting requirement

simply not possible to compare the relative progress made by these different avenues of funding, which is a critical component to the management of such a diverse portfolio.		will be implemented that we believe will address the inadequacies of the current annual reporting for the National Laboratories.
Bioenergy Research Centers		
The COV recommends that there be extensive oversight of these centers, that there be strong scientific advisory committees, and that a rigorous set of evaluation procedures be established that will provide frequent feedback and ensure that the activities of the BRC remain on track. It is expected that LMSD will conduct annual site visits and reviews of the three BRCs. It is imperative that LMSD provides sufficient support to enable these site visits.	BER agrees with the recommendations, and all are already in place.	1. BER Program managers conducted extensive oversight of the BRCs, including a "Lehman Review" six weeks after initial funding (November 2007) and annual, two-day, onsite reviews for each BRC (September/October 2008). 2. The BRCs report on at least a quarterly basis to BER, biweekly phone conferences are held among the BRCs and BER. 3. All three BRCs already have scientific advisory committees.
The COV recommends that this collaboration [with the JGI] receive the same oversight as the BRCs, to ensure that the Centers are provided with the required sequencing support.	BER agrees with the recommendations.	BER coordinates the JGI sequencing requirements from the BRCs. BER has augmented funding at the JGI specifically for BRC use and coordinates both the amount of sequencing and the selection of sequencing targets. BER is conducting a comprehensive review of the JGI's science, operations, and management in December 2008.
Computational Biology		
The COV recommends this program be decoupled from DOE's supercomputing program.	BER believes that it is critical to continue the partnership between the GTL program and the Office of Advanced Scientific Computing Research (ASCR). This partnership will continue to take advantage of ASCR's full expertise and resources. These include applied mathematical and simulation tools, midrange to High Performance Computing (HPC), and network investments that can serve the broad range of	1. GTL program staff are working closely with the ASCR Office on a strategic plan that will address the needs of computational biology and bioinformatics focused much more broadly than HPC applications. These activities range from weekly meeting by Program Managers in BER and ASCR to joint community involved workshops that serve to formulate the basis of a sound and realistic strategic

	computational biology and bioinformatics needs of BER programs.	plan in computational biology and bioinformatics. 2. BER and ASCR are coordinating to support a new area of multiscale modeling for computational biology that will impact our missions in bioenergy, bioremediation and carbon sequestration. 3. BER and ASCR will be jointly sponsoring a community workshop in 2009 to address exascale computational biology.
Structural Biology		
LMSD should play a principal role in the development of facilities for x-ray spectroscopy, x-ray scattering, and x-ray crystallography optimized for applications in structural biology at the National Synchrotron Light Source II (NSLS II) currently under development at Brookhaven National Laboratory (BNL).	The development of the NSLS II will indeed enable new types of experiments in structural biology. BER will be actively engaged in the process of assessing proposals and funding beamlines, instrumentation and infrastructure for biological applications at the NSLS II. This is particularly the case for spectroscopy, scattering and imaging capabilities that may have a significant impact on research in BER mission areas. There is a very large investment in the field by NIH and other public and private agencies, and BER will coordinate its activities with these agencies.	1. BER will establish a planning group of program managers in structural biology and the biological research programs to monitor the NSLS II plans. 2. BER will continue discussions with the research community, the NSLS II scientists and management and the Office of Basic Energy Sciences to determine the best investment of BER's limited funds in the NSLS II. 3. BER will hold workshops involving both experts in light source technologies and leading scientists in BER programs to assess the value of specific technologies for BER research.
The COV recommends that DOE explore how this [development and commercialization of pixel-array detectors abroad rather than in the US] occurred, in light of the federal technology transfer mandate, given this substantial investment, and steps should be taken to ensure that this loss not be repeated.	BER has played a significant role in the development of detectors for use at x-ray and neutron user facilities. The pixel array detector (PAD) offers major advantages, and BER has provided some funding for a large U.S. consortium developing such a detector, for which NIH has been the primary source of Federal government support. A Swiss PAD is now commercially available, ahead of the U.S. detector. It is not yet clear when the latter will be available. BER will work with other agen-	BER and NIH will organize a meeting of all funders of the U.S. PAD project to determine the current status and the best path to a commercial detector. BER will also continue to work with NIH and other federal partners to explore effective and timely technology transfer for our mission needs.

	cies to determine the best way to ensure that it is not delayed further.	
The COV recommends that the BER should have a much stronger presence at the SNS/ORNL, in the areas of neutron scattering, neutron reflectivity and neutron crystallography, as applied to critical problems in structural biology.	BER acknowledges the value of increased utilization of the capabilities at the SNS.	1. BER is engaged in discussions with the Director of the Neutron Scattering Science Division at ORNL about the development of experimental stations at the SNS, and will request a concept paper from ORNL defining the priorities for new investments by BER for biological experimental stations at the SNS. 2. BER will initiate discussions within DOE and with NIH and NSF regarding the best approach to developing the life science capabilities at SNS.
The COV recommends that the SB program remain focused on the more general area of structural biology, rather than more narrowly on the needs of any specific program(s), such as GTL	The structural biology program has always focused on the needs of the national life science community and will continue to do so. Specialized needs of programs within BER will be met by those programs. For example, the Genomics: GTL program has made major continuing investments in x-ray scattering and imaging and infrared spectromicroscopy beamlines at the Advanced Light Source.	BER will continue to coordinate DOE mission-relevant investments in structural biology user facilities with other agencies. Our intent is to ensure that our BER-mission priorities in bioenergy, environmental remediation, and carbon sequestration are served, while contributing to the support of the full range of life science applications of these facilities.
Radiochemistry/Instrumentation		
The COV recommends that the DOE-OBER continue to support basic research that builds on unique DOE capabilities in physics, chemistry, engineering, and computational science … BER should also explore the application of these imaging technologies for the study of plant and microbial metabolic networks and the regulatory systems underlying cellular differentiation, specialization, and interactions with the environment.	BER agrees with this recommendation	1. BER led a November 2008 workshop for feedback from the relevant scientific community to help align the BER Radiochemistry and Radionuclide Imaging Instrumentation research with the BER missions. 2. BER will solicit, review, and award projects under the new research scope in Fiscal Year 2009, subject to the availability of funds.

The COV's specific comments and recommendations include that: "*Over the years the principal management of this office has been very closely linked with the Principal Investigators and Institutions where the program has major investments. The positive side ...The downside of this system is that it is difficult for new institutions or programs with fundamentally new ideas to break into the program."*	BER agrees with the need to involve new institutions and investigators, and notes that a substantial number of new projects were funded at universities as a result of the last program solicitation prior to the reduction in the program budget in 2006, and the pilot project solicitation in Fiscal Year 2008.	BER will ensure that the reconfigured program will be widely publicized to encourage investigators not previously funded to apply.
The COV believes that this [the medical imaging agent/drug development territory] departs from the fundamental radiochemical instrumentation mission of the program and raises the most significant questions concerning potential overlap with NIH missions. One path forward would be to refocus on developing a strong program in basic radiochemistry and radio-instrumentation over a broad range of potential applications, including medical ones.	BER agrees with this recommendation.	1. As noted above, in Fiscal Year 2009, the program will be reconfigured to reflect BER's energy and environmental missions, distinct from NIH focus on developing disease diagnostics and medical therapeutics. The program will develop a new scope for the Radiochemistry and Radionuclide Imaging Instrumentation research. 2. BER will encourage transfer of new technology arising from these research projects to medical research programs in other Federal agencies and in the private sector.
Artificial Retina		
The COV is surprised and somewhat disturbed that such a stunning success story [Artificial Retina], which highlights the abilities of our National Laboratories, the personnel in LMSD, our nations universities and the private sector to join forces to address a significant human health challenge, and which has had such significant success in every aspect of the endeavor will soon be terminated. The rationale behind this decision was not clear to the COV.	BER takes great pride in knowing that we have provided the fundamental science needed to launch the artificial retina project. The goal of the project was not to actually complete the device for commercialization, but rather to generate the scientific knowledge and proof-of-concept for developing this type of advanced sensor-based instrumentation using hard-soft interfaces and novel materials. DOE policy presumes that the private sector will take advantage of the BER investments and complete the development of a commercial	BER will fund research to complete the design, construction, and animal testing of the 240 microelectrode array device and transfer this technology to our private sector partner.

	product.	
Carbon Sequestration		
The COV enthusiastically supports continued joint funding opportunities between DOE and USDA, and encourages the two agencies to consider including a special programmatic focus on understanding how crop plants will respond to future predicted climate fluctuations and breeding varieties adapted to projected climate extremes.	The joint USDA-DOE Plant Feedstock Genomics for Bioenergy program agrees that genomics can contribute significantly towards understanding responses of bioenergy crops to environmental stresses resulting from climate change.	1. The joint USDA-DOE Plant Feedstock Genomics for Bioenergy program has already initiated placing a greater program emphasis on using genomics to understand bioenergy crop response to nutrient and water use, two key impacts expected from climate change predictions. 2. The program will continue to work with stakeholders in the plant breeding community to translate fundamental research knowledge into practical outcomes, such as developing new varieties adapted for geographically and ecologically diverse environments.
Joint Genome Institute		
The COV recommends that the JGI maintain this high level of community involvement through the CSP program.	BER agrees.	Additional capacity being added to the JGI's sequencing pipeline should enable continuation of this program as well as continued attention to BRC sequencing needs.
The COV recommends that JGI's investment into informatics be increased significantly, not just to keep pace with current sequencing demands, but also to anticipate future needs associated with data generated via next generation sequencing.	BER agrees with the COV that informatics is vital to the success of any high-throughput sequencing operation and that sequencing throughput has outpaced informatics analytic capacity (a problem not unique to the JGI). The JGI has initiated a strategic planning effort that specifically addresses future informatics and data management needs.	Informatics is a critical focus of an impending review of the JGI. Following the review in December 2008, and the completion of the JGI's strategic planning efforts, and subject to the availability of funds and other program priorities, BER will consider placing greater emphasis on informatics at the JGI.
The COV recommends that LMSD require a more balanced portfolio of CSP panels and actively engage in ensuring an immediate resolution of this inadequacy. This is an easy problem to solve and should have been accomplished by the 2006 review panels.	BER agrees that the CSP review panels should include broad representation from the scientific community.	BER will work with the JGI to ensure that the CSP panel composition is scientifically diverse and fairly balanced, beginning with the Fiscal Year 2009 CSP review.

The COV recommends that the CSP program adopt the same type of rigorous review procedures–with thorough documentation–used by other programs in DOE or similar sequencing programs that have been funded by the National Science Foundation (e.g., Microbial Sequencing or Comparative Plant Genomics).	Until three years ago, reviews were conducted by BER; consistent with other DOE User Facilities, the JGI was permitted to establish its own review process. The current JGI process is directly modeled on the NHGRI large scale sequencing review process.	This will be a focus of the December 2008 review of the JGI, and BER will revisit the need to implement any changes, including more rigorous documentation, following the review.
The COV recommends that the DOE provide a more hands-on approach to administration of the JGI, at least those portions funded by LMSD.	BER agrees to assess the best approach to administration of the JGI and notes that the entire JGI budget is funded by the Biological Systems Science Division, which will make it straightforward to institute changes if they are needed.	1. Management has been made one of the key topics for the December 2008 review of the JGI. 2. Potential changes in the BER administration of the JGI will be addressed after the December review.
We concur with the previous COV recommendation that JGI consider how its resources could be used to support some "big science" sequencing efforts. We urge JGI to consider soliciting community ideas for large-scale transformative sequencing project.s	BER agrees.	1. With the initiation of plant and metagenome sequencing projects (and the BRC sequencing program), this is being done. 2. In particular, the plant community is working with JGI staff to define a list of plants (consistent with DOE missions) to sequence and a white paper has been prepared on fungal sequencing. 3. The JGI is developing a strategic plan that will also help articulate a vision for its future.
The COV urges DOE to ensure that this increased requirement [sequencing capacity devoted to BRCs] is not met at the expense of the community-available sequencing	BER agrees.	BER will work with the JGI to ensure appropriate resource allocation to meet all user needs. BER expects that increased sequencing capacity using next-generation sequencing technologies (e.g., 454 and Illumina) will help offset greater sequencing demand.
Low Dose Radiation Research		
Although the Program already funds innovative proposals, the COV recommends	BER agrees that more use should be made of supporting pilot studies for high risk / high	1. Low Dose Program solicitations already ask for high risk / high payoff research

increasing the number of small pilot projects to ensure that riskier ideas have a chance to be tested and developed for larger scale support.	payoff research.	applications. More emphasis will be placed on choosing these types of projects in the programmatic reviews, awarding one or two-year pilot studies. 2. The program manager will communicate the value of such research to the Lab Low Dose Radiation Research SFAs.
ELSI		
The COV recommends that BERAC consider establishing a scientific advisory committee for ELSI, which would aid the PM in the development of solicitations. The membership of the advisory panel should include expertise in social sciences.	BER believes a formal scientific advisory committee is not an appropriate or efficient way to gain guidance on ELSI program goals or activities. The ELSI program devotes only about $2 Million annually for research projects and education and other activities, and BER does not see a formal advisory committee as needed for this small a program.	BER will continue to hold workshops to explore the range of potential ELSI topics and to define the high impact activities that ELSI can support in BER mission relevant topics. BER will actively seek to include new and diverse participants with broad scientific backgrounds in these workshops and in the ELSI program.
The COV recommends the gradual expansion of this important program, provided that the solicitations can be refined to generate a larger number of applications worthy of funding.	BER acknowledges the value in broadening the scope of this program within current budget considerations.	BER will actively seek opportunities for engaging broader research participation and soliciting ideas for future program solicitations within current budget considerations.