MINUTES

Biological and Environmental Research Advisory Committee (BERAC) Meeting
Office of Biological and Environmental Research
Office of science
U.S. Department of Energy

DATE: April 29-30, 2004

LOCATION: Academy for Educational Development, Washington, DC. The meeting was announced in the Federal Register on April 2, 2004.

PARTICIPANTS: Approximately 75 people were in attendance for part of all of the meeting. Eighteen BERAC members were present:

Keith Hodgson	Richard Hallgren
James Adelstein	Will Harrison
Eugene Bierly	Steven Larson
Michelle Broido	Patricia Maurice
David Burgess	Lisa Stubbs
Joanne Fowler	Victoria Tschinkel
Robert Fri	Warren Washington
Ray Gesteland	Barbara Wold
Richard Gibbs	John Wooley

Seven BERAC members were not present:

Jonathan Greer	Janet Smith
Margaret Leinen	James Tiedje
Lou Pitelka	Isiah Warner
Mel Simon	

(Information on the BERAC membership can be found at:
http://www.science.doe.gov/ober/berac/members.html)

Thursday April 29, 2004

Ray Orbach, Director Office of Science (viewgraphs on BERAC meeting website)
http://www.science.doe.gov/ober/berac/orbach04_04.ppt

OneSC – The Office of Science has been reorganized (http://www.screstruct.doe.gov/)

- We previously had a complicated organizational structure especially regarding lab-site office links
- OneSC roll-out was announced on April 1

- There is now a direct relationship between SC-1 and the labs
- Oak Ridge Office & Chicago Office assistance and key roles in OneSC
- US government responsibility to ensure labs operate as best they can and in service to US. OneSC will help.
- Working to develop new long term vision of the labs – What are the labs thinking? What are we thinking? Relationship meant to be interactive.
- Consistent with President's management agenda

DOE/SC 20-year facilities outlook
(http://www.science.doe.gov/Sub/Facilities_for_future/facilities_future.htm)

- ITER negotiations continue and continue… Two parties that have offered sites (EU and Japan) are negotiating between themselves. We have stepped back for now. All 6 parties should meet in next few months. Difficult task. Four months since both sites put proposals on the table. Have two 100% solutions on the table.
- Leadership class computer competition. February 2004 solicitation. ~50Tflop sustained speed machine. 200-250 Tflop peak speed machine. Four proposals received and reviewed. S1 announcement in 1-2 weeks. $25M in FY04 budget so need to get money out. $25M in FY05 request. Wonderful proposals. Each different. Span a range of exciting opportunities. Hoping there will be no "losers" so that all these great ideas can be kept alive. (NOTE – Secretary Abraham announced on April 12 that Oak Ridge National Laboratory will lead this effort http://energy.gov/engine/content.do?PUBLIC_ID=15871&BT_CODE=PR_PRESSRELEASES&TT_CODE=PRESSRELEASE)
- Next four facilities -
    - GTL Protein production and tags – CD-0 signed. PED in FY05 budget.
    - Linac coherent light source (LCLS) – remarkable facility with remarkable opportunities for the physical and biological sciences
    - Rare isotope accelerator
    - Joint Dark Energy Mission (with NASA) – not ready to move forward yet
- GTL Characterization and imaging – CD-0 signed
- All top 12 SC facilities getting started in one way or another

Currently doing FY06 budget. Hopeful that FY05 will be passed before October 1 but this is an election year so we may well be on a continuing resolution through the end of the year and beyond.

We are not allowed to compete labs against universities. Will/may create new FFRDC for RHIA.

First GTL facility will be competed among DOE labs. Second facility (Characterization and Imaging of Molecular Machines) will be competed among universities. Last two facilities will be split among labs and universities.

Issue of balance between facilities and research funding. Not a large BER issue at this point but it could become an issue. BERAC will/may need to weigh in. For BER ~25%

now facility operation and 75% research. High Energy Physics ~50:50 in contrast. Need to keep this in mind as we go forward.

Questions:

Thank you for reorganization. Will make interaction with labs easier. Budget question. Last week AAAS held their annual budget forum. Some large national issues. Budget guidance for out years speaks of 1.5% for inflation and only 0.5% for real growth. Thoughts? Reality of learning to live with guidance from OMB. FY05 growth for SC is only for LCLS and hydrogen research. We are the stewards of $3.3-3.4 B and we must do the best we can with that for the American people.

Very hopeful that the Energy Bill will finally pass so the SC can be reauthorized after many years. Whole facility outlook based on things in that bill. We are the easy part of the Energy Bill – people like science – but there are tensions. Critical for us.

Ray Gesteland, University of Utah, BERAC (written report not yet available since not yet approved by BERAC)

Synthetic genomics. Charge by the Secretary. Catalyzed by publication by Venter and Smith on synthetic synthesis of bacterial virus with BER funding.

Committee members – Mildred Cho, Stanford
George Church, Harvard
David Galas, Keck
Charles Rice, Rockefeller
Mark Johnston, Washington U
Gerald Joyce, Scripps
James Tiedje, Michigan State
Ray Gesteland, U of Utah

Currently using one gene at a time approaches. Are there more efficient approaches?

Venter publication is nothing new or revolutionary. Incremental improvements in old technology. Modest technical advance here is ~10X increase in effiency. Make small (~42 base pair) fragments covering the whole genome for both strands of the DNA. Short pieces here made very accurately using purification for more effective rejoining. Optimized rejoining efficiency. ~2 weeks from start to finish.

Still an error problem. ~10 errors per genome. Could use reinfection of bacteria to select for the phage put back together correctly.

Limitations for scalability to chromosome sized fragments. Not ready yet. Accuracy. Starting materials not perfect. There are ways to correct for errors that arise. Cost still

high though coming down already. Commercial world working on lowering costs of making small synthetic pieces of DNA.

Can this become routine? Can we take advantage of this opportunity for DOE needs? (This was the charge to BERAC from the Secretary.) May be able to look at groups of genes rather than one at a time for testing hypotheses, custom making pathways, making new organisms.

10-100 fold improvements needed. Also improvements in error rate, cost, automation.

This is the way that genetics is going to be done and genome information is going to be used in the future! Benefits seem clear. All you would need is the sequence information, not necessarily the organism itself, to study parts of or entire organisms. Democratizes science since all will have access to sequence information though not necessarily organisms.

DOE applications clear. Others too, e.g., vaccine development.

Again – nothing new or revolutionary here.

What are the concerns? Are new ethical issues being raised? No. Mildred Cho previously published on this in Science based on determining a minimal genome. Could enable bioterrorism – reconstruction of pathogens from sequence. Committee considered the NAS Fink report. Issue of microbial release into the environment and escape of genes. Can consider/include ways to include protective genetic mechanisms in the reconstruction/design process. Ownership and patent rights issue. What is a “product of nature”? Material Transfer Agreements might be minimized since the information can be pulled from the data bases directly.

Questions/Discussion

Very important research. How much money will it take to push this forward? Didn’t deal with this issue. A genome scale initiative? No. Focused, thoughtful investments. A distributed or center focused research activity? Distributed. Lots of individual challenges to be solved.

Concerned that the risks have been downplayed. “No new concerns for negative consequences being raised.” Are we doing enough to address the old concerns and consequences? Not trying to downplay or minimize potential risks.

No real difference in kind? There is a difference in quantity of what can be done in laboratory settings for example. A statistical issue of small versus large amounts of a substance or material. Easy to be swept away by the excitement of the research and the potential benefit.

Stepping “eyes wide closed” into a genetic arms race? Why a high priority for the government to do this faster when we are behind in understanding of implementation strategies for this type of technology.

Nothing here about the biocomplexity issue.

New federal advisory committee to set policy in this area – National Science Advisroy Board for Biosecurity, http://www.biosecurityboard.gov/.

We need this technology and capability.

How will the concerns be dealt with on a long term basis? This committee wasn’t charged with this responsibility. Ray Orbach has recently started an SC-wide Integrated Ethics Management effort to look at issues like this across all of SC. SC management intends to take these (and other) issues head on.

Data isn’t there yet make decisions about what will happen if things get out into the environment. We need to learn a lot more so that we can make decisions about the risks.

Issue of DOE priorities? Is this a priority for DOE without significant new investments about the risks? NO. Would argue that this is in fact a next significant step if we are in the microbiology business. Absolutely need to be able to assay the functions of large groups of genes and this is the way to do it. This is the foundation of GTL as BERAC has framed it over the past years.

SUMMARY OF REPORT STATUS: Sense that we do need continued reflection on the report. Need to work further with Ray’s subcommittee to incorporate comments from discussion. Can add new portions to the report to reflect additional perspectives.

We also need to schedule more about this committee’s effort and the broader federal effort at the next meeting.

Ari Patrinos, Associate Director of Science for Biology and the Environment
The State of BER (viewgraphs on BERAC meeting website)
http://www.science.doe.gov/ober/berac/patrinos04_04.ppt

BER is now a half billion dollar program. Most diverse federal program in any one office or place. Blessing and curse (especially in times of tough budgets).

Budget – Record breaking earmark year. Ok to be against earmarks in general but not against specific ones.

Genomics:GTL – many names changes over time. This is where we are now. This is no longer an acronym. Understanding complete biological (microbial) systems. Flagship program now sold on the basis of DOE mission needs.

Core projects – Large, multi-investigator projects.

Recent solicitation to develop new tools and capabilities – imaging, computing and modeling of pathways, metabolomics and microbial genomics, protein production and tags pilots (for Facility 1)

Four GTL facilities to underpin the high throughput needs of the program.

Environmental sampling – both ocean and land. New opportunities for discovery and applications of new genes.

JGI Production Genomics Facility – Community Sequencing Program. Transition from human genome (and other) sequencing to a scientific user facility for the broader community. Dolphin may be sequenced in partnership with the Office of Naval Research. Sequencing needs are growing but comparable growth of agency commitments to sequencing not necessarily keeping up.

Structural biology facility upgrades. Leveraging major facilities built and operated by Basic Energy Sciences resources. Partnership with NIH in several cases.

Low Dose Radiation Research Program. Project of great interest to Senator Domenici.

Medical Science program. A small investment with large impacts. Wonderful collaboration with NIH. Example of the kinds of interagency efforts that should be pursued more often.

Radiopharmaceuticals a key area of DOE research leadership.

Imaging of moving subjects and exciting and important area especially for infants and people with movement disorders. Major computational challenges. NIH and BER co-funded a JASON study last summer on computational challenges in medical imaging.

Artificial retina project – labs, universities, industry – multi-institutional success story. These kinds of projects are perfect examples of the remarkable, high impact contributions that our program can make.

Atmospheric Radiation Measurement sites part of our Climate Change Research Program. Part of our contribution to the National Climate Change Science Program. ARM program now over 12 years old. Originally a 10 year program. Never funded at more than 50% recommended level. Addressing clouds as key uncertainty in climate models.

BER program's principal goal is to develop and improve global circulation models used for climate change prediction. Three permanent sites, a new mobile site, and unmanned aerial observation vehicle (UAV)

Climate modeling has a significant effort as part of SciDAC (Scientific Discovery through Advanced Computing) to improve climate modeling software to take best advantage of most powerful computers.

Better computers let us better model and predict climate.

A fully coupled climate model is the “holy grail” of the field.

Carbon cycle is an integral part of our program and of the climate science program – carbon fluxes, carbon cycle, carbon sinks and sources, carbon impacts.

AmeriFlux – measures fluxes from and into the biosphere.

Impacts of elevated carbon dioxide (FACE program) on ecosystems.

Carbon sequestration – Ocean sequestration. Iron fertilization experiment. Joint effort with NSF. Increased carbon uptake but need to address potential negative impacts as well. Probably best to leave the oceans alone. Terrestrial studies now with capability to link to genomic resources and analyses.

Throughfall displacement experiment – impacts of higher/lower rainfall on an ecosystem. Long term research investment to study potential impacts of global warming.

Scaling initiative. New effort. Solicitation just closed today (http://www.sc.doe.gov/grants/Fr04-14.html). Studying ecological processes from the ecosystem to the molecular scale.

Environmental Remediation Sciences division combining ongoing programs and new programs.

Natural and Accelerated Bioremediation Research Program (NABIR). Many exciting advances. Some applications already showing success. Example of success of Derek Lovley’s research on Geobacter and uranium. Field Research Centers a key part of this program.

Environmental Management Science Program (EMSP) – Newest addition to this program. Fate and transport of contaminants.

Environmental Molecular Sciences Laboratory (EMSL). Our premier facility. Broad capabilities in environmental molecular sciences and computational research. Excited to finally have 900 MHz NMR operational. Grand challenges and new part of national lab contracts – concentrated effort bringing large teams with access to multiple instruments to rapidly advance a field.

Savannah River Ecology Lab (SREL). The other newest addition to our program. Working to integrate in BER program. Strong history of ecological and remediation research. Significant capabilities for BER.

Four new charges for BERAC:

- New approaches to cloud modeling? Abrupt climate change research? Warren Washington and Climate Change subcommittee
- COV review of Environmental Remediation Sciences Division – Michelle Broido lead. This process has already been very useful to BER.
- Broader role of BER in neuroprosthesis research? Lead to be determined.
- BERAC input on user facility operational hours and on measures for interim progress on BER long term measures.

Lots of solicitations for new research. Very proud of our role as a competitive program.

Proud of our partnerships with other agencies across all of our research programs.

New competitions for lab contractors underway. A leadership priority.

PNNL 300 Area. Problem at PNNL. BER steward of PNNL. Need to get out of this area while maintaining research activities.

Tough decisions. Getting out of Medical Reactor at MIT. Pressures from OMB. Ongoing negotiations with MIT and NIH about the future of the reactor. Part of tough decisions for us to move forward with exciting new program like GTL is our decision to get out of the basic research part of structural biology especially. This decision was also driven by NIH's growing investment in this area.

New interactions with the Biotechnology Industry Organization (BIO). Exciting opportunity to engage the industrial and environmental sector of BIO with our programs, especially GTL. Just participated in the first Congress of this new BIO sector with GTL playing a prominent role.

Under Secretary Bob Card gone. David Garman, Assistant Secretary for EERE now acting in this role. Bob Card came to DOE looking to rid DOE of BER. In the end he became our biggest fan. Now we are starting again with a new person whose "goals" for BER aren't known.

Jill Banfield, U.C. Berkeley – Science talk
Structure, Reactivity, and Behavior of Nanoparticles in the Environment
http://www.science.doe.gov/ober/berac/banfield04_04.ppt

Rachel Samuel, DOE Deputy Advisory Committee Manager
Gloria Sulton, DOE Office of General Counsel

DOE Advisory Committee Office approves BERAC meetings, Federal Register announcements, committee renewals, and membership packages. Members provide advice and recommendations for BER. They are expected to bring their expertise to the table. Legal requirements: FACA (Federal Advisory Committee Act) 1972-structuring and monitoring activities. Some government leaders were receiving advice from self serving interest groups. FACA Management final rule was revised in 2001. Included things like court cases and other statues that have been passed. At DOE, we have a manual that is also under review now, and it is still in a draft. Hope to be published before the end of this year.

Purpose of Advisory Committee: To conduct business openly. Provided to public. Materials are all available for public inspection. Entire meeting is on the record. BERAC members are prohibited from assuming responsibility or authority for DOE functions. DOE Advisory Committees: establishment: under agency authority, by statute, by President. We have 22 Federal Advisory Committees. 17 are statutory. 15 are discretionary.

Concerns and sensitivities: Gloria Sulton from General Counsel will address Conflict of Interest. Scope and objectives are set by the DOE. It is important for members to know what they are. As members, we try for it to be balanced in points of view and functions to be performed. We have other requirements at our Department--be diverse. Expectations--commitment. Understand the objectives of the committee. If in doubt, ask your committee's Designated Federal Official (DFO). Candid observations are very helpful.

Reminders: Ethics and conflict
Financial: not subject to criminal statute that Feds are. You should not participate in a matter that could have a direct or substantial effect on a company, institution, or organization that you are affiliated with. The level of our discussions rarely get to specific grants or proposals that would impact our organization. If you have any concerns talk to a DFO if you feel bias or are concerned with the integrity of a report submitted by the committee. It is the integrity of the committee's work that they want to protect.

Advisory Committee members to adhere to general Conflict of Interest requirements. Refrain from your use of membership for private gain. Should not use inside information. Shall not use your position in any way to coerce or appear to coerce any person. Seek immediate guidance if you are offered a gift. Gift rules: practical matter. Consider: how would someone on the outside perceive this? Not subject to post employment restrictions.

Questions

We are becoming involved in Committee of Visitors. What is official status?

Status does not change unless you have received some kind of other appointment. They have looked closely at COV. COV does not specifically fall under the same things as advisory committee members--not appointed by the Secretary. Air on the side of caution. (David Thomassen NOTE: BER appoints its COVs as BERAC subcommittees so the status is no different than any other BERAC subcommittee.)

Steve Larson, Memorial Sloan-Kettering Cancer Center, BERAC
Update on Radiochemistry Charge (viewgraphs and report on the BERAC website)
Report - http://www.science.doe.gov/ober/berac/Radiopharm.pdf
Presentation viewgraphs - http://www.science.doe.gov/ober/berac/larson04_04.ppt

Original BERAC charge

- "(in view of major recent opportunities) to reassess how BER support might best stimulate directions in radiopharmaceutical research that are most likely to find translation into routine medical practice."
- Driven by concern for shortages
  - Key personnel, now and future
  - Optimized facilities and infrastructure

Subcommittee recommendations approved by BERAC in original report:

- Centers of Excellence
- Training of Radiochemists and other chemists in allied disciplines, such as structural biology, medicinal chemistry
- Collaboration and joint planning with NIH and other key governmental agencies
- Regulatory review with FDA to facilitate probe development

Progress since last BERAC meeting:

- Partnership with NIH
  - Agreement on common goals
    - BERAC recommendations and NIH Road map
  - Collaboration
    - Role definition: DOE physical chemical and biologic science; NIH translation into man
    - National Institute for Biomedical Imaging and Bioengineering (NIBIB), exploring joint programs with respect to nuclear medicine centers of excellence for technology development and training

Dr. Orbach received a strong letter in support of the BERAC recommendations from NIH Director Dr. Zerhouni. Dr. Orbach responded that DOE intends to continue to developing radiopharmaceuticals and also intends to continue to support training of radiochemists

and radiopharmaceutical chemists. This helps establish a framework for collaboration between NIH and DOE.

Discussion of revised/updated report –

Q: What will your subcommittee be giving to us. A: I hope you feel you've had enough time to ask questions. We should then endorse the report and proceed to the next steps and provide more detail on this program.

Q: Lots of interest at universities on radiochemistry. Are you thinking of a different approach to radiochemistry, yet molecular imaging is a very high-interest area? A: The report does talk of individual components. There is a renewed need for radiochemists who are skilled at making these probes. Need post doc programs for those with PhDs in chemistry who can get training and move forward.

This is a field that benefits from bringing all kinds of chemistry together. We have at DOE the infrastructure to train people at the intersection. This is the kind of field that will reel new young chemists in. We need to nucleate this area for repopulation. There are nuclear chemistry summer schools and they have a good record of populating this field.

There is a growing appreciation in big pharmaceuticals to use these probes to accelerate pharmaceutical development. They use PET, but they need trained people. There are a lot of vacancies in this field. This field has shown itself to be extremely valuable clinically. At Memorial Sloan-Kettering they do 30 scans a day just based on a clinical need.

Q: Would like to see more in depth information on responsibilities/roles between NIH and DOE, particularly with FDA. A: They will involve representatives from NIH in the planning phase. They appreciate the fact that the resources are at the labs and the testing phases are at NIH and that does give them distinct complementarity.

Our school of pharmacy is interested in this area. Psychiatry school, etc are interested in both of these programs. It may be that engineering programs are interested in these areas, too.

We've experienced that a number of people with degrees in organic chemistry may use their skills to make probes and may help to design probes. It becomes possible to rationalize the design of these probes. There are other tracers other than radio tracers. There are magnetic and optical tracers that need to be developed in parallel.

Q: The letter from the director of NIH mentions regional centers. Do they have to be regional, in the day and age of the Internet [it doesn't seem necessary], or can they be more distributed? A: Certain physical assets and resources made by cyclotrons have to be near the source of use due to short half lives.

Q: This is a 50,000 foot level report. We need more details pertaining to distribution of activities between the two agencies. Is there anything on the level of a grand challenge

that might float to the top? A: In terms of grand challenges, it may be premature, so we are still in the general stage and we can move quickly to make this more specific. DOE provides radiotracers and NIH provides the molecular imaging centers. It is time consuming, but if you work with the biologists to tell them what tracers and probes you have, with their input you can create experiments that couldn't have been done otherwise. For example, imaging stem cells in real time---imaging the initial colonization in the bone marrow and the cells proliferate from that point and repopulate.

Another value of stem cell research will be to study the control of endothelium development in tumors. We should be able to study this process, and how to interrupt it, in real time. This work will benefit from the discussions with the biologists. Need these interdisciplinary groups to get to the details you are asking for.

Chair - Does the group feel comfortable with adopting the report as a framework to engage NIH? OK, we'll do so. The report is adopted.

Michelle Broido, University of Pittsburgh, BERAC
Discussion of two BERAC charges.

Over the past several years we have discussed the Environmental Management Science Program (EMSP, now part of BER), the Natural and Accelerated Bioremediation Research Program (NABIR), and value of lab and field-based experiments. Mesoscale experiments are highly instrumented experiments where the size of the experiment is a few to many 10s of square meters. These have some of the complexity of field studies but they are more highly instrumented than larger field studies.

The first charge deals with a proposal from Idaho National Engineering and Environmental Laboratory (INEEL). History is important. Until recently INEEL was focused on the cleanup of a weapons processing site. In 2003, INEEL was transferred to the Office of Nuclear Energy.

A lot of contamination is in the subsurface and it has been there a long time. When INEEL was an Environmental Management (EM) laboratory it developed a subsurface science initiative. BERAC was asked to review INEEL's proposed mesoscale science experiments.

The ideas were focused on EM needs because INEEL was an EM lab at the beginning of the study. The key question is whether there is there a need for such facilities? If BERAC decides that they are needed, there should be additional discussion on those facilities at a subsequent meeting. This is an important consideration in the subcommittee's deliberations and recommendations.

The subcommittee's focus was not on the scientific merit of the mesoscale facility. The subcommittee met in February for a full day of presentations. INEEL staff members are thanked for their fascinating and well done presentations and discussions. The take home

message from the presentations was the overall premise that laboratory studies are not sufficient for studies involving contaminant transport in the subsurface. The arguments---if there were a single facility housing a number of mesoscale experiments, there would be certain economies of scale achieved---data management, extraction, sophisticated instrumentation---that wouldn't need to be duplicated and instruments would be dedicated that could be used on long time scales.

Is there a need for experiments at the mesoscale? Yes, clearly. However the subcommittee didn't agree with the premise that there must be constant interplay between laboratory and field studies. This is only needed when testing appropriate hypotheses. Mesoscale experiments are needed when dictated by hypotheses but they are not required in all cases. Different scientific inquiries require dramatically different experiments.

What about the facility being planned at INEEL? INEEL is establishing itself as a leader in this area. INEEL is an appropriate site to invest in studies of the vadose zone that might include mesoscale capabilities, but this doesn't mean they need to invest in this facility.

Remember that the subcommittee did not look into the details of the proposed facilities themselves. The committee did not envision how a centralized facility could address the needs of the scientific community. On the other hand, would some kind of facility or facilities in general on mesoscale experiments be important to DOE? There are a number of applications for mesoscale experiments across DOE. For example, carbon sequestration is important to Energy Efficiency and Renewable Energy (EERE), SC and Fossil Energy and benefits from mesoscale studies.

The bottom line - mesoscale experiments are important to some key DOE missions. INEEL has a wonderful group of scientists who can address these issues. However, the subcommittee does not endorse a centralized facility for mesoscale research.

Comments, questions, clarifications?

Comment: We need to think about the questions you are asking and what is the best approach. We have been looking at hydrologic observatories that are highly instrumented. The biggest question is what are the most important questions in hydro-geo science today? We need to see why or how this site would be used to answer the fundamental questions. The idea of mesoscale experiments is important. In recent discussions of Genomics:GTL, with microbes, you are dealing with samples that don't have a long shelf life. A well-instrumented field site is very important and would be a tremendous advancement in the field. People have to do the biology analyses immediately and this has to be driven by the fundamental questions. There doesn't appear to be anything here on the molecular and nano-scale networks---a whole new field. You'd want to pick a site carefully and you wouldn't want to pick a mesoscale site right at the beginning. The whole idea of having a mesoscale site is very important. Need to think about the technologies and doing this in the future.

Those ideas are not included in the report because it wasn't raised in the discussions. We didn't go into depth and detail on the physical nature of these facilities.

How do nanoparticles form and migrate? How does spatial temporal heterogeneity affect that? If the right questions were to come, wouldn't your view of this be quite different?

The subcommittee endorses mesoscale experiments, but they should be physically located at the most logical place for each experiment, but not at a central location.

It depends. If you are there to develop new technologies, you might have more flexibility at a central facility.

The subcommittee has been clear that the second part deals with INEEL. I don't think there is any inconsistency here.

Subcommittee report accepted by BERAC.

The subcommittee's second charge was to determine whether or not there is need for additional field research sites for BER's environmental remediation mission. The NABIR program does have one field research center (FRC) at Oak Ridge National Laboratory (ORNL) that has been successful for supporting needs of NABIR. The subcommittee expanded the charge to ask if there were facilities or instrumented capabilities that were needed beyond those provided by the FRC.

The benefits of the ORNL FRC for researchers: A direct connection to the contaminant mix at a site. Doing fundamental research on real contaminants. When you go to a site things you weren't aware of come to the surface. Filed sites raise awareness of economic, regulatory aspects, etc. The complexities and heterogeneities present in the field have to be addressed.

By having FRCs you foster more field research than would otherwise would occur. It is a daunting task to develop FRCs de novo. It helps to bring the novice researchers to a site to further the number of scientists who are working in the field. Field projects are more interdisciplinary than lab projects. Samples from the field are taken back to the lab so it enhances what happens in the lab.

The subcommittee believes it is important to have additional FRCs. They should be focused on issues, not necessarily on contaminants, that are expanded from what can be achieved or learned at the ORNL FRC. They should have broad applicability. There should be a range of questions and experiments that should be addressed---more than the issues upon which NABIR is focused. Should have issues and capabilities that would be of interest to EMSP.

It is important that FRCs be focused on DOE problems---radionuclide contaminants of environment including mixed wastes. Can include organic solvent plumes.

Prioritizing locations or features of additional sites: They should have combination of interesting physical and biological properties. There should be an array of chemical waste streams to facilitate the broadest hydrological , biological and geological studies.

Models are critical. Models are a basis for data integration. Models help clarify what is known and what is not known. You need a way to organize what you know and don't understand. Models can be used to fill in the gaps of knowledge and help in conducting field experiments.

Budget? How do you balance the expenses of one or more FRCs against the whole portfolio? There are currently 4 bioremediation programs. NABIR, EMSP, EMSL, Savannah River.

NABIR and EMSP budgets: The subcommittee felt that 10-15% of these budgets should be used to provide operational support for FRCs. If a new site were developed that is as well characterized as the ORNL site was, it would be a cost savings that could allow at least two more sites to be developed. 10-15% of the budget should be operational support, 15% for research, 15% for lab based studies, etc.

This could leave from 0-25% of the budget for additional activities. The subcommittee recommended some mesoscale experiments when the right questions are asked and if they are collocated with lab or field experiments that are complementary. There are some mesoscale capabilities that would be important.

The other thing that is important is synchrotron-based research. There is a report that was drafted at the time the subcommittee met---a parallel organization to BioSync that made a report on the use of synchrotrons for environmental studies. There is a need for an interagency study on how to develop this. The subcommittee recommends that US synchrotrons also be used for environmental research.

The other two subcommittee recommendations: (1) Because of the criticality of modeling/theoretical studies to the science mission of the Environmental Remediation Science division, there should be a partnership between BER and the Office of Advanced Scientific Computing Research. (2) The subcommittee was also concerned that the EMSL is not as robust a partner in the general area of subsurface science remediation as it could be especially on radionuclide work since EMSL wasn't designed to work with radionuclides in the facility. The subcommittee recommends that this deficiency be corrected.

BERAC agreed that items raised during the presentation and discussion should be added to the report and included in the transmission letter to Dr. Orbach. The subcommittee can be repulsed at Dr. Broido's discretion. The charge and report should be expanded to reflect the committee's and BERAC's deliberations and discussion.

Bill Valdez, SC Office of Planning and Analysis

Joel Parriott, Office of Management and Budget (OMB)
BER Roadmap for Long-Term Performance Measures
(Presentation on the BERAC website - http://www.science.doe.gov/ober/berac/valdez04_04.ppt)

Discussion of links between program planning, budgeting, and performance targets.

For development of the FY 2005 Program Assessment Rating Tool (PART) SC developed new performance measures. Ari has to report every 3 months. SC is the only science agency that has a suite of performance measures. This serves as an indication of what you are going to deliver for the money.

The SC website explains the measures, what they mean, etc.
(http://www.sc.doe.gov/measures/)

Every 3 years, OMB will look back at progress being made toward each program's long term measures. OMB has asked the program, with BERAC's help, to develop a roadmap that for each measure will show the performance plan.

Objectives come from the strategic plan. The performance plan comes from that. Critical path analyses are being done and the critical pathway needed to achieve BER's goals has ben set. (Material not available for distribution)

Expectations from OMB.

The bottom line on the roadmaps, that is important to OMB, is that BER has long term measures that tell where it will be in 15 years but it also needs to know and be able to demonstrate where it will be at intermediate stages, say 3 year intervals.

The goal in developing these intermediate measures is to do as little harm as possible, e.g., don't want to predict dates of discoveries and then be held accountable for discoveries that aren't made on time. The people who make decisions on budgets need to know where the program is headed and to have ways of knowing if it is getting there. If BER and BERAC can help OMB lay out the pathway to let us know you've made it, or if you've discovered something more important that you predicted, if you can describe how you got there, we'd be in good shape.

By combining these two things we are seeking the lowest common denominator and this should decrease not increase the workload. The roadmaps are needed by September of this year in conjunction with the OMB budget. Since this will contain budget sensitive data, it won't be released until January.

Q: Is the roadmap a FED-ONLY thing? BERAC can help in what it is asked to do. It needs to understand what it can do to help. The next full BERAC meeting is in November. We need to know what we can and can't do. We need to hear your thoughts on what you'd like.

Joel: When you craft the long-term measures, people made assumptions where the program would be 15 years out. Don't know what the assumptions were, but we should expect realistic budgets. Everyone has a different definition of realistic budgets.

You as a committee should be able to sit down and think of the intermediate steps. How you interface with DOE on that is up to DOE. Bill: it was valuable to have the advisory committees look at performance metrics. It's like the good housekeeping seal of approval when the advisory committees are involved. Some advisory committees changed certain aspects of their performance metrics and they did. It would be useful to have the advisory committees look at the roadmaps and provide their views. Need to talk to Ray and others.

Joel: Doesn't see how these are proprietary budget documents---they don't have dollars in them.

I think BERAC didn't fundamentally change the variables, but there were tweeks that were valuable. If we have the data in enough time and can discuss it, we could provide input.

Joel: You are in essence writing a charge letter for the committee that will be reviewing this in 3 years. At that point that committee will revise the long-term measures because science will have changed in that time.

When BERAC was asked to do this the first time was tight so our ability to do more than tweak was limited by about a 36 hour time frame. Would be better to have more time to do this in a more measured way. There is more time this time. Will complete the first draft of the program plans by the middle of this month. Assuming Ray approves, they can be sent off to the advisory committees soon after that.

Q: You acknowledged that discoveries don't happen or don't happen on the dates we wanted them to. What if there is no widget or direct application, but only knowledge that we shouldn't be going a certain way or using a certain strategy that we thought we should? Would OMB call that a success?

Joel: In physics one of the most important discoveries was that the rate of expansion of the universe was accelerating yet the field initially set out to do the opposite. Don't want to cause agencies to fund low risk research. This is one of the areas where DOE BER is differentiated from NIH. As long as the failure is via a high quality process, that is fine.

Bill: They will update the strategic plan on an annual basis and will change roadmaps on the web, though they won't be making a hardcopy.

Joel: We treat basic research differently from applied research.

Q: What do you envision the category "key external factors" to be?

Bill: There is guidance---it is the analog to the significant shifts to the SC budget. It is what has caused you to change your direction. At this point they developed boiler plate language for the programs and they modified it for the circumstances. At some point these planning processes will stop being new, they will be embedded into our strategic planning processes. The advisory committees will help form those kinds of categories. You will know this request is coming and you will help us fill in that kind of data.

Joel: We don't consider the fact that programs "never get enough money from the president's budget" as a key external factor. Climate change stuff is a huge interagency process and there would be a number of external factors involved there.

In the '05 budget going to the hill, there's guidance for the out years. This relates to Orbach's 20 year facilities plan. We have concerns on the administration side that we have no way of responding to this 20 year plan and this may be raising expectations way beyond where they should be.

The unique thing about SC budget is that it is stable---doesn't matter who is president, etc. A reasonable assumption is that it will still be flat. With a current services budget you keep what you have and you pay salary increases. Most people say inflation is about 5%, but budgets you saw are flat. This means we can't afford a current services budget let alone new facilities.

Q: What is the interplay between the program assessment roadmaps and GPRA?
A: GPRA has been subsumed somewhat so they don't do two separate processes.

Q: If the score goes from 55 to 85 and the budget doesn't go up, why do we bother to do this? Joel: It was a necessary but not sufficient method for budgeting in the government. If SC had pushed back and said we aren't going to do this, it wouldn't be pretty. This is a tool, but there are many other factors for setting budgets. (There have even been cases where low scores were actually used to justify higher budgets so it cuts both ways.) It's not just the scores only, but we view this as part of OMB's management toolkit. Your point is well-taken, but who said everything is rational?

Bill: Despite difficulties, there were some good things that came out of this that helped crystallize BER's performance planning process in a way that made sense to them.

Joel: The committees of visitors process has come out of this. The committees of visitors, if done properly, will be more important than any budget document/justification you could write.

Ari: We welcome the visitors and their contribution. The net result for BER is that they discovered things they would not have been done had it not been for the board of visitors. The process opened our eyes to their tremendous potential.

BER is only reporting on 5 metrics (and most just have yes/no answers).

NO PUBLIC COMMENT.
Meeting Adjourned at 5:00 p.m.

Friday April 29, 2004

Ari Patrinos, Associate Director of Science for Biology and the Environment
BERAC review of BER facility operating hour definitions.
(viewgraphs on BERAC meeting website) http://www.science.doe.gov/ober/berac/facilities.ppt

Always attempting to make our user facilities more efficient. One measure of the success or failure of DOE managers. Are the facilities serving in a cost effective way? BER came into facilities game rather late. 20 years ago we hardly had any facilities. Only in the past 5 or 6 years has BER focused more on scientific user facilities. BER has an important niche in the facility business and it benefits from the experience and expertise from its sister offices in SC with their experiences in building light sources, etc. Our facilities, more than anything, are unconventional, in the DOE SC way of doing things.

Question on measuring the use of specific NMR instrument for example. OMB efficiency hours are always based on a suite of instruments rather than on every instrument in a facility.

The numbers are all about 98% of maximum hours which is meaningless and confusing. This is driven by the president's management agenda.

Are these reasonable metrics?

It would be interesting to compare it to another high-tech activity perhaps instrumentation at a university or in a medical facility. You may be overpromising and overachieving or overpromising and underachieving.

When this exercise was first launched, he didn't see these exercises as adding value. At the time it seemed like a meaningless task. There is some value in benchmarking. It is the science you want to judge. At the very least, if you can have some of the processes "down" that you can be guaranteed you are not failing in that arena. You can get a better assessment of whether you are doing the science right and if you are taking on the right science problems, etc. We want to make sure the process part is done right and that's where we seek validation.

Regarding EMSL, there are certain instruments that have high down time and some instruments have down time under certain specific configurations. So, you could be using a laboratory for a specific configuration that would make the uptimes go up, but the instruments wouldn't be used in more risky protocols.

That's why the selection of instruments needs to be well thought out. Don't want to operate blindly.

Are you using this to justify future budget increases for these facilities? NO, there are no budget increases. These are used to justify continuing existence.

The dilemma here pales by comparison to the process going forward if we get the GTL facilities. If we are successful with the GTL facilities we'll have to do a more rigorous job in our assessments.

Another unconventional facility: the mouse house in ORNL. The definition of an operating hour is not clear.

BER is encouraged to stay with what we have and not create additional metrics right now. Zero order is useful. If OMB accepts these metrics, then you go ahead with them until they say something different.

Jeremy Berg, Director National Institute of General Medical Science (NIGMS), NIH
NIGMS and the NIH Roadmap for Medical Research
(viewgraphs on BERAC meeting website) http://www.science.doe.gov/ober/berac/berg04_04.ppt

Challenges for NIH:

- Accelerate the pace of discovery in the life sciences
- Translate research more rapidly from laboratories to patients and back
- Explore novel approaches; need to do more than incremental changes.

NIH Director Zerhouni asked for a roadmap. Involved NIH, scientific, and health care communities. There were a large number of initiatives on the table that were winnowed down to a small set. A framework of priorities.

There are 3 sets of initiatives:

- new pathways to discovery
- research teams of the future
- re-engineering the clinical research enterprise into something that is crucial to the translation part of the roadmap.

The biological data of the future: most methods suffer from being destructive, qualitative, difficult to develop a cumulative knowledge base and move forward, less quantitative. The other aspect to finely integrate this with the success of human genome sequencing and complex environmental factors to put this together to improve quality of health and decreasing cost of health care.

Bench → Bedside→ Practice

There are implementation groups charged with coordinating activities in different areas. One of the driving force for these initiatives was to find things that impacted all the NIH institutes. Jeremy is co-chair of two implementation groups.

Key elements of roadmap funding and management. All institutes contribute equally and proportionately to all roadmap elements. Zerhouni has authority to transfer 1% of the funding of each institute to the central roadmap funds which are then distributed.

The mechanisms for funding---there's a certain amount that is intramural

Overall budget is $128 M for roadmapping effort.

The scale of the roadmap is small scale in that it is less than 1% of the NIH budget, although integrated over all the institutes and 6 years, is that it is about $2 B. The roadmap is not causing proposal success rates to drop as some researchers feared.

<u>New pathways to discovery</u>:

Molecular libraries of imaging probes
The use of small molecules as probes. Three recent developments make small molecule/chemical genomics initiatives feasible. The human genome project, modern synthetic chemistry, and compound collections. Pharmaceutical companies will have access to screening library compounds.

There are plans for 6 national screening centers. One will be at NIH and there will be a public database.

The picture that is envisioned: an investigator develops an assay and gets access to a screening center where the assay will be customized. Screening will be done so results are available. There will be some chemical modification capability in the centers. PubChem is the database. Synthesis capabilities to make new fluorescent probes will be available.

An RFA was issued in 2004 for fluorescent probes for cellular imaging. Want to get a factor of 100 increase in sensitivity.

Structural Biology
Many physiologically and pharmaceutically important proteins are membrane proteins. Few membrane protein structures are known. We are doing just as well with membrane proteins as with soluble proteins if we are willing to tolerate a 25 year offset. Need to decrease the steepness of the curve. Centers for Innovation in Membrane Protein Production.

Filling strategic gaps in the overall (ongoing) program---but there won't be huge increases in funding. Goal of the ongoing Protein Structure Initiative is to make 3-D atomic level structures available. They've focused on improvement in technology and methodology and to make reagents and materials available. Trying to capture both the successes and failures to start improving the methods.

Many structures will be deposited in the database (required), even though they may not be published. Progress and when protocols were abandoned are on the web. PDB, TargetDB, PepcDB is under development. They want to make all targets that have been looked at available to other scientists.

403 structures determined in first 3 years. Doubling each year. 70% for PSI

One concern they heard is that we'd be producing structures with no functions based on sequence.

Lessons learned:

- Structural genomics pipelines can be constructed and scaled up
- High throughput operations work for many proteins, but not all
- Genomic approach works for structures
- Bottlenecks for some protein classes
- A coordinated, 5-year target selection policy must be developed. (They are spending a lot of time thinking about how many structures to get—if set too high, scientists will go for the easiest ones that may not be the most interesting.) One aspect of the new implementation is to get this coordinated selection policy in place.
- Homology modeling methods need improvement (if 40% homology)

PSI-2 large scale centers goals:

- Increase the number of sequence families that have at least one experimental structure determined.
- Increase the number of sequenced genes for which homology models can be built
- Increase the biomedical significance of the structures
- Requires between 4 and 6,000 unique structures.

This next phase will be an interacting network with 3 or 4 components - large scale centers and specialized centers for tech dev and challenging problems, etc.

This effort is moving more toward human proteins.

Bioinformatics and Computational biology
The cornerstone - National Centers for Biomedical Computing. Applications received on January 23, 2004. $12 M to fund 4 centers. Directed toward developing software for driving biological projects. All software will be open source. They are making plans for R01 projects to interact with national centers.

Multi and interdisciplinary research: Multidisciplinary research means two scientists from different fields work on a problem and go away unchanged by the interaction. Interdisciplinary research results in interactions that forge a new discipline. The challenges to make this work cut across federal agencies and the academic community.

Many academic systems favor independent investigators. Need to be clear on who is the single driving force. Interdisciplinary science requires interdisciplinary peer-review.

NIH director's pioneer award - 500,000/yr for 5 years. The NIH peer review system is frustrating and conservative. The pioneer awards are a way to compensate. 3-page nominations. Multi-tiered process that ends up with interviews. A large number of applications have been received.

Re-engineering the clinical enterprise is a large scale initiative. It is clear that clinical research is challenging because of a lack of infrastructure and coordination with the regulatory side. Trying to develop networks that track patients.

www.nihroadmap.nih.gov The roadmap site changes rapidly and often. Trying to get the research community to contribute. Need to see mechanism for how they receive comments.

Q: Have priorities shifted on the roadmap? No, articulation may have shifted. All programs include underrepresented groups. The health disparity issue may be a driver.

Q: To what degree is the roadmap and its sequestered funding filtering down to the institute study sections? This should mean that more money is available. The roadmap is a framework for all of NIH's work rather than just a small, new program. The roadmap is identifying crucial areas for moving forward.

Q: Can you make a personal prediction where we'll see a demonstration or showcase? A: It's a huge area. The idea for building multipurpose networks for clinical trials where there is much better coordination between investigators wanting to relate problems.

Gene Bierly, American Geophysical Union, BERAC
Two subcommittee reports (viewgraphs on BERAC meeting website):

- Reconfiguration of the Atmospheric Science Program (http://www.science.doe.gov/ober/berac/ASP.ppt)

Atmospheric Science Program reconfiguration recommendation: Reconfigure the atmospheric chemistry and environmental meteorology programs into an aerosol program that addresses radiative forcing in the atmosphere.

Research is needed that emphasizes radiative forcing from natural and anthropogenic aerosols. The results will be used to provide input into climate models with a goal of reducing uncertainty in model output. Aerosol forcing appears to be of the same magnitude as the effect of Greenhouse Gases, but much more uncertain.

Two areas of greatest uncertainty: indirect effects of aerosols on clouds and the role of black carbon and organic aerosols on climate.

The US Climate Change Science Program recognizes that aerosol research is growing in importance. There are concerns that uncertainties associated with aerosols are not being addressed adequately. DOE (BER) volunteered to look into the problem.

- Committee of Visitor Review of the Climate Change Research Division (http://www.science.doe.gov/ober/berac/COV_CCRD.ppt)

Climate Change Research Division Committee of Visitor Review - March 1-3, 2004.

COV is an opportunity to have a group of interested and knowledgeable peers take a detailed look into how a program(s) is managed and operated and to help management in its operation of their programs.

COV was charged to:

- Assess some of the research program management processes in the Climate Change Research Division in BER
- Provide as assessment of the processes used to solicit, review, and recommend proposal funding actions
- Assess the processes used to manage ongoing research programs, especially the decision-making processes

What the COV found:

- Details on individual programs not completed
- Need more than one year of data, three years would seem to be adequate
- Need information on declinations, withdrawals, solicitations, pre-proposals, rejections because of irrelevance, and grants
- Documentation by Program Managers should be standardized especially in proposal jackets
- Program Managers need to keep records of why they take certain actions, especially changes in budgets, declinations, and return of pre-proposals
- Merit reviewer pools need to be refreshed

Also:

- Integration of Climate Change Research Division (CCRD) programs into Climate Change Science Program (CCSP) needs constant work and work with other agencies
- National labs are a great resource and their work needs to be better integrated into a DOE presence in the CCSP
- CCRD staffing is too thin to do an adequate job in all programs

John Houghton, BER
Genomics:GTL Roadmap Status (viewgraphs on BERAC meeting website)
http://www.science.doe.gov/ober/berac/GTL_Roadmap.ppt

GTL roadmap - Much higher stakes than the last roadmap he was involved in on carbon sequestration. Roadmap called for in the pending Energy Bill, but regardless of whether it passes or not, a GTL roadmap is essential for us to plan the GTL program, in particular the facilities.

What is a roadmap? A vision about the future and a description about how to get there. Described what we know now, and what kinds of science, capabilities and technologies we need to get to our vision.

We have been getting broad input from the scientific community through past and current workshops.

Q: What is the timeframe? Our plan is to finish it in the fall. There will be lots of review of the products via external people. Will ask BERAC to form a subcommittee because there is some chance there will be some output prior to your next BERAC meeting.

Marv Frazier, Director Life Sciences Division, BER
Proposal for a BER Distinguished Scientist Fellowship (viewgraphs on BERAC meeting website) http://www.science.doe.gov/ober/berac/DSF_Award.ppt

Goal: To help develop and sustain scientific excellence in Biological and Environmental Research at the National Laboratories. Proposed to be a seven-year renewable fellowship for a total of $1.4M ($200K/year).

Eligibility: Must be full time employees of a National Laboratory (NL) or other DOE facilities; Must have worked for a minimum of 10 years at a National Laboratory or other DOE facilities; and Must have shown sustained scientific excellence in biological and/or environmental research.

Selection Process: Nominations – made by the Laboratory leadership and be endorsed by the Laboratory Director; Eligibility – determined by an independent peer-review panel of distinguished scientists from outside the National Laboratory System; and Selection – from the list of eligible candidates by BER senior staff members; Review and Endorsement – by BERAC.

Restrictions: Twenty total awards could be in place at any one time; Six awards (maximum) to any individual National Laboratory or DOE facility.

Selection criteria: Evidence of sustained scientific excellence; Significant scientific achievements; Honors and awards; Peer-reviewed publications quality (high impact journals) and quantity; Proposed research relevant to BER programmatic goals; and Recommendations from individuals at non-affiliated institutions (6 letters)

BERAC endorsed the plan as long as it is rewarding excellence. Let mid-term scientists see that if they are good at a national laboratory there is something higher they can aspire to. For young people in the national laboratory system, they can see there is a future.

Think a little more about why you're doing this. Is that the appropriate way to reward past excellent? Encourage top people to do important stuff for BER?

This might not be the best reward system.

Keith would like to help put this program together and he'd like to differentiate this from the development of the rewarding process. BERAC would only be involved in the process not the merit review aspects.

No Public Comment

Next meeting – November 3-4, 2004, at the American Geophysical Union.