

## **Report on the Biological and Environmental Research Advisory Committee's (BERAC) Consideration of the Genomes to Life Facilities Plan**

BERAC Committee Meeting, December 3-4, 2002

At the Advisory Committee meeting held December 3-4, 2002, BERAC devoted a significant fraction of its time to discussion of the Genomes to Life (GTL) program with focus on the planning for GTL facilities. The GTL facilities plan is one component of the broader GTL science initiative, which itself is an integral component of the BER life sciences portfolio as it evolves to capitalize on the wealth of information that is coming from genome sequencing efforts. An overview presentation of the GTL facility plan and four specific talks on each of the proposed facilities were made to BERAC. This served as the background and framework for a considerable amount of discussions and questions. The short report that follows provides BERAC's view of the plan as an outcome of this process. This report was developed after the meeting and transmitted to members for their review and approval, a process that was completed by mid-February 2003.

**BERAC remains extremely enthusiastic about GTL and the impact and major discovery potential of its science program in the coming decades.** GTL is a new and different scientific agenda that has generated a great deal of excitement in the scientific community encompassing university investigators, DOE laboratory investigators and aspects of the private sector. GTL, integrated within the broader BER life sciences program, is off to a very strong start in taking a leadership role in redefining modern biology in a national context, developing in parallel the potential to optimally serve the specific scientific mission interests of BER and DOE. BERAC encourages strong support for the whole GTL initiative as it holds a key to future energy and societal benefits from biological sciences.

**Several unconventional facilities are needed to support the GTL science plan.** It has become increasingly clear that in order for GTL to reach its very aggressive goals and have maximal scientific impact, its researchers will need access to and the support of several new, and unconventional facilities. These new facilities need to be brought into operation and be effective if GTL itself is to succeed as a science program. If done well, they will have terrific catalytic impact, assuring success of the GTL scientific agenda and indeed refashioning how biology is conceived and done over the coming 20 years. By taking the lead in this endeavor, DOE can make a seminal contribution to future research, with an impact that is similar to that provided by conception of the genome project nearly two decades ago. For this reason, BERAC most strongly endorses and supports the concept of these GTL facilities and urges that they be put on the critical path for DOE facility development in an appropriately phased manner.

**Unconventional facilities need to be born and raised unconventionally.** BERAC strongly believes that these unconventional facilities mandate equally unconventional planning and implementation for making choices in siting, design, management and provision for facility evolution. Here, BERAC urges caution and recommends several specific areas described below that need both immediate and longer term attention. The design process and operating principles must be custom-tailored to the specific scientific opportunities and needs of GTL and to the user community each facility will serve. It is essential to consider each major management issue now - from choices about siting to setting the science agenda and measuring success. Doing this will further establish DOE's leadership role in the wider area of the biological sciences.

**The risk side of the equation.** It should be recognized that there are differences between conventional and unconventional facilities. DOE should not assume that its past experience with conventional facilities can be migrated and applied across the board to these new unconventional ones. Although the ability to draw on elements of the most successful and relevant conventional facilities is obviously a DOE strength, and BER has experience in this regard through its stewardship of the Production Sequencing Facility and the Environmental Molecular Sciences Laboratory, the proposed GTL facilities must have a different character for several reasons. Success in their missions will require considerable flexibility, technical innovation and a much more integral connection to the scientific programs they will support.

The challenge will be to map the most relevant elements of DOE experience onto the needs and mission of the proposed GTL facilities. At the same time – and equally as important – BER, with the support of DOE Office of Science, must assume the responsibility to identify and discard aspects of past facility design and operation that *do not* match the new needs of new GTL facilities. We strongly recommend that the frame of reference for inventing a new unconventional facility go beyond conventional thinking for development and operation. BERAC believes that this is the time for a major and concerted effort to draw analysis, advice and input from the private sector, from the university community, from other entities such as The Institute for Genomic Research and Sanger Centers and other private institutes, and from prospective users of the facilities. This process has indeed already begun and needs to be vigorously continued and expanded so that input can be obtained from a broad range of future stakeholders. Moreover, while involved users will include GTL scientists from the National Labs and from universities, it is critical that the definition of “user” for this planning stage be the broader one that helps to justify facilities of this magnitude and assure the “buy in” of the broad scientific community. A possible process to accomplish this would be a series of smaller, more focused planning workshops that involve broad representation - an example of which was the National Human Genome Research Institute's Airlie House planning retreats.

**Managing user expectations.** BERAC also believes that involving a diverse group of prospective users, now and throughout development of these facilities, is important for managing community expectations which are typically unbounded. Shared ownership of the facilities and real buy-in for the user community - and the acceptance of associated

responsibilities, including being asked to participate directly in solving its problems - will work to buffer natural tendencies toward impatience and resentment that such large investments will inevitably foster when the facilities do not instantly deliver all conceivable and desired forms of output.

### **Specific Considerations:**

**Siting.** As stated emphatically before, BERAC very strongly recommends a wide-open, broadly advertised and competitive process for siting these facilities. This is critical to the future success of the facilities and to ensure that they have the broadest impact and depth of penetration into the scientific user community. Sites associated with National Labs are an obvious set of candidates, but more non-conventional sites - especially ones with close ties to universities or institutes with more experience in high-throughput biology, in underlying technologies and in their management - must also be evaluated. Choices should be based upon peer-review of a competing set of proposals and recommendations of a review committee constituted as carefully as possible to avoid conflicts of interest. The commitment of the host institution(s) to support the facilities, to invest in bolstering their competitiveness and to aggressively ensure their role in serving offsite users, should be included along with concentration of relevant expertise as criteria in choosing sites.

**Setting the scientific agenda.** The agenda must be defined and in part driven by the outside community of GTL and other prospective users. A limited fraction (5-10%) of the activity should be directed and allocated by the scientific leadership of the facility as an incentive to attract the very best possible scientists to run and contribute to further development of the facility. However, the remainder of the agenda should be set by outside users, many of who will be engaged in and funded by the DOE-BER GTL science program. This will need to be an ongoing process, and here some of the mechanisms that DOE has already established and proven in its structural biology and microbial DNA sequencing programs can provide a model; however, the agenda should be tuned specifically to the mission of each facility and will not be the same for each of them. GTL science activities that will depend upon, and take advantage of, products and services from these facilities should be priority weighted in some fashion. The integration of the goals and priorities of these facilities and the goals of the GTL projects and scientific agenda will be essential to success of both the facilities and the scientific program.

**Managing evolution of the facilities and their scientific agenda.** At this point in time, the four planned facilities differ quite significantly in their level of maturity. More specifically, the scope, requirements and technologies for detailed design and beginning an operational phase of Facility I (protein production) are well in hand. Facility I also has special management challenges unique to a facility that will make, catalog, store and distribute physical reagents to users. The technologies that will be most useful for Facility III (characterization and imaging of molecular machines) are in part less well defined and this facility is much more likely to

utilize imaging technologies that are not yet mature. Construction starts on all four facilities should be staggered accordingly. BER is encouraged to continue focused pilot or R&D programs where it appears further technology development will lead to more effective choices. BERAC feels that it is extremely important that there be a single oversight mechanism that oversees all four facilities and coordinates their development (in effect a GTL facility management board or oversight committee). This oversight group must have real authority to make changes in direction, balance and budget to best optimize the ability of this set of resources to most effectively enable the goals of the GTL science portfolio.

**Evaluating success.** BERAC strongly believes that the long term success and effective operation of the GTL facilities, including their location, will only be achieved if they are subjected to rigorous peer review on a regular basis. This is vital both to maintaining the vigor of the science and to maximizing the impact on the broad scientific community. To the degree possible, this review should be coordinated among the operational facilities. Success of the facilities can be measured in part by criteria articulated by the National Academy, OMB and the DOE BESAC report; that is, using expert review to assess quality, leadership and relevance.

**Summary:** DOE-BER had the vision and insight at the beginning of the genome project to make it happen and to invest in parallel to develop key technologies that allowed scaling up production and reducing costs. DOE-BER is again positioned with the GTL program to provide leadership in the post-genomic era, especially in ways that map to DOE mission needs in energy and the environment. DOE-BER has the experience to lead new technology development that can be realized by these four unconventional facilities that bring together a range of disciplinary capabilities and expertise under one umbrella. The development of technology and the collection of new experimental data coupled with computational and modeling capabilities that are such an important and integral component of GTL will lead to breakthrough discoveries in basic and applied biology. The potential gains from establishing and operating these GTL facilities primarily in support of the GTL science program merit going forward with enthusiasm and expediency. BER is strongly encouraged to maintain rigorous attention to the design, siting and management issues.