Hearing on Biological Research for Energy and Medical Applications at the Department of Energy Office of Science

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Testimony of Jay Keasling
Acting Deputy Director, Lawrence Berkeley National Laboratory
CEO, Joint BioEnergy Institute

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Introduction

Mr. Chairman, Ranking Member Inglis and distinguished members of the Committee, thank you for the opportunity to testify at this important hearing. And, thank you for your strong and consistent support for science and the innovation process. My name is Jay Keasling and I am the CEO of the Joint BioEnergy Institute and the Acting Deputy Director of the Lawrence Berkeley National Laboratory (Berkeley Lab), a Department of Energy (DOE) Office of Science laboratory operated by the University of California. I am also a professor at the University of California, Berkeley, in chemical and biological engineering.

The Joint BioEnergy Institute (JBEI) is a scientific partnership led by Berkeley Lab and including the Sandia National Laboratories, the University of California campuses of Berkeley and Davis, the Carnegie Institution for Science and the Lawrence Livermore National Laboratory. JBEI's primary scientific mission is to advance the development of the next generation of biofuels – liquid fuels derived from the solar energy stored in plant biomass. JBEI is one of three DOE Bioenergy Research Centers (BRCs) funded by the Office of Biological and Environmental Research (BER).

Lawrence Berkeley National Laboratory is a world-leading multidisciplinary science laboratory founded in 1931 by Nobel Laureate Ernest Orlando Lawrence. Eleven scientists associated with Berkeley Lab have won the Nobel Prize and 55 Nobel Laureates either trained at the Lab or had significant collaborations with the Lab. It has a very distinguished history in several fields of science including physics, chemistry, biology, computing, energy efficiency and earth sciences, among others.

Today, Berkeley Lab is mobilizing its strong bench of scientific and engineering talent to lead the scientific advancement and technological development of solutions to the energy and environmental challenges facing our planet. Much of this good work is funded by the Office of Biological and Environmental Research within the DOE's Office of

Science. I am delighted to be here with you today to share information about this productive and good use of federal research dollars, and to share a few thoughts about BER, the BioEnergy Research Centers and more generally on biology-based opportunities in energy and other fields.

Overview of Testimony

The energy and environmental demands facing our nation and the world are daunting and require a broad and balanced mix of solutions – from advancements in science and technology to bold changes in policy and human behavior. BER is aggressively advancing the scientific knowledge and the technological know-how needed to address these grand challenges with its unique cadre of experts and facilities. From the development of biofuels, to cost-efficient remediation of toxic environments, to changing the way we understand and predict the global impacts of climate change, BER serves a crucial and irreplaceable role in the federal research enterprise.

Today I want to draw your attention to four key areas:

1. BER's arsenal of research resources, such as the BRCs and the Joint Genome Institute, are unparalleled in the nation's science and technology complex and are hotbeds of potentially game-changing energy and environmental research.

2. The BRCs' development of cellulosic biofuels, especially next generation, environmentally benign, drop-in biofuels, will contribute significantly to new technological approaches to transportation fuels.

3. Synthetic Biology, a transformational approach to biological energy and medical challenges, holds great promise for the design and development of sustainable, safe, bio-based products.

4. In order to make rapid and meaningful progress, DOE's basic and applied energy research and development activities must collaborate closely and strategically. The BRCs are an excellent model for building stronger alliances between these two areas.

BER's Arsenal of Resources

Championing large scale and team-centric biology-based approaches to big problems have propelled BER to a world-leadership position in the biological sciences and in the development of biology-based technologies. Since spearheading the Human Genome Project in 1986, BER has led the development of modern genomics-based systems biology that today is enabling cutting-edge research into sustainable energy alternatives and global climate change solutions.

At the core of BER's strength are its unique facilities and world leading scientists. From the three BRCs to the Joint Genome Institute, BER is providing American research institutions and companies the intellectual horsepower and the specialized tools and equipment needed to make progress quickly. Also, BER is careful to ensure that it and its facilities utilize and leverage one another as well as other DOE assets to support its mission.

A case in point: each of the BRCs has access to the tremendous genomic research capabilities of the Joint Genome Institute (JGI). JGI was created in 1997 to unite the expertise and resources in DNA sequencing, informatics, and technology development pioneered at the DOE genome centers at Berkeley Lab, Lawrence Livermore National Laboratory, and Los Alamos National Laboratory. By combining these efforts, the significant economies of scale achieved enabled the JGI to be the first to publish the sequence analysis of the target chromosomes 5, 16, and 19, in the journal *Nature*. Following this accomplishment, the DOE JGI went on to advance basic science by sequencing scores of microbial species as well as several model organisms and provided this information freely to public databases.

Building on its success, in 2004 the BER established JGI as a national user facility. The vast majority of JGI sequencing is conducted under the auspices of the Community Sequencing Program, surveying the biosphere to characterize organisms relevant to the DOE science mission areas of bioenergy, global carbon cycling, and biogeochemistry. Today, JGI's largest customers are the BRCs, which utilize the JGI's skills and tools to sequence the genomes of prospective biofuel feedstocks, such as the poplar tree and the grass arabidopsis, or of potentially highly effective organisms for cellulosic deconstruction, such as those in the hindgut of termites or on the rain forest floor.

Additionally, JGI works with institutions and companies from around the country, including from the Chairman's and Ranking Member's home states. These projects include:

Scott Baker, PNNL, Richland, WA	fungus *Trichoderma reesei*	Developing strains with boosted production of biomass-degrading enzymes for industrial use in making biofuels
Toby Bradshaw, University of Washington	poplar tree	First tree genome sequenced laid groundwork for developing trees as potential feedstocks for cellulosic ethanol production
Maud Hinchee, ArborGen, Summerville, SC	eucalyptus tree	Fast-growing woody plant is one of the DOE's candidate biomass energy crops for cellulosic ethanol production
Jeff Tomkins, Clemson University	plant Aquilegia Formosa	Used as a model system to study how plans adapt to changes in the environment, especially as a result of climate change

BER's leadership role in biological sciences and technology development continued with its request for proposals in the summer of 2006 to establish three centers to research and develop cellulosic derived ethanol. Inspired by a joint BER-EERE workshop, the report, "Breaking the Biological Barriers to Cellulosic Ethanol: A Joint Research Agenda," provided direction for a program that would more directly effect large-scale solutions to our energy and environmental challenges. The workshop, in which I participated along with my UC Berkeley colleague Chris Somerville (Executive Director of the $500 million, BP funded, Energy Biosciences Institute), provided a cohesive research strategy that could best be realized through the creation of dedicated, collaborative scientific research centers.

This Committee and the Congress also played a critical role in the establishment of the BRCs. From the biofuel provisions in the Energy Policy Act of 2005, research agencies' budget authorizations in the America COMPETES Act, and the appropriations that made the Centers possible, you and your colleagues have demonstrated your leadership and your understanding that new approaches are needed to attack these big problems.

All of the BRCs are up and running and are making great progress. As an addendum to this testimony I have attached the recently updated "Bioenergy Research Centers Overview" (07/09) which includes information about the three centers, our progress and successes. JBEI's sister centers are profiled below.

> The **DOE Great Lakes Bioenergy Research Center** is led by the University of Wisconsin in Madison, Wisconsin, in close collaboration with Michigan State University in East Lansing, Michigan. The Center Director is Timothy Donohue, and other collaborators include: DOE's Pacific Northwest National Laboratory in Richland, Washington; Lucigen Corporation in Middleton, Wisconsin; University of Florida in Gainesville, Florida; DOE's Oak Ridge National Laboratory in Oak Ridge, Tennessee; Illinois State University in Normal, Illinois; and Iowa State University in Ames, Iowa.

> The **DOE BioEnergy Science Center** is led by the DOE's Oak Ridge National Laboratory in Oak Ridge, Tennessee. The Center Director is Martin Keller, and collaborators include: Georgia Institute of Technology in Atlanta, Georgia; DOE's National Renewable Energy Laboratory in Golden, Colorado; University of Georgia in Athens, Georgia; Dartmouth College in Hanover, New Hampshire; and the University of Tennessee, in Knoxville, Tennessee.

Each of the BRCs has pulled together the best of the national laboratories, academics, and the private sector to build a new model for interdisciplinary research. Working collaboratively, the three BRCs have the potential to provide a better investment for the federal dollar than a single large center. As has been pointed out by many, the days of Bell Labs and Xerox Labs are behind us. Therefore, it is critical that the federal government continue to invest in high payoff research that will bring transformative technology to the marketplace, maintain the leadership position of the United States in technology development and support the creation of new economic sectors. As example, let me describe JBEI to you in more detail.

As noted earlier, the Joint BioEnergy Institute (JBEI) is a six-institution partnership led by Berkeley Lab and based in the San Francisco Bay Area in a new research facility in Emeryville, California, within commuting distance of its partner institutions. JBEI is designed to be an engine of ingenuity, dynamically organized with all the scientific teams working together in a single location, under one roof, to enable researchers to share ideas and address cellulosic biomass problems at a systems-wide level. Within 60 miles of JBEI are some of the world's foremost expertise and facilities for energy, plant biology, systems and synthetic biology, imaging, nanoscience, and computation, plus the highest concentration of national laboratories and world-class research universities in the nation.

Organized like a start-up company (for example, my title is CEO), JBEI is designed to be nimble and flexible, able to focus and refocus resources quickly, efficiently and effectively – not the typical mode for basic scientific research. This organizational structure is critical to JBEI's success. For example, research avenues that are unproductive as related to meeting biofuels development targets may be quickly redirected. Ideas that show the most promise are invested in aggressively and resources are allocated to ensure rapid progress.

Biofuels: The Next Generation

Although biofuels have been in use, and in some stage of development for decades, the federal government and industry have not invested adequately in the basic science and technology development needed to advance more useful and sustainable forms. Ethanol derived from corn starch and other starch based biomass is a good place to start and have demonstrated the viability of bio-based fuels as useful and effective alternatives to fossil fuel. However, ethanol, especially when derived from starches, presents problems that must be overcome.

From the limitations of using existing transportation infrastructure, such as our inventory of automobiles and fuel distribution networks, to the inefficient utilization of the feedstock, starch derived ethanol is ultimately not the best way to address our energy security or global climate change challenges. New ways must be developed, and BER's investment in the BRCs is one critical path that holds great promise.

At JBEI, we are focusing on developing "next generation" biofuels that are compatible with existing infrastructure and utilize feedstock more efficiently. To do this we are taking a whole-systems approach to ensure that our research is applicable on large scales. The research revolves around four interdependent efforts that focus on (1) developing new bioenergy crops, (2) enhancing biomass deconstruction, (3) producing new biofuels through synthetic biology, and (4) creating technologies that advance biofuel research. The magic of this approach, as well as similar approaches at the other BRCs, is that advancements and discoveries in any of the four areas can be shared with and employed by each other, and by industry. In other words, commercially applicable developments made at the BRCs can speed improvement in various components of biofuels production before game changing discoveries are made and perfected.

JBEI researchers are engineering microbes and enzymes to process the complex sugars of lignocellulosic biomass into biofuels that can directly replace gasoline. However, the process and the research begin much earlier than the conversion of sugars into fuels. First, we must develop better biomass and better technologies for deconstructing the tough cellulosic bonds. Below are three examples of work through which JBEI researchers will improve the fermentable content of biomass and transform lignin into a source of valuable new and sustainable fuels.

The conversion of cellulosic biomass to biofuels begins with pretreatment—the use of chemical or physical treatments to loosen the tight linkages among cell-wall components, making the biomass easier to degrade. A new development in pretreatment research is the use of ionic liquids—salts that are liquid rather than crystalline near room temperature. Ionic liquids can dissolve both lignin and cellulose; their use, however, has required large amounts of antisolvent to recover the dissolved cellulose. JBEI researchers have studied solvent extraction technology based on the chemical affinity of boronates to complex sugars and determined optimal pH and temperature conditions for recovering sugars from the ionic liquid–biomass liquor.

To find other ways, including new and better enzymes, to break down lignocellulose, JBEI researchers have analyzed microbial communities in Puerto Rican rainforest soils that boast some of the planet's highest rates of biomass degradation. Scientists used the Phylochip, a credit card–sized microarray developed at Berkeley Lab that can quickly detect the presence of up to 9,000 microbial species in samples. Using bags of switchgrass as "microbe traps," the researchers conducted a census of these soil microbes to identify the most efficient biomass-degrading bacteria and fungi.

Through re-engineering microbes, JBEI researchers have used synthetic biology and metabolic engineering techniques in *Escherichia coli* and *Saccharomyces cerevisiae* (yeast) to produce advanced, "drop-in," fuels that perform better than ethanol. The scientists redirected central metabolic, fatty acid, and cholesterol biosynthetic pathways to produce candidate gasoline, diesel, and jet fuel molecules. JBEI also has developed a new metabolic pathway that potentially could produce both advanced fuels and other molecules (e.g., polymer monomers) that might otherwise be produced from petroleum, paving the way to replace a significant portion of petroleum-based products with sugar-based products. I will discuss this in more depth later in the testimony.

Close collaborations with industry is critical to the whole systems approach and to the process of getting discoveries and technological improvements to the market. At JBEI, we collaborate with companies in a number of ways to achieve this goal. We have an Industry Advisory Committee, comprised of leading companies in a number of sectors that relate to biofuels: agriculture, biotechnology, chemicals, oil and gas, automobile and aerospace. Currently this committee is comprised of representatives from the following companies: Arborgen, Boeing, BP America, Chevron, DuPont, GM, Mendel

Biotechnology, Plum Creek, and StatoilHydro. These companies meet annually for a review of JBEI's research and provide feedback from an industry perspective. They are able to identify challenges and opportunities that are difficult to perceive from the lab bench, but critical to address in the marketplace.

We also have an Industry Partnership Program though which companies can collaborate with JBEI in a variety of ways to best meet their needs. JBEI partners with companies to expand the scope of its biofuels research and take JBEI's fundamental discoveries the next step in development by focusing on an applied research problem in tandem with a company. In one example, JBEI is planning to work with a company on testing the compatibility and efficacy of our inventions with their processes. In another, JBEI has leveraged industry funding from Boeing and StatoilHydro to develop an economic model of a cellulosic biorefinery that will identify those aspects of the process that would most benefit from cost reduction.

JBEI ensures that its discoveries offer value to industry by patenting those inventions that we expect to be commercially valuable. Thus far, JBEI has produced 30 inventions and copyrighted or filed a patent application on 21 of them. JBEI actively promotes these inventions to the public and the target markets, not only to ensure that Fairness of Opportunity is met, but to find the most qualified licensee in each case.

Although we are making significant progress, I do not want to leave here today having given you unrealistic expectations. I estimate that whole-system, cellulosic to drop-in biofuels production on a mass scale is still at least a decade away. However, as stated before, we and our colleagues at the other BRCs are rapidly developing solutions for various aspects of the biofuels enterprise that may come to market much quicker. Synthetic biology offers more immediate opportunities.

The Promise of Synthetic Biology

As an example, I would like to describe my personal research in synthetic biology and how this exciting field offers great promise, not just for the development of game-changing biofuels, but for other bio-based chemical, consumer and medical products.

I started my career at Berkeley in the early nineties when it was very difficult to engineer biology. I began with the idea that one could engineer microorganisms to be chemical factories to produce nearly any important chemical from sugar. Unfortunately, there were very few tools to engineer microorganisms to produce chemicals. So, we began by developing tools to control the expression of genes that had been transferred to cells so that we could accurately control the production of the chemical of interest. There was really no name for what we were doing, but now it is referred to as synthetic biology.

At the time, I was somewhat ostracized by my colleagues for focusing on the development of tools for engineering biology – even though the development of tools is at the heart of every engineering field. As an example, Gordon Moore famously recommended that Intel spend at least 10% of its budget on the development of tools. Obviously, tools help to move science forward.

One of our most important and well-known applications of these tools has been engineering microorganisms to produce the anti-malarial drug artemisinin. There are 300-500 million cases of malaria at any one time, with 1-3 million people dying from the disease each year, 90% are children under the age of 5. While the quinine-based drugs that have been so widely used to treat malaria are no longer effective, artemisinin combination therapies are highly effective in treating malaria.

Because the drug is extracted from a plant that naturally produces it in rather low yield, artemisinin combination therapies are too expensive for most people in the developing world to afford. To increase the availability of the drug and decrease its cost, we engineered a microorganism to produce a precursor to the drug by transferring the genes responsible for making the drug from the plant to the microorganism. Through generous funding from the Bill & Melinda Gates Foundation, we were able to complete the science in three years. That science was greatly enabled by our previous work on developing biological tools. The engineered microorganism was further optimized and a production process developed by Amyris Biotechnologies. The microbial production process has been licensed by Sanofi-Aventis, which will scale the process and produce the drug within the next two years.

Artemisinin is just a start. Just as synthetic biology is being applied to develop new fuels, I believe that similar processes and techniques can also be applied to the production of many other products – from chemicals and medicine to consumer and commercial products. Today, companies like Amyris and DuPont are leading the way in the development of more sustainable, bio-based products that traditionally have utilized fossil fuels. Investing in cleaner, non-petroleum based manufacturing methods for non-fuel products should also be a significant focus of our energy and global climate change federal research agenda. Limiting this research to just fuels would be a mistake and a lost opportunity.

Collaborating for Success

I wanted to bring to the Committee's attention an important issue that, if addressed effectively, could greatly improve the Department's ability to develop solutions to great problems and help to move them to the marketplace. Energy research and the development of energy and environmental technologies at DOE demonstrate an unfortunate disconnect between the basic sciences and applied technology development at DOE.

Instead of dwelling on the problem, however, I prefer to concentrate on the huge upside presented by closer collaboration. If the Office of Science and DOE's applied research and development programs were more strategically and organizationally aligned, the progress that could be made would be astounding. Just as JBEI and the other BRCs are taking a whole-systems approach, so must the Office of Science and the DOE technology offices work together to establish objectives, to coordinate activities and to jointly invest in programs and projects. The BRCs provide a great opportunity for this type of collaboration.

There are signals that this is occurring. A recent instance is the announcement by Secretary Chu that EERE's Office of Biomass will fund a biofuels pilot plant for use by the Office of Science/BER-funded BRCs and other users across the nation. The pilot plant would translate the technologies created by the Joint BioEnergy Institute (JBEI) and its sister BRCs beyond laboratory scale to facilitate their commercialization. The facility will have capabilities for pilot scale pretreatment of biomass, production of enzymes for biomass deconstruction (cellulases, hemicellulases, and lignases), and fermentation capacity for advanced biofuels production and purification in quantities sufficient for engine testing at partner institutions.

Finally, I would like to share one last example of a potentially dynamic and productive collaborative effort. More foundational research is needed to develop the underpinning technologies in synthetic biology (SC), and to apply synthetic biology to test beds like microbial production of transportation fuels and specialty chemicals (EERE). An example of this foundational research is that conducted at the National Science Foundation-funded Synthetic Biology Engineering Research Center (SynBERC), a collaboration of the University of California campuses at Berkeley and San Francisco, Stanford University, Harvard University, and the Massachusetts Institute of Technology. BER could play large role in this foundational research, which would complement its work at the Joint Genome Institute, and advance its mission-focused research in many fields. Specifically, the funding of a biological fabrication facility dedicated to the construction and characterization of biological components would increase the speed and reduce the costs of the development of microorganisms that produce biofuels, commodity and specialty chemicals, and pharmaceuticals.

Conclusion

I hope that my testimony has illustrated for you the remarkable role that BER has and will continue to play in our nation's research and innovation enterprise. Your actions and the support of the Congress, however, will determine whether these efforts described today are ultimately successful. This is a marathon, not a sprint, and requires consistent and continuous nourishing and care. Additionally, the Department has a huge burden to shepherd their programs in a coordinated, strategic and efficient manner. To meet the monumental tasks before us, just in the area of advanced biofuels, will require more than what BER can do alone **–** all of DOE's resources, in coordination and collaboration with industry and other federal agencies, must be brought to bear.

Finally, thank you, again, for holding this important hearing and for inviting me to participate. Please let me know if I may ever be of any assistance.