Testimony

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The Future of Biotechnology: Solutions for Energy, Agriculture and Manufacturing

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Chairwoman Comstock, Ranking Member Lipinski and Members of the Committee, thank you for holding this very important hearing and for inviting me to participate. I applaud the committee for exploring the great potential that advanced biology has to address the nation's grand challenges and to stimulate innovation and economic growth.

As the Biosciences Principal Deputy at Lawrence Berkeley National Laboratory (Berkeley Lab), I am privileged to enjoy a front row seat as some of the world's best scientists push the boundaries of engineering biology. Over the course of a 30-year career as a biologist, I have been employed in industrial and drug discovery biotechnology. Most recently, I served as Assistant Director for Biological Research at the Office of Science and Technology Policy in the Executive Office of the President where I was the principal author of the National Bioeconomy Blueprint. Although my testimony represents my personal views and does not necessarily represent the views of Berkeley Lab or those of the Department of Energy (DOE), I do want to take a second to recognize the leadership role of both in driving the nation's engineering biology capabilities forward. Funding from the DOE Office of Science's Office of Biological and Environmental Research (BER) has nurtured world-class scientists and supported the creation of cutting edge tools at Berkeley Lab and throughout the DOE national laboratories that are internationally unique and extremely productive. Leveraging BER's investments in new and dynamic ways is a key feature of my testimony.

By 2050, the global population is expected to exceed 9 billion people. To feed all of those people, the world will need to increase agricultural productivity by 60 percent. Further challenging our ability to feed the planet is a predicted 40 percent decrease in crop yields by 2050 – as much as 80 percent by the turn of the next century. An ever-growing population is also expected to increase worldwide demand for energy by over 50 percent within the next 30 years. Creating an unvirtuous cycle, growing energy consumption will increase the production of carbon dioxide and cause climate changes, such as decreased rainfall, that challenge food production and contribute to disease. Another growing threat is posed by pathogens resistant to existing pharmaceuticals. With more than 25 percent of drugs used today derived from plants, competition for land to grow food and plants for medicines create the potential for shortages. These challenges are great, and biology can be harnessed to address them in sustainable and more efficient ways.

Biology can improve agricultural yields, increase nutrients in the soil, and reduce the need for water and for fertilizers. It can be used to create bio-solutions to reduce the demand for livestock-based protein sources such as beef and poultry for a planet with more people and fewer resources. It can convert non-food biomass into fuel, electricity, and commodity and high-value chemicals and, in the process, replace fossil fuels. It can convert microbes into low-cost producers of drugs and alter microbiomes, which are beneficial microbial communities, to improve human and animal health. It may even be able to produce novel biomaterials with desired properties that do not yet exist – such as shatter-proof bio-glass – having an array of uses and potential to create new markets in the way that the discovery of the novel material Kevlar did in the 1960s to revolutionize everything from tires to racing sails to body armor.

How is this happening? What about biology today leads my colleagues and I to have such great optimism about the future and about the value proposition for the nation and the world of investing in advanced biology? In a sentence, biology has reached an important inflection point. Similar to the advances made in information technology decades ago with the advent of programmable electronics, biology can now be programmed to more efficiently and effectively address challenges and opportunities.

Although engineering biology is an extremely sophisticated and complicated effort that brings together many fields of scientific and technological research, it is not over generalizing to describe its underlying foundation as the ability to program DNA. Where computer coding languages use ones and zeros to program computers, DNA is a coding language that uses As, Cs, Gs, and Ts, the four building blocks of DNA, to program biology. Farmers and botanists have been "programming" DNA for centuries in the quest for better food and material sources. And, scientists have been programming biology using genetic engineering for decades, applying it to a vast array of useful purposes - therapeutics, food, and consumer products.

Today, biology is poised to exponentially expand its application across broad areas of science and technology. Genome sequencing is fast, cheap, and has revealed a staggering array of biological diversity and metabolic potential that scientists have only scratched the surface of being able to understand. Synthetic biology tools and methods, advances in biological imaging technologies, and high performance computing-aided analysis have opened doors to new discoveries regarded as impossible only a generation ago. The promise is great, but the process of programming biology is still slow, expensive, and lacks tools, facilities and other platforms that are publicly available to researchers broadly. My testimony will focus on the opportunity and challenge of democratizing engineering biology in a way that will unleash the power of America's research biologists at universities, national laboratories and in industry.

Although genome sequencing has accelerated at an impressive pace as a consequence of the Human Genome Sequencing Project, advances in genetic engineering have not kept pace in allowing scientists to concomitantly benefit from this wealth of genome sequence information to create public benefit. As I mentioned, biological engineering is still relatively slow. It can take years to engineer simple microbes to produce desired products and even longer to engineer plants to be more productive, resilient crops. And because of the competitive landscape, I know from firsthand experience having worked in industry, that when a company makes a significant advance and creates new products through engineering biology it is often reticent to share the tools and technologies it has developed – naturally, it wants to maintain its competitive advantage. This means that those who follow often must spend time and money solving problems that have already been solved by others.

However, new emerging technologies such as synthetic biology and gene-editing, combined with powerful computation capabilities, promise to advance scientists' ability to engineer biology. As you will hear from other members of this panel, researchers now have the capability to create novel applications that were previously unimaginable across a broad variety of national and societal needs. The challenge is to create an ecosystem in which these new capabilities (expertise, tools, facilities, methods, knowledge) are widely available, easy to access, and domain neutral, meaning they can be used for a wide variety of desired purposes.

New engineering-biology research platforms promise to greatly accelerate the discovery of solutions to national and global needs, and in the process democratize engineering biology to enable researchers everywhere to drive advancement across fields and industrial applications. An excellent model for such democratic research platforms exists in the national laboratories, where national user facilities allow any researcher in academia, government, and industry to competitively apply to utilize and benefit from a broad range of world leading scientific instrumentation and expertise, from genome sequencing, to high performance supercomputing, to the world's most powerful electron microscopes, provided through support from the federal government.

Currently missing from the collection of national laboratory user facilities is a biofoundry: a high-throughput, open, public engineering-biology facility powered by capabilities in physical sciences and supercomputing to develop freely available tools, technologies, and knowledge needed to drive a sustainable national bioeconomy. Such a facility could accelerate scientific discovery, reduce costs, and cut the time to market for new bioproducts needed to transform energy, agricultural and industrial manufacturing processes for human and environmental benefit. It would build on and capture a greater return on DOE's existing investments in genome sequencing, synthetic biology, and other engineering biology research capabilities. A major asset of such an effort would be an open and public knowledge repository available to all research sectors interested in effectively engineering biology for useful purposes.

Berkeley Lab has made an initial investment to launch a prototype of an open biofoundry to address this unmet need, and has undertaken early proof-of-concept work to create bio-based products using novel technologies. The effort is aimed at establishing a robust, democratic platform technology for the engineering of biology for a wide variety of desired purposes. This effort will also create a public knowledgebase envisioned to provide the fundamental advances needed to transform manufacturing to accelerate the creation of biological solutions to national needs such as reducing energy intensity and negative environmental impacts of traditional manufacturing.

Ensuring that the nation has a well-trained workforce in engineering-biology is another critical reason to democratize all aspects of the field – including education and workforce training. To address this need, Berkeley Lab has also launched a workforce initiative to collaborate with individual community colleges and national organizations to further incorporate biological engineering and biomanufacturing into community college curricula and programs, and to promote undergraduate research for making renewable fuels and chemicals. Approximately 75 community colleges across the country have biomanufacturing programs and are engaged in conversations now with Berkeley Lab, and in the near future, the Berkeley Lab will make biological tools available for students to manufacture renewable fuels and chemicals and create new industrial production organisms. These efforts provide opportunities for community college students to do exciting cutting-edge research with advanced technologies, and valuable experience to enhance employment and career prospects.

In addition to technological and workforce challenges, economic challenges have inhibited the acceleration of biomanufacturing for both large and small companies. The so-called production organism is regarded as the most important determinant of the economics of the biological production process, and bioprocessing facilities represent the largest capital expense for a company. A 2015 National Research Council report, entitled *Industrialization of Biology*, recognized that the biomanufacturing of products is poised to greatly expand in scale and scope if future advances in feedstocks, production organisms, and fermentation and processing are realized. A federally-coordinated and strategic engineering biology initiative perhaps like the National Nanotechnology Initiative, could not only help solve several of the fundamental research challenges that impede the expansion of biomanufacturing but also address some of the significant economic challenges in the process.

How can the national laboratories help? Recent industry listening sessions held by Berkeley Lab indicate that in addition to user facilities, national laboratories can serve at least four unique and important functions for industry. First, many companies currently involved in biomanufacturing have expressed concerns that they face specific research challenges, such as the lack of suitable production organisms or readily available software solutions, that are considered "off-mission" by investors yet are likely to greatly accelerate the success of "on-mission" efforts. National laboratories could address such industry needs by creating and curating a diverse array of novel "domesticated" production organisms and freely available software solutions to greatly expand industry opportunities for engineering biology toward biomanufacturing.

Second, possible applications of published research from the academic sector must be carefully validated by companies before they can be usefully integrated into standard operating procedures, a process that is often time-consuming for companies and frequently unproductive. National laboratories could establish biological engineering validation platforms with standardized assurances and certifications that could greatly reduce company external technology validation timelines.

Third, because traditional manufacturing of some products involves the use of toxic solvents and high temperatures, which are energy intensive and result in significant greenhouse gas emissions and hazardous waste, many large companies are considering moving from traditional manufacturing toward biomanufacturing to reach corporate sustainability goals. However, a transition from traditional to biomanufacturing faces many hurdles, including significant capital expenditures and lack of technical expertise in-house. Without human capital having technical expertise capable of successfully driving such a transition, investors are wary if not unsupportive. National laboratories are already beginning to respond to this challenge by providing opportunities for companies to "embed" industry researchers for purposes of transferring engineering biology technologies and expertise directly to companies through hands-on training to forge industry capacity in biological engineering.

Fourth, companies agree that fermentation process scale-up is a major challenge and potential hurdle to production of chemicals and fuels. Successfully predicting production organism performance across scales – from microtiter to shake flasks to small fermenters to production scale fermentation – remains an aspiration, achieved likely only via intensive interdisciplinary efforts involving chemical engineering, cell physiology, automation, statistics, and modeling. Understanding the basic biological principles of "the science of scale" is an undertaking likely characterized as "off-mission" by corporate investors but perhaps well suited for national laboratories, especially those with existing flexible pilot scale fermentation facilities and supercomputing and modeling capabilities such as Berkeley Lab.

To fully realize the potential of biomanufacturing through the creation of robust engineering biology platforms, the development of measurement infrastructure is imperative. Standards, reference data, predictive models and other forms of biometrology will enable the types of predictability, specialization, interoperability, and reliability central to other manufacturing settings to fuel commerce from engineering biology. Berkeley Lab has engaged the National Institute of Standards and Technology (NIST) as a partner in its prototype biofoundry efforts, and appreciates that NIST's leadership in the development of standards and metrology for biomanufacturing and risk-assessment in evaluating new biotechnologies will help forge a responsible path forward.

I applaud the committee for its interest in the topic of engineering biology and believe that a vision for a strong long-term research and development program, including research in the ethical, environmental, and social aspects of engineering biology, is needed for the U.S. now that biology is at this critical inflection point. In the way that the 21st Century Nanotechnology Research and Development Act of 2003 provided for strong interdisciplinary nanotechnology research that included societal, ethical, and environmental concerns, the nation could similarly benefit from a research initiative that paves a path toward real-time technology assessment engaging in fundamental, problem-oriented research on the broad-ranging implications of these new engineering biology technologies. It is critical that research in this area explore responsible innovation and ways in which engineering biology research responds to, creates, and interacts with social and ethical issues. In addition, the provision for technical expertise to inform the development of guidelines and safeguards for new products, processes, and systems of engineering biology will lay a solid foundation on which to build a robust and responsible biomanufacturing future.

In conclusion, I would like to briefly raise the issue of America's competitive standing internationally in advancing engineering biology for national needs. Many countries such as the UK and other European nations have developed roadmaps that will guide their investment decisions in a coordinated and efficient manner. Also, in October of this year, over 60 science and technology ministers from around the world met in Korea to discuss the development of global science and technology innovations, and the resultant declaration invited the Organisation for Economic Co-operation and Development to explore innovation policy frameworks needed for the "next production revolution", a large part of which is expected to involve biomanufacturing solutions around the world. The federal government must help to ensure the nation's leadership in advanced biosciences by developing a more cohesive, coordinated and aggressive initiative. A focused and coordinated national engineering biology initiative would help drive U.S. leadership in biomanufacturing, enable new fundamental discoveries, deliver solutions to national challenges, and fuel the U.S. bioeconomy.

Thank you.

Dr. Mary Maxon is the Biosciences Principal Deputy at Lawrence Berkeley National Laboratory. Previously, she was Assistant Director for Biological Research at the White House Office of Science and Technology Policy (OSTP) in the Executive Office of the President where she was the principal author of The National Bioeconomy Blueprint. Before moving to OSTP, Dr. Maxon ran the Marine Microbiology Initiative at the Gordon and Betty Moore Foundation, which supports the application of state-of-the-art molecular approaches to the field of marine microbiology with the goal of developing comprehensive models to detect and validate environmentally-induced changes in marine microbial ecosystems. Prior to that, Dr. Maxon served as Deputy Vice Chair at the California Institute for Regenerative Medicine, where she researched and drafted intellectual property policies for California stem cell grantees in the non-profit and for-profit research sectors. Previously, she was Associate Director and Anti-infective Program Leader for Cytokinetics, a biotechnology company in South San Francisco. Her biotechnology experience also includes a position at Microbia, Inc., based in Cambridge, Massachusetts, where she contributed to the discovery and development of the Precision Engineering technology for production of commercial products from microorganisms using metabolic engineering. Dr. Maxon received her Ph.D. from the University of California, Berkeley in Molecular Cell Biology, and did postdoctoral research in biochemistry and genetics at the University of California, San Francisco.