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December 6, 2011

Mr. Ted Wackler
Deputy Chief of Staff
Office of Science and Technology Policy
The White House
Delivered to: *bioeconomy@ostp.gov*

Dear Mr. Wackler,

Thank you for the opportunity to share, on behalf of my colleagues in Life Technologies, our thoughts on the National Bioeconomy Blueprint. We commend you for undertaking this initiative and for highlighting the importance of the Bioeconomy.

Life Technologies (NASDAQ: LIFE) is a leading global biotechnology tools company dedicated to improving the human condition. Our products, including cutting-edge instruments such as high-throughput DNA sequencers, are used to make life-saving biomedical research breakthroughs, to advance personalized medicine and regenerative science, to enhance food and water safety, and to solve and prevent crime with 21st century forensics. Our company's history attests to the rapid growth and evolution of the Bioeconomy. Twenty years ago we were a small company focused almost exclusively on supporting and enabling biomedical research. Today, we have annual sales of nearly $3.5 billion, over 9000 employees, and thriving businesses applying our biological knowhow to criminal justice, energy, the environment, food safety, animal health, and more. A recent report from Battelle highlights the vast reach genomics is having across multiple industry sectors already, even though the genomics revolution has just begun.[1]

[1] Battelle Technology Partnership Practice, *Economic Impact of the Human Genome Project*, http://www.battelle.org/publications/humangenomeproject.pdf.

We would also like to recognize the efforts the Administration has already taken to support the Bioeconomy. Your unflagging support for the National Institutes of Health (NIH) and science funding generally has been instrumental to driving the Bioeconomy, and will only grow in importance during these difficult economic times. Your work to expand biology based efforts in other agencies and departments is forward-thinking and provides the seeds for further growth in the life sciences. And interesting and important projects like the NIH-DARPA effort to develop integrated microphysiological systems for drug efficacy and toxicity testing move the field forward, faster.

**Bioeconomy Barriers**

You asked for input on roadblocks to achieving the full potential of the Bioeconomy. Outdated regulatory frameworks and processes are a drag on the bioeconomy. One of the most important steps the Administration can take to propel this sector is to timely adapt the regulatory environment to technological evolution. Our experience is that the record to date is mixed. Three examples illustrate the point:

- **Regulatory Pathway for Next Generation Sequencing**. Research and clinical trials using Next Generation Sequencing (NGS) are already showing how powerful the tool could be in human health care.[2] The Food and Drug Administration (FDA) has been working effectively with

[2] Matthew N. Bainbridge et al, "Whole-Genome Sequencing for Optimized Patient Management," *Science Translational Medicine* 3, no. 87 (2011), 1-6.

"Results of First Whole-Genome Sequencing Clinical Trial for Triple-Negative Breast Cancer Patients Will Be Presented at 2011 CTRC-AACR San Antonio Breast Cancer Symposium," *Life Technologies*, 1 December 2011, http://www.lifetechnologies.com/us/en/home/about-us/news-gallery/press-releases/2011/results-of-first-whole-geome-sequecig-cliical-trial-for-triple-e.html.

stakeholders and providers of NGS systems to understand the technology and to shape a nimble regulatory pathway that will allow disparate and rapidly evolving systems to be cleared in a timely way. Such a pathway is absolutely essential if NGS is to reach its scientific and economic potential, and the effort to date is to be commended.

FDA is taking steps toward elucidating that pathway by working closely with industry to identify a set of standards, methods, and quality metrics that both industry and end-users could access. Standardized, well characterized reference materials and methods for validation are critical. There are existing reference standards and collections within government, such as the Genetic Testing Reference Materials Coordination Program (or GeT-RM) at CDC, and the Standard Reference Materials held by NIST, as well as reference materials and controls provided or certified by CAP and other stakeholder groups. Recommendations for validation are being written by organizations like the Clinical Laboratories Standards Institutes, the Association for Molecular Pathology and others. FDA would be well-served to build on this knowledge base rather than constructing a collection and set of methods from scratch. Finally, a platform-independent clinical grade variant database would complete the collection and advance the field.

- **Draft FDA Guidance on Research Use Only/Investigational Use Only (RUO/IUO) products.** While much of this June 2011 draft guidance is non-controversial, there are provisions in it that would impose inappropriate and burdensome requirements on manufacturers of RUO/IUO products. Full enforcement of this draft guidance will cut off the supply of equipment and reagents used in many Laboratory Developed Tests, jeopardizing patient access to newborn metabolic screening and various personalized medicine diagnostics. Despite concerns raised in formal comments to the FDA by hospitals, universities,

manufacturers, patients, public health labs, and others that provisions of the guidance are dangerous, on questionable legal ground, and unwarranted by any evidence of harm, the FDA has signaled its intention to proceed to final guidance with few if any changes. The result is a drag on innovation with no obvious public or private benefit. The imposition of these onerous new requirements through a Q&A style draft guidance document that contains novel legal frameworks, in violation of FDA's own Good Guidance Practices, adds to stakeholders' frustration. This guidance should be significantly revised.

- **Veterinary Biologics.** In the veterinary biologics arena, an outdated USDA post-market batch release authorization process for USDA-CVB licensed veterinary diagnostic test kits causes significant delays and unnecessary expense. Currently, USDA's Center for Veterinary Biologics (CVB) requires that two kits from every serial that may be selected for testing must be sent in, and that two kits from every marketed serial that may be called upon during CVB investigations be retained. A batch cannot be released until CVB provides a release authorization, which can take one to three weeks. Instead, CVB should rely on manufacturer quality systems to ensure that nonconforming product does not enter into commerce. This can be done via records review during periodic inspections, as is done for many products regulated by USDA and FDA. Serious violations could result in CVB pulling a firm's license, which should ensure compliance with quality systems. CVB could and should place the burden on manufacturer quality systems not to release nonconforming product, rather than conducting the testing itself.

There are other basic ways in which our joint potential is constrained. The terms and conditions of grant programs that seek private sector participation are often a deterrent to commercial participation. For example, recently the Department of Energy (DOE) released a solicitation seeking ideas and

projects for deploying green manufacturing processes. We had an idea for replacing a toxic solvent in our processes with a plant-based one. Unfortunately, under the (common) terms of the RFP, applicants were required to provide indirect cost and fringe benefit data that we either do not keep or are not able to make public. As a result, we did not participate. The bioeconomy is filled with companies unaccustomed to government contracting and without government accounting infrastructures. Basic grant program terms can cause companies to withdraw from public private partnerships and otherwise attractive grant programs. An awareness of this type of potential structural impediment when developing programs could generate increased private participation.

**Research Priorities**

With respect to research priorities, we encourage the Administration to continue its strong support for the NIH. A recent report from United for Medical Research quantifies the enormous impact NIH funding has on US employment and on the international competitiveness of the US medical innovation industry.[3] As described below, two other research areas that can provide a lift to the bioeconomy include synthetic biology and the application of genomics to public health.

**Synthetic Biology.** Using bioengineering to design living systems holds the promise of new health care and alternative energy products, as well as the creation of new research tools. Synthetic biology research takes place in many agencies and departments within the federal government. A cross-agency and coordinated research agenda, developed in consultation with the private sector, would support advances in synthetic biology and ensure progress.

[3] Everett Ehrlich, *An Economic Engine: NIH Research, Employment, and the Future of the Medical Innovation Sector*, http://www.unitedformedicalresearch.com/wp-content/uploads/2011/08/UMR_An-Economic-Engine.pdf.

Development, validation and categorization of tools for scaled DNA construction and engineering will make the essential suite of parts and technologies available “off the shelf,” including new model organisms, chemistries, and genomics. Identification and characterization of novel hosts and properties could be followed by methods to grow and manipulate hosts more effectively and characterize their metabolism in detail.

A large stable of synthetic biology parts will require naming conventions to form a metagenomic "catalogue" of tools. Validated methods and standards for characterization, annotation, homology and domain criteria will support collaboration and comparability while reducing confusion as will development of software for genetic circuit design and function, as well as chassis context design and modeling. This working parts library could then be extended from model organisms into hosts of industrial importance.

Finally, increased computational abilities are critical for the development of synthetic biology. “In silico” capabilities, such as development of CAD and simulation software tools for genetic circuit design and function and computational methods for de novo parts design will enable bottom up de novo genome/organism design. While the private sector intends to fully participate in these efforts, government support, coordination and partnership will enable the field to progress rapidly.

**Genomics and Public Health.** As high throughput nucleic acid sequencing becomes more powerful and less expensive, it can be used in a wider range of applications to answer questions previously out of reach. We propose two broad applications of genomic technologies be prioritized to address the important impact of microbes on human health and disease.

According to data from the Centers for Disease Control and Prevention (CDC), food-borne illness costs the United States $150 billion per year – a major challenge to public health. Preventing outbreaks, or even shortening their duration and spread will have a significant impact on the cost of food-borne illness in terms of lives as well as dollars. Next generation sequencing can be used in the context of food safety or other pathogenic outbreaks as a complement to conventional epidemiology. This use of "genetic epidemiology" allows for rapid, more specific and detailed tracking and tracing of the cause of outbreaks, and is a powerful tool in investigations.

NGS facilitates whole genome typing by interrogating every base in a microbial or viral genome. This fine-scale characterization can lead to rapid, single base resolution strain tracking, leading to more sensitive detection of outbreak clusters, especially when caused by common PFGE types or serotypes. NGS also facilitates rapid development of outbreak-strain specific detection assays that can be immediately deployed for clinical, food, or environmental testing. For example, sequencing of the recent German *E. coli* O104:H4 outbreak strain with the semiconductor-based Ion Torrent system led to the rapid identification of strain-specific TaqMan assays. The declining cost and increasing power of whole genome sequencing is rapidly reaching a point where a full sequence could augment or replace PFGE fingerprinting as the primary typing method in PulseNet.

In order for NGS to become accepted as a method for routine microbial epidemiology studies, the instruments and methods need to undergo rigorous validation and standardization. This will include the development of methods and analyses that are compatible with existing typing schemes (e.g., PFGE and MLST). Similarly, there will need to be standardized methods for interpretation and reporting so that results from disparate local sites can be efficiently conglomerated at the CDC. Improved communications and

resources between CDC, FDA, and USDA on food safety will assist not only conventional epidemiology, but also the new "genetic epidemiology."

Life Technologies is pleased to be a leader in the Bioeconomy. We thank the Administration for its interest in and commitment to these issues, and we look forward to working with you.

Sincerely,

Mark Stevenson

Cc: Janet Lambert