To:
Dr. John P. Holdren
Director, Office of Science and Technology Policy
Executive Office of the President
725 17th Street NW, Room 5228
Washington, DC 20502

Submitted Through: bioeconomy@ostp.gov

From: Claude R. Canizares
Vice President for Research and Associate Provost, Massachusetts Institute of Technology (MIT)

Date: Dec 6, 2011

Subject: Recommendations Concerning Bioeconomy Blueprint; Request for Information

Dear Dr. Holdren:

I am writing in response to the Office of Science and Technology Policy's (OSTP) October 7, 2011 Request for Information (RFI) regarding the development of a National Bioeconomy Blueprint.

We very much welcome the opportunity to comment on the bioeconomy framework. We believe key to this idea is convergence, or the merging of the life and physical sciences with engineering, as a superstructure to support the next stage of advance in a host of areas. This response will focus on the portion of the bioeconomy blueprint related to the future of biomedical research and the opportunities lingering at the intersection of existing efforts.

Background

Leading MIT researchers recently published a white paper entitled, "The Third Revolution: The Convergence of the Life Sciences, Physical Sciences, and Engineering (2011)," which outlines the way forward for biomedical research.[1] This white paper builds on the National Academies report, "A New Biology for the 21st Century: Ensuring the United States Leads the Coming Biology Revolution (2009)."[2] This effort is also strengthened by additional reports including a recent Food and Drug Administration (FDA) report, "Driving Biomedical Innovation: Initiatives for Improving Products for Patients (2011)"[3] and the recently released National Academies

[1] The MIT paper is available online at http://web.mit.edu/dc/Policy/MIT%20White%20Paper%20on%20Convergence.pdf
[2] The past NAS report is available online at http://dels.nas.edu/Report/Biology-21st/12764
[3] The FDA report is available online at: http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/ucm274333.htm

report, "Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease (2011)."[4]

As MIT Professors Phillip Sharp and Robert Langer explain in the July 2011 *Science* article[5] outlining the convergence framework:

> The next challenge for biomedical research will be to solve problems of highly complex and integrated biological systems within the human body. Predictive models of these systems in either normal or disease states are beyond the capability of current knowledge and technology…there is an increasing need to merge expertise that goes beyond the interdisciplinary intersection of fields to the emergence of new disciplines. In recent decades there have been two biomedical revolutions: molecular biology and genomics. We believe the convergence of fields represents a third revolution (1, 2), where multidisciplinary thinking and analysis will permit the emergence of new scientific principles and where engineers and physical scientists are equal partners with biologists and clinicians in addressing many of the new medical challenges….[C]onvergence will be key to advances in many crucial areas, such as using microfabrication to analyze single cells, the development of targeted nanoparticle therapeutics, the integration of large data sets to create personalized medicine at the bedside and microsensors that can detect the onset of disease.

We envision convergence as an organizing framework for understanding pathways to move forward through a bioeconomy blueprint.

Section 1: Grand Challenges

As you know, the current state of medicine is such that costs are high and biomedical investment is not perceived to be lowering those costs. On top of that, we are facing the demise of blockbuster drugs. Despite the genomics revolution, medicine is still intrusive and not specifically targeted. Given the reality that the U.S. spends a larger portion of its gross domestic product (GDP) on health care than any other industrialized country; that a quarter of the Medicare budget is spent in the last year of life; and that, relative to GDP, the total U.S. investment in research and development (R&D) is falling in comparison to emerging global leaders, we have to change the paradigm for biomedical research to help reverse these trends.

In accordance with changing the paradigm for biomedical research and in keeping with the grand challenges identified by President Obama, (including smart anti-cancer therapeutics, early detection of disease from saliva samples, and advanced regenerative medicine for organ transplants), we propose one grand challenge with several short term challenges within.

The grand challenge we suggest tackling is to replace symptomatic disease with prediction of disease.

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[4] The recent NAS report is available online at: http://dels.nas.edu/Report/Toward-Precision-Medicine-Building-Knowledge/13284

[5] Phillip A. Sharp and Robert Langer, "Promoting Convergence in Biomedical Science," Science 29 July 2011: Vol. 333 no. 6042 p. 527. This article is available online at http://www.sciencemag.org/content/333/6042/527.short

Prediction of disease would allow treatment before disease symptoms manifest to the patient. Based on this model, individuals would be scanned for diseases continually and treated at the first cellular indication, before the onset of manifested symptoms. This idea takes the concept of prevention to a new and more active stage.

This would require an integration of data into models of disease states that have predictive value at the level of an individual. In order to address this challenge, we need to advance the science of normal and disease states, integrating medical records, genomic data, understanding of the systematic structure of cellular processes, and environmental and clinical data from individuals to create models to predict disease states as well as their prevention or treatment.

In addition to related technology advance, three areas in which to begin this work are briefly outlined below.[6]

- **The Single Cellome.** We should focus on what we don't know. Start with enhancing current understanding of health and disease by complete understanding of the healthy and diseased cell and its components as well as how it reacts to its environment.

- **The Human Phenome Project.** We need to get ahead of disease. Change the medical paradigm to less physically intrusive, continuity-inspired medicine. This will include high throughput parallel analysis at multiple stages including imaging methods that detect metabolism at the level of individual cells.

- **Living Laboratories**. The current animal models are insufficient to enable to next stage of advance. We need to develop effective methods of analyzing human systems. This includes the development of sophisticated human tissue, even whole organ systems, to characterize normal and disease processes.

While academics and practitioners work towards these advances, there are concrete steps government can take to help achieve this goal. Several recommendations are outlined below.[7]

<u>Recommendations: The Federal Role</u>

- **Establish a biomedical innovation culture within government based on the convergence framework.** Scientific research has historically been funded in separate stovepipes by science-mission agencies. Mechanisms to enable and foster better connections need to be institutionalized. One option is to establish think-tank environments within each research agency where agency detailees from across the executive branch could be invited to visit and collaborate on the research priorities of the host institution. This might be initially be coordinated by the National Science and Technology Council (NSTC).

[6] These concepts were outlined during a daylong convergence workshop at MIT on September 30, 2011 that included representatives from academia and industry, as well as agency leaders and Boston-area clinicians.
[7] These recommendations have been adapted from a selection of recommendations included in the MIT White Paper, "The Third Revolution: The Convergence of the Life Sciences, Physical Sciences, and Engineering." That paper is available online at http://web.mit.edu/dc/Policy/MIT%20White%20Paper%20on%20Convergence.pdf

- **Support a diverse portfolio of federal government investment.** Individual investigator grants for smaller projects are a time-honored, respected tradition. Small projects often lead to innovation and new discoveries, and support for them should continue. At the same time, it is vital to also direct resources to large-scale projects that include multiple principal investigators. These undertakings allow researchers from many disciplines to conduct systematic inquiries into general target areas while pursuing their own specific interests.

  Since collaboration and innovation in research methods are more difficult if individual researchers are isolated in separate departments at their institutions, we suggest the founding of centers at institutions across the country that would include multiple principal investigators. A group of agency and academic experts should convene and use a systems approach to design these centers around national research priorities.

- **Educate, expand, and support the next generation of researchers based on the convergence model.** Universities increasingly understand that the merger of scientific and engineering fields is a reality for the successful future of the life science enterprise. New efforts need to be undertaken to educate the next generation of researchers to work in cross-disciplinary fields. While a deep disciplinary background remains vital, including a robust cross-disciplinary education is essential additional preparation for our future scientists. A promising example of a program that currently enables such collaborative learning, and that can encompass convergence approaches, is the National Institutes of Health (NIH) Training Grant. We recommend that the training grant model be expanded and also utilized at other agencies.

  In addition, we must strengthen the pipeline of future researchers by addressing the diversity problem in our educational system. To that end, careful consideration should be given to the recommendations contained in two recent studies, including the 2009 report by the Council on Graduate Schools (CGS), "Broadening Participation in Graduate Education,"[8] and the 2010 report, "Gender Differences at Critical Transitions in the Careers of Science, Engineering, and Mathematics Faculty"[9] released by the National Academies.

Section II: Research and Development

The ambitious goal, as described in the previous section, of bringing an end to symptomatic disease would require the scientific community to unite across existing siloes and examine the promise lingering at the intersections of current efforts. Such a battle cry could offer momentum to a coordinated cross-agency effort that would move national competencies and capabilities closer to realizing the promises made for the genomics era and the era of personalized medicine.

We would recommend that the Office of Science and Technology Policy (OSTP) convene a cross-agency working group through the National Science and Technology Council (NSTC)

[8] More information about the CGS report is available online at http://www.cgsnet.org/default.aspx?tabid=365
[9] The NAS report is available online at http://www.nap.edu/catalog.php?record_id=12062

mechanism to take steps towards such a goal.

Section III: Moving Life Sciences Breakthroughs From Lab to Market

One of the aspects of technology commercialization that the Office of Science and Technology Policy (OSTP) should consider in its bioeconomy effort involves enhancing and overcoming impediments to university technology transfer. In response to the National Economic Council and Office of Science and Technology Policy's March 25, 2010 Request for Information (RFI) on Commercialization of University Research, Dr. Susan Hockfield, MIT President, offered a detailed explanation of the MIT innovation ecosystem with specific recommendations for broad application of this successful model.[10] The recommendations discussed below draw on those proposals.

Recommendations: Fostering Commercialization through the University Innovation Ecosystem

The following recommendations for government action would enhance the impact of federally funded research and improve the process of transferring research in the lab to commercialization by the private economy.

- **Implement Model Innovation Centers.** Implement additional pilot model innovation centers across the U.S. at research universities to develop, document, and assist in nationwide dissemination of "best practices" for encouraging innovation and entrepreneurship by students, faculty, staff and alumni. This could include expansion of the new National Science Foundation (NSF) I-Corps effort, but additional models as well. The pilot centers, for example, could more closely draw on MIT's Deshpande Center approach of close proximity between researchers and advisors. They would engage in a variety of activities including connecting university researchers with technologies of potential commercial value to industry and capital; educating and mentoring; business plan preparation; creating ties to regional businesses; and providing grants or seed money. These centers would also disseminate best practices and form the nucleus of a community amongst U.S. universities enhancing innovation.

- **Support On-Campus Mentoring Services.** Support expansion and escalation of mentoring services based on the proven MIT Venture Mentoring Service model at research universities across the U.S. Additionally, support formation of an Innovation Mentoring Consortium that would enable the sharing of knowledge, experiences, and best practices amongst mentoring organizations to enhance effectiveness and further increase innovation output.

- **Add Technology Transfer Costs to Indirect Cost Pool**. Many schools, particularly in the current economic climate, lack funding to build a patent portfolio and employ well-trained staff to create successful technology transfer offices. Many existing offices are now facing cutbacks. Allowing technology transfer costs (e.g., patents and staff) to be included in the indirect cost pool for federally funded research (and perhaps excluded

[10] Please refer to the full comments, "Recommendations Concerning Commercialization of University Research; Request for Information - May 26, 2010," online at http://web.mit.edu/dc/policy.html

from the administrative cost cap) could provide schools with the resources to bolster and build their Technology Licensing Office (TLO) programs.

At the same time, federal programs (including at the National Institutes of Health, Departments of Energy and Agriculture) are increasingly asking for "matching funds" or cost sharing from non-profit universities for infrastructure and applied research. This is a very detrimental move in the wrong direction, and these cost-sharing policies should be reversed. University funding streams, unlike those in the private sector, do not have a profit pool that could be allocated to such sharing.

- **Promote Policies that Encourage Entrepreneurship**. Encourage government and universities to examine their rules and regulations to eliminate barriers to responsible faculty/staff entrepreneurship. Medical schools and teaching hospitals have high potential for entrepreneurship that could benefit society broadly, while also contributing to economic growth, consistent with high standards of integrity. In those institutions, policies that strongly promote openness of relationships, appropriately overseen by senior faculty committees, can ameliorate the potential problems that arise from the needed medical faculty connections to biomedical industry.

- **Host Technology Innovation Fairs**. Federal R&D agencies involved in bio-medical research should cooperatively consider holding joint annual technology innovation fairs that bring groups of outstanding university inventors together with supporting government agencies, companies, venture capital (VC) firms, and financial institutions in emerging technology sectors. The recent Advanced Research Projects Agency – Energy (ARPA-E) Energy Innovation Summit could provide a very useful model.[11]

- **Support Small Firm/University Collaborations**. Encourage research agencies, where appropriate, to adopt the Defense Advanced Research Projects Agency (DARPA)-hybrid model for a portion of their funding as part of their research and development (R&D) portfolios. This approach provides awards for collaborative efforts involving small firms and university researchers. This would be especially useful at the National Institutes of Health (NIH); the proposed National Center for Advancing Translational Sciences (NCATS) could pilot this approach there.

- **Examine How to Attract More Venture Capital Investment.** While this Request for Information (RFI) is seeking solutions that fill in the gaps of venture funding and finance, and alternatives to them, there is much more we need to understand about capital availability in this sector. Accordingly, there is a need to conduct an in depth data-based examination of the factors that induce Venture Capital firms (VCs) to invest in early-stage technologies, and the structure and stability of that funding. Typically, for example, VCs only invest in physical-science-based technologies when they are near commercialization, yet life science advances will increasingly need to rely on engineering physical science developments and longer term funding may be required for these. They invest in relatively fewer startups during economic downturns creating significant

[11] Further information on the ARPA- E Energy Innovation Summit is online at http://www.ct-si.org/events/EnergyInnovation/

instability; we need to consider what factors are leading to these decreases in VC investment rates. If these issues are studied and better understood incentive systems could be devised to influence these trends.

- **Encourage SBA Investment in New Technology Startups.** Examine the policies of the Small Business Administration (SBA) to be sure that adequate emphasis is placed upon new businesses with high growth potential (i.e., "gazelles"). In particular, there should be an explicit focus in agencies' administration of the Small Business Innovation Research (SBIR) Program for new technology startups and new business recipients that will accelerate technology implementation.

- **Enhance and Add Tax Credit Programs to Encourage Technology Transfer.** In addition to improving some of the structural problems in the research and development (R&D) tax credit and making it permanent, provide additional credit for funding for collaborations between industry and university researchers to accelerate technology transfer. This is available now for energy technologies and should be extended more broadly, including to bio-medical research firms. Also consider dropping the incremental feature of the current credit, so it rewards significant, sustained R&D investments by firms. We refer you to work completed by the Information Technology & Innovation Foundation (ITIF) on this subject, including a recent overall report, "Expanding the Research and Development Tax Credit to Drive Innovation, Competitiveness and Prosperity."[12]

- **Provide Post-Degree Visas**. Foreign-born immigrants have an unusually strong record of starting firms and bolstering our science talent base. This has long been an historic competitive advantage for the U.S. that few nations have been able to match. We rely heavily on foreign-born post docs in the health science area, in particular, and also offer graduate education to many from abroad. These are important talent pools we should encourage to stay in the U.S. In order to preserve this strength, the U.S. should award five-year, post-degree visas to all foreign students in accredited university programs in STEM and management fields. These special visas should be converted easily into green cards, and their holders fast-tracked to U.S. citizenship if they continue employment in U.S. science and technology-based research and enterprises, or if they start their own U.S.-based companies.

Section IV: Workforce Development

We applaud the President's efforts on workforce development with community colleges earlier this year with his announcement of the expansion of the Skills for American's Future Initiative. We agree that industry partnerships with community colleges across the country can build a nation-wide network that could maximize workforce development strategies, job training programs, and job placements. As part of that effort, we also applaud the launch by the Manufacturing Institute, the affiliated non-profit of the National Association of Manufacture

[12] The ITIF report is available online at http://www.itif.org/publications/expanding-research-and-development-tax-credit-drive-innovation-competitiveness-and-pros

(NAM) of a certification program between industry and community colleges.[13] In the biomedical field, production remains a significant portion of pharmaceutical and device costs; community college certification developed in coordination with biopharma firms for skills needed in this sector could be an important effort.

Section V: Reducing Regulatory Barriers to the Bioeconomy

MIT views the regulatory science effort underway at the Food and Drug Administration (FDA) as critical to improving regulatory delays and barriers for drug and device approvals.

Concerning university research, there are two specific areas of regulatory burden that continue to affect efforts to participate in what is described as the bioeconomy. These include agency and university shared research expenses via the ongoing A-21 discussion, as well as conflict of interest regulations as most recently exemplified by the National Institutes of Health (NIH) regulations on this issue.

Regarding specific recommendations, we refer you to the comments on A-21 submitted in July 2011 by the Association of American Universities (AAU) to the A-21 Task Force of the National Science and Technology Council (NSTC).[14] Regarding the conflicts of interest issues, we refer you to the ongoing work of the Council on Governmental Relations (COGR), and specifically to the document COGR prepared in response to the NIH proposed regulations in 2010.[15]

Section VI: Public-Private Partnerships

The highest impact opportunities for public-private partnerships related to the bioeconomy revolve around data. Applying the convergence framework to shared pools of existing data would revolutionize the capacity and scope of biomedical research. For instance, it would enable progress in validating surrogate markers, advancing predictive toxicology, and identifying and validating predictive clinical biomarkers (genetic and other) of response. Enriched data sets would also advance efforts to map established outcomes to observational, clinical, and lab data, and to learn about disease sub-types from data.

Regarding specific improvements in the regulatory process for drugs, diagnostics, and devices, the NEW Drug Development ParaDIGmS (NEWDIGS) program at MIT is working towards leveraging drug data to deepen collective understanding of progressive or adaptive licensing approaches through retrospective simulations. Given further access to the pool of data held by federal agencies, MIT researchers would seek to simulate adaptive licensing designs on historical cases of drug development to understand impact on time, risk of late stage attrition due to safety issues, economics and public health impact. This effort would be unique since the simulation would include all key stakeholders to understand perspectives of regulators, pharmaceutical companies, payers, providers, patients, and public health personnel.

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[13] More information available online at http://www.whitehouse.gov/the-press-office/2011/06/08/president-obama-and-skills-americas-future-partners-announce-initiatives

[14] The AAU A-21 Task Force letter is available online at http://www.aau.edu/WorkArea/DownloadAsset.aspx?id=12432

[15] The COGR response to the NIH Conflict of Interest Regulations is available online at http://www.nacua.org/documents/COGR_Comments_NIH_COI_ProposedRule.pdf

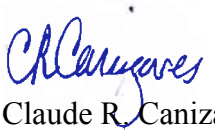
In addition, since manufacturing and clinical outcomes are currently completely siloed, the MIT Biomanufacturing (BioMAN) Program at the MIT Center for Biomedical Innovation (CBI) would be interested in understanding the relationship between outcomes data in clinical trials (safety, efficacy, immunogenicity) to manufacturing process information.

These shared pools of data would drive advancements in ongoing research and would also enable important new questions to be explored. However, a public-private process with access to university expertise is the only way this data will get unlocked and become truly accessible for research. The federal government could play a key role both as a convener of public/private interests and as a leader in unlocking access to data across federal agencies.

In closing, I want to express MIT's appreciation for the recognition and efforts of the Office of Science and Technology Policy (OSTP) to help frame research as an economic driver. As explained in the introduction, we believe the bioeconomy blueprint efforts correspond closely with efforts underway at the National Academies (NAS), National Institutes of Health (NIH), and the Food and Drug Administration (FDA) and among a growing number of universities across the country manifesting their own version of the convergence model. This culmination of these efforts indicates that we are at an inflection point for life science research that, if navigated correctly, could encompass new fields of knowledge and yield revolutionary advances in a wide array of areas.

I hope you find this submission useful in developing the National Bioeconomy Blueprint. MIT's faculty and staff stand ready to assist you as you move forward in these efforts. If your offices have any follow up questions, please contact Amanda J. Arnold in MIT's Washington, DC Office at [redacted]

Sincerely yours,



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