Response to Request for Information on the Biotechnology and Biomanufacturing Initiative

From: Maria Zuber, Vice President for Research, Massachusetts Institute of Technology
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MIT appreciates the opportunity to respond to the Request for Information (RFI) on the National Biotechnology and Biomanufacturing Initiative (NBBI). We think the general approach we lay out below is relevant to many of the specific questions raised in the RFI.

We should start by noting that two MIT faculty played key roles in drafting the recently released report from the President's Council of Advisors on Science and Technology (PCAST), *Biomanufacturing to Advance the Bioeconomy*, and we assume that the report will help guide the Administration's work in this area.

While there are many approaches that can contribute to the growth of the bioeconomy, we want to focus on one that is broad and may be overlooked — what we call "Convergence."

By Convergence we mean the integration of engineering, the physical sciences, computation, artificial intelligence, and the life sciences, which has the potential to create advances in broad areas of the economy, including medicine, energy, and agriculture. Examples of technologies that could result from Convergence include virus-built batteries, protein-based water filters, cancer-treating nanoparticles, mind-reading bionic limbs, and computer-engineered crops. Convergence can lead to a wider range of products and more economic growth than life sciences or traditional biotechnology could by themselves.

Below are some ways the federal government could institutionalize a Convergence approach.

ARPA-H. The Advanced Research Projects Agency – Health (ARPA-H) should become a model for taking the Convergence approach. One reason ARPA-H was needed is that the National Institutes of Health, despite its many strengths, is siloed in a way that causes cross-disciplinary and novel proposals to be undervalued.

The bioeconomy has much to gain from an ARPA approach to biomedicine and biotechnology – an approach that emphasizes a focus on the solution of specific problems, a team-based approach, linkages between engineering and science, risk-taking, milestones designed to enable projects to fail quickly or advance, and partnerships between academia and industry.

NSF. The Directorate for Technology, Innovation, and Partnerships (TIP) at the National Science Foundation (NSF) should also promote a Convergence approach. TIP was created, in part, to foster problem-based, use-inspired fundamental research that crosses disciplinary lines to address national issues. TIP can carry out that mission both through existing programs like its Convergence Accelerator and through new ones that could create centers that would bring together researchers across disciplines to conduct fundamental, use-inspired research to solve specific problems.

NIST. The National Institute of Standards and Technology (NIST) should also play a key role in creating the bioeconomy, especially given its expertise in manufacturing and in working with industry. Among other activities, it could help develop standards and biomanufacturing protocols. The Manufacturing Extension Partnerships and ManufacturingUSA Centers can help disseminate information to improve biomanufacturing and other aspects of the bioeconomy.

Cross-Agency Collaboration. A number of federal agencies – not limited to those discussed above – run programs that could help create a thriving bioeconomy. They need to work together in a coordinated fashion. This should mean that agencies truly work together to plan an overall program and decide how each can contribute; it should not mean just stapling together individual agency budgets and program plans that have been developed separately.

Research related to the bioeconomy and research coordination would be enhanced by implementing the bioeconomy R&D sections of the "CHIPS and Science Act" (Division B, Title IV, P.L. 117-167). In particular, the creation of an interagency committee to collectively oversee the planning, management, and coordination of the NBBI could improve coordination among bioeconomy-relevant agencies. Research would, of course, also be enhanced by fully funding the research spending authorized in "CHIPS and Science."

Education. If Convergence is to become a widespread approach to research and problem-solving, it needs to be inculcated during schooling. Federal support of graduate students should encourage and support cross-disciplinary work. Some federal fellowships and traineeships could be devoted exclusively to backing cross-disciplinary research. Federal agencies like NSF could fund efforts to develop undergraduate curricula that emphasizes Convergence, while still giving students solid grounding in disciplines.

We also encourage ARPA-H to develop programs to assist graduate students and to expose them to the cross-disciplinary research we hope the agency will fund. In general, funding from agencies using the ARPA model has not been ideal for supporting graduate students because of the high-risk milestones. ARPA-H should develop programs to help graduate students that are not overly tied to individual research projects.

Technology Transfer. University research can help create a bioeconomy only if discoveries and innovations make it out of the lab and into widespread use. The federal government can encourage technology transfer, the development of incubators, the development and sharing of business expertise, and the availability of patient capital – all of which are needed to successful spin-out university advances.

One tool for this that the government has not yet funded are the grants that were authorized under Secs. 10389, 10391 and 10392 of the "CHIPS and Science Act." Funds under Sec. 10391 might, for example, help other schools or consortia of schools undertake the planning needed to create entities like The Engine, the incubator and funder of "tough tech" – including bioeconomy companies – that MIT created as an independent entity.

Partnerships. In working to enable more regions to become bioeconomy hubs, the federal government should encourage partnerships with universities and other entities that have already demonstrated an ability to foster the bioeconomy. Those partnerships can bring together entities from different regions.

Biomanufacturing Examples. Modular, small-footprint biomanufacturing systems are an emerging technology that could strengthen the robustness of the manufacturing capacity in the U.S. for reagents, diagnostics, biologic medicines, or food alternatives. Such automated solutions for production could also create jobs for manufacturing in regions where limited capacity presently exists, and for individuals with diverse types and levels of education.

(MIT has demonstrated a fully automated end-to-end prototype for generating biopharmaceutical drug substances and vaccine candidates with support from the Defense Advanced Research Projects Agency and the Gates Foundation. A women-owned and operated start-up company Sunflower Therapeutics is advancing this concept to commercial use. One Sunflower system has the capacity to produce the annual supply of insulin for South Dakota as an example.)

Regional facilities outfitted with different types of small-footprint manufacturing technologies (small molecules, RNA, proteins, cells) throughout the country could provide manufacturing centers for innovation in local ecosystems for new bio-enabled products and a "warm" manufacturing base for pandemic readiness.

Another example. A critical raw material for many products needed for alternative foods, medicines, and diagnostic applications is proteins. Total protein production for these classes of products may require as much as 1,000-fold greater volume, while spanning exceptional diversity in types of proteins (for example, milk, beef replacements, vaccine components, cell therapy reagents). Efficient synthesis of complex proteins remains difficult for such diversity and underlying strains appropriate for manufacturing are not widely available for broad innovation by the research community. (MIT has started the Alternative Host Research Consortium as one community to develop the science for protein production and new biology that provide a starting point for further development of products and manufacturing uses.)

Additional recommendations to promote Convergence research and hasten bioeconomic growth, can be found in *Convergence: The Future of Health*, a 2016 MIT report that still has relevant insights. It was co-chaired by Phillip Sharp, Susan Hockfield, and Tyler Jacks and drew on ideas from dozens of researchers from over 30 academic and federal institutions. The report is available at www.ConvergenceRevolution.net.