MITRE's Response to the OSTP RFI Supporting the National Biotechnology and Biomanufacturing Initiative

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About MITRE

MITRE is a not-for-profit company that works in the public interest to tackle difficult problems that challenge the safety, stability, security, and well-being of our nation. We operate multiple federally funded research and development centers (FFRDCs), participate in public-private partnerships across national security and civilian agency missions, and maintain an independent technology research program in areas such as artificial intelligence, intuitive data science, quantum information science, health informatics, policy and economic expertise, trustworthy autonomy, cyber threat sharing, and cyber resilience. MITRE's 9,000-plus employees work in the public interest to solve problems for a safer world, with scientific integrity being fundamental to our existence. We are prohibited from lobbying, do not develop or sell products, have no owners or shareholders, and do not compete with industry. Our multidisciplinary teams (including engineers, scientists, data analysts, organizational change specialists, policy professionals, and more) are thus free to assess and analyze complex challenges from all angles, with no political or commercial pressures to influence our decision-making, technical findings, or policy recommendations.

MITRE has broad expertise in the life sciences, including biotechnology, immunology, infectious disease, microbiology, epidemiology, biology, and biomedical engineering, which it uses to provide subject matter expertise and technical awareness of emerging biotechnologies to numerous federal agency sponsors. This includes horizon scanning, technology assessments, and test and evaluation to rapidly identify, develop, and mature emerging biotechnologies, with the goal of improving military, economic, and global health security.

Introduction and Overarching Recommendations

In the past 10 years, the pace of innovation within and industrialization of the bioeconomy has increased substantially.[1] Driven by market opportunities and global crises (such as the COVID-19 pandemic), technologies that enable the use of biology to address a broad range of industrial applications have accelerated from basic academic research to full scale industrial manufacturing.[2] The continued development and industrialization of the bioeconomy will have tremendous impacts in areas such as human health, manufacturing, the environment, and agriculture.[3]

[1] Safeguarding the Bioeconomy. 2020. National Academies Press, https://pubmed.ncbi.nlm.nih.gov/32352690/. Last accessed January 18, 2023.

[2] A. Hunger, et al. When biosecurity is the mission, the bioeconomy must become government's strategic partner. 2022. Center for Strategic and International Studies, https://www.csis.org/analysis/when-biosecurity-mission-bioeconomy-must-become-governments-strategic-partner. Last accessed January 18, 2023.

[3] J. Dileo, et al. Maintaining U.S. Leadership in Advanced Biotechnology & Growing the Bioeconomy. 2022. MITRE, https://www.mitre.org/sites/default/files/2022-05/pr-22-00151-01-maintaining-us-leadership-in-advanced-biotechnology-growing-the-bioeconomy.pdf.

With these advances come global competition (such as with China)[4,5] and new biological threats that will necessitate intentional policy and investment to secure the bioeconomy and protect US geopolitical interests. Failure to win this international competition can harm U.S. security interests by (1) decreasing leadership and preeminence in the bioeconomy, which undermines U.S. economic competitiveness, and (2) increasing dependency on foreign supply chains due to lack of industrial base capability and capacity, which undermines U.S. health system operations and resilience to transnational threats or crises.

This biodefense mission offers a potent use case for the bioeconomy as it exists at the intersection of national, economic and health security. It is imperative that the U.S. assess, promote and protect biotechnology elements as critical infrastructure, including its facilities, supply chains and trained workforce. We therefore recommend that the administration consider including biomanufacturing within the Department of Homeland Security's Critical Manufacturing Sector supporting Presidential Policy Directive 21, and "Supply Active Pharmaceutical Ingredients and Biological Precursors" should be designated as a National Critical Function. Doing so refines and clarifies roles and expectations for all entities working to protect biomanufacturing assets.

The ongoing response to COVID-19 clearly demonstrates the criticality of this sector and the imperative to both **innovate and industrialize** capability and capacities, avoid strategic dependencies, and retain a leadership role in global health security. MITRE, working in collaboration with leaders from government, industry, and academia, has previously analyzed the biopreparedness industrial base and proposed a comprehensive set of recommendations as well as developed a ten-point action plan.[6,7] This work and these documents provide the foundation to our answers in this RFI response.

Questions Posed in the RFI

1. For any of the four categories outlined above (health, climate and energy, food and agriculture, and supply chain resilience):

c. How else can the Government engage with and incentivize the private sector and other organizations to achieve the goals outlined in (a)?

Successfully advancing national-level S&T priorities, such as biotechnology, in a manner that enables us to win the competition with China will require significant strategic collaboration

[4] C. Ford, et al. A "Horizon Strategy" Framework for Science and Technology Policy. 2021. MITRE, https://www.mitre.org/sites/default/files/2021-11/prs-21-1440-horizon-strategy-framework-science-technology-policy.pdf.

[5] Mid-Decade Challenges to National Competitiveness. 2022. Special Competitive Studies Project, https://www.scsp.ai/wp-content/uploads/2022/09/SCSP-Mid-Decade-Challenges-to-National-Competitiveness.pdf.

[6] Building a Sustainable Biopreparedness Industrial Base. 2022. MITRE, https://www.mitre.org/sites/default/files/2022-04/pr-21-2885-building-a-sustainable-biopreparedness-industrial-base.pdf.

[7] M. Mansoura, et al. 10-Point Action Plan: Sustaining A Biopharma Industrial Base for a More Secure Nation. 2021. MITRE, https://www.mitre.org/sites/default/files/2021-10/pr-21-2355-10-point-action-plan-sustaining-biopharma-industrial-base.pdf

between government, industry, academia, and international partners.[8] The National Science and Technology Council should embrace a leadership and coordination role within this public-private collaboration. Although the Council has not normally embraced this role, it does have limited experience doing so that has yielded significant outcomes.[9]

An oft-overlooked aspect of prior S&T collaboration that will be especially important here is commercialization. Strategies for critical research initiatives should include proactive transition plans to facilitate rapid, at-scale manufacturing and productization. Standards for biotechnology product nomenclature, properties, and descriptive materials that clarify the need for products as well as the offerings from biotechnology manufacturers are also needed. Relatedly, the U.S. will need to expand its biomanufacturing capacity to ensure future national security and economic prosperity from these R&D investments.

4. How can the Federal Government, in partnership with private, academic, and nonprofit sectors, support a data ecosystem to drive breakthroughs for the U.S. bioeconomy? This may include technologies, software, and policies needed for data to remain high-quality, interoperable, accessible, secure, and understandable across multiple stakeholder groups?

To support the further utilization and democratization of biology-as-a-technology, the federal government could support the development of a decentralized ecosystem for life science innovation. Such a system would leverage and integrate current trends in information technology, synthetic biology, biomanufacturing, and others to make the tools of modern biotechnology available to people the world over in a safe and secure manner. As part of this infrastructure effort, the federal government should help facilitate trusted information sharing between public and private stakeholders. This trusted information sharing can and should lead to the creation of biotechnology data standards, as well as standards for data sharing and use to protect intellectual property and prevent data tampering. Said standards should ideally be corroborated with (or used to pioneer) transnational, global biotechnology data standards as well.

The federal government should explore developing an independent public-private partnership to enable data sharing and open discussions of bioeconomic issues of concern (e.g., common safety and security vulnerabilities) while protecting government and industry partners' privacy and interests. An approach similar to the MITRE-managed, Aviation Safety Information Analysis and Sharing (ASIAS) public-private partnership would be beneficial, as it allows rapid dissemination of threat information across the bioeconomy and sharing of best practices while protecting government and industry partners' privacy and interests.[10] This could also involve

[8] D. Blackburn. A Discussion Response to "Government and the Evolving Research Profession". 2023. Issues in Science and Technology, https://issues.org/evolving-research-policy-wright-forum/. Last accessed January 18, 2023.

[9] D. Blackburn, et al. A National Science and Technology Council for the 21st Century. 2021. MITRE, https://www.mitre.org/sites/default/files/2021-09/pr-21-2388-national-science-technology-council.pdf.

[10] FAA Aviation Safety Information Analysis & Sharing (ASIAS). 2023. Federal Aviation Administration, https://www.asias.faa.gov/apex/f?p=100:1. Last accessed January 18, 2023.

developing novel mechanisms and incentives for reporting data related to accidents (e.g., theft, loss, release of biological material), near-misses, and cyber vulnerabilities.

6. What can the Federal Government do to expand and scale domestic biomanufacturing capacity and infrastructure? What level of investment would be meaningful and what incentive structures could be employed?

Sustaining the biomanufacturing industrial base requires an integrated system of actions across the whole of government. MITRE recommends four interrelated courses of action (COAs) as a systematic approach that the federal government should undertake simultaneously to be effective. The first COA is defining and implementing a biomanufacturing strategy, which should be tied to the appropriate policy, authorities, and accountabilities to execute against it.[11] Second, the federal government should identify the financing infrastructure(s) to enable sustained investment in biomanufacturing capability and capacity, including an adequate and trained workforce. Third, the USG needs the situational awareness to act on risks and threats to market access and capacity of the industrial base, including economic competition from other nations. Fourth, the USG needs to reframe the government and industry relationship from a transactional model to one of long-term collaboration and mutual benefit.

8. How can the Federal Government partner with state and local governments to expand domestic biomanufacturing capacity, with a particular focus on underserved communities?

The federal government could partner with state and local governments to create biotechnology clusters that connect college programs (both four-year and community colleges) with government and academic activities. Designed correctly, this effort could not only help spur innovation but also support broader efforts to leverage historically underserved communities. Direct student relationships with employers should be a part of these efforts. This can be done through a combination of training and internships prior to graduation so that students have opportunities immediately after graduation.

Such efforts should leverage ongoing activities, such as the Virginia Advanced Pharma Manufacturing and R&D Cluster.[12] This cluster will expand the domestic supply chain for essential medicines and critical active pharmaceutical ingredients via a range of projects that "include expanding a nascent pharmaceutical manufacturing corridor in central Virginia through investment in new wet lab space, development of critical infrastructure to sustain industrial

[11] The President's Council of Advisors on Science and Technology recently offered a similar recommendation: https://www.whitehouse.gov/wp-content/uploads/2022/12/PCAST_Biomanufacturing-Report_Dec2022.pdf.

[12] Advanced Pharmaceutical Manufacturing (APM) Cluster. 2022. U.S. Economic Development Administration, https://www.eda.gov/funding/programs/american-rescue-plan/build-back-better/finalists/virginia-biotechnology-research-partnership-authority. Last accessed January 18, 2023.

capacity in Petersburg, and engagement with local business to enhance the regional pharmaceutical supply chain. The project will also catalyze a new partnership between Virginia Commonwealth University and Virginia State University (a historically Black college) to create new pathways for underserved residents to high-quality training and jobs in the pharmaceutical industry."[13]

MITRE further recommends creation of publicly accessible lessons that leverage biotechnology matters in important degree fields beyond biotechnology-specific degrees, such as data science, materials science, and various engineering specialties. MITRE undertook a similar effort on artificial intelligence (AI), which helped a wide range of students understand AI within the contexts of their fields of study.[14]

10. How can the U.S. strengthen and expand the biotechnology and biomanufacturing workforce to meet the needs of industry today and in the future? What role can government play at the local, state, and/or Federal level?

As the bioeconomy expands, the U.S. biotechnology industry will require personnel with a broad spectrum of biotechnology knowledge and skills ranging from technicians with basic understanding of biological concepts to experts with doctoral degrees and years of experience in applied research. Developing the workforce will require new policies and programs that expand biotechnology education/training at all levels, provide for upskilling and retaining of workers, and encourage cross-disciplinary training.

Given the growing overlap between biotechnology, information technology, and engineering, this workforce will include (1) experts in biological principles (e.g., molecular biologists, geneticists, computational biologists, systems biologists, microbiologists, biochemists, bioethics) and (2) positions where expertise lies in a non-biologically related STEM field (e.g., engineering, materials science, chemistry, data science, cybersecurity) with a working understanding of biological principles.

To ensure that the U.S. builds the necessary workforce, MITRE recommends conducting a national workforce study to identify critical career fields and then predict and prioritize overcoming gaps. Understanding and quantifying the specific challenges to the bioeconomy workforce is a critical step in creating targeted mitigation strategies, identifying synergies with other national STEM initiatives, and targeting opportunities to scale U.S. interests in this field. MITRE has conducted a related study on the Defense Industrial Base subset for the U.S. Department of Defense (DoD).

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[13] U.S. Department of Commerce Invests Approximately $52.9 Million to Boost Virginia's Pharmaceutical Industry Through American Rescue Plan Regional Challenge. 2022. U.S. Economic Development Administration, https://www.eda.gov/news/press-release/2022/09/02/us-department-commerce-invests-approximately-529-million-boost. Last accessed January 18, 2023.

[14] B. Eidson. Generation AI Reaches 10,000 Students—and Begins a New Chapter. 2022. MITRE, https://www.mitre.org/news-insights/impact-story/generation-ai-reaches-10K-students-and-begins-new-chapter. Last accessed January 18, 2023.

A strong biotech workforce will require development efforts at multiple levels: K-12, where many individuals in marginalized groups can lose interest in STEM; university and graduate school, where efforts should be made to retain students and expand access to specialized fields beyond just biology itself; the skilled technical workforce, which would most benefit from apprenticeship and partnership programs; and the experienced workforce, which provides an opportunity for reskilling and upskilling.

To be successful in expanding biotechnology related degrees, efforts at K-12 should focus on creating the broadest interest and aptitude in STEM among all students, but special efforts should be made retain the interest of marginalized groups. The broad, general efforts can be scaled across all STEM fields, but must include branding of the biotechnology fields such that it creates an interest in biotech while building STEM skills necessary to be success at the university level or in the skilled technical workforce. A key component of a national biotechnology workforce study should be to identify opportunities to coordinate efforts with other career fields of national importance (e.g., microelectronics, quantum, and AI).

At the university level, efforts to retain students across all demographics need to be bolstered by expanding university programs to create a career ready workforce by creating more specialized coursework both for biological sciences (e.g., computational biology) and for adjacent fields needed in biotechnology (e.g., material science). The coursework should be paired with industry experience so that students can both apply their skills and develop a love for their field—and in many cases a job offer upon graduation.

The workforce study should include an analysis of the geographic location of biotechnology employers combined with community colleges and training centers to create the skilled technical workforce. Federal information from the study can be used to help state and local government target their efforts. These efforts should include by historically Black colleges and universities (HBCUs) and universities that serve large Veteran populations. Most importantly, however, these efforts should be managed by a staff knowledgeable about what makes these programs successful, especially any reskilling programs for Veterans given the high failure rate of reskilling programs that don't consider interest, aptitude, and job placement opportunities.

Finally, efforts for career switching, reskilling, and upskilling of adjacent workforces should be an immediate area of focus. Efforts beginning at K-12 can take decades to grow a biotechnology worker. Experienced workers in adjacent fields, however, can be trained up quickly. As such, the workforce study should identify which fields and geographic areas are most likely to have interested workers and specially align to state and local government initiatives. One area of exploration could be women reentering the workforce after a pandemic-related hiatus. Given the abundance of biology degrees and that over 25% of individuals with biology degrees work outside of areas requiring biology degrees and industries, there may also be opportunities to reskill early career biology graduates for biotechnology.[15]

[15] Field of Degree: Biology. 2022. U.S. Bureau of Labor Statistics, https://www.bls.gov/ooh/field-of-degree/biology/biology-field-of-degree.htm. Last accessed January 18, 2023.

11. What strategies and program models have shown promise for successfully diversifying access to biomanufacturing and biotechnology jobs – including those involving Historically Black Colleges and Universities, Tribal Colleges and Universities, and other Minority Serving Institutions? What factors have stymied progress in broadening participation in this workforce?

Recently, tailored talent development and university research programs have shown promise in diversifying access to biomanufacturing and biotechnology jobs. Programs such as Amgen's HBCU BioTech Fellows & Bristol Myers Squibb's "Tomorrow's Innovator" programs focus on developing and training biotechnology talent from HBCUs for jobs in the field post-graduation. Also, university programs such as the DoD's HBCU and Minority-Serving Institutions Research and Education Program have created Centers of Excellence at HBCUs, charged with providing training to underrepresented students pursuing STEM disciplines, complemented by internships at defense laboratories, collaborations with DoD researchers to address science and technology challenges, and K-12 student training to proactively build STEM talent pools.

17. What risks are associated with international biotechnology development and use, and how can the U.S. Government work with allies and partners to mitigate these risks?

In the coming decade, rapidly lowering biotechnology barriers to entry could allow bad actors (e.g., rogue states, super-empowered individuals, small groups of zealots/extremists) to assemble, synthesize, and potentially globally distribute pandemic-class agents.[16] USG and its allies and partners could mitigate this risk in the following ways:

- Empowering and supporting the creation of global "bottom-up" biosecurity through biosecurity workforce development and self-monitoring within academia, industry, and communities writ large.
- Identifying and addressing security issues through enhanced biosecurity standards and international cooperation.
- Working with academia and industry to reduce life sciences information hazards.
- Using human and signal intelligence methods to detect and monitor connections between affiliates of extremist groups with ideologies suggesting mass civilian casualties, the collapse of civilization, or the extinction of humanity would be a desirable outcome and individuals with the technical skills to assemble pandemic-class agents.
- Investing in global early warning systems capable of reliably detecting pandemic-class agents, as well as rapid diagnostic test deployment and pandemic-proof personal protective equipment development and distribution.

[16] K. Esvelt. Delay, Detect, Defend: Preparing for a Future in which Thousands Can Release new Pandemics. 2022. Geneva Centre for Security Policy, https://dam.gcsp.ch/files/doc/gcsp-geneva-paper-29-22.