DAY ONE PROJECT

A National Bioeconomy Manufacturing and Innovation Initiative

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December 2020

Summary

The COVID-19 pandemic has devastated the world. In the same year, record fires, hurricanes, and weather wreaked havoc on the United States. These disasters have had devastating economic effects on American lives. To combat COVID-19, foster economic recovery, and address climate change, the United States should implement a National Bioeconomy Manufacturing and Innovation Initiative. The U.S. bioeconomy is composed of healthcare, agriculture, and life-science companies and contributes an estimated 2% of the U.S. GDP.[1] This figure is expected to rise in the coming decade. The bioeconomy also contributes to addressing climate change by reducing U.S. dependence on petroleum-based products and creates American jobs through a growing biomanufacturing sector. Biomanufacturing is the production of products via biological and biosynthetic mechanisms, such as fermentation-based production of industrial ethanol. To fully realize the potential of the bioeconomy, the United States must invest in cross-cutting research and development (R&D) across the areas of healthcare, food & agriculture, energy, environment, and industrial applications.[2] The pillars of this "National Bioeconomy Manufacturing and Innovation Initiative" should focus on (1) cutting-edge R&D, (2) development of fundamental and publicly available tools, and (3) biomanufacturing. The initiative should be coordinated out of the Executive Office of the President via a National Bioeconomy Coordination Office. The initiative should be supported by senior leadership positions at each federal agency with equities in the U.S. bioeconomy, as well as by appropriated funding.

Challenge and Opportunity

In the past year, COVID-19 has devastated the lives of Americans and the U.S. economy. The pandemic has exacerbated gender, race, and economic inequalities and killed hundreds of thousands of the most vulnerable Americans. In the same year, climate change has led to record wildfires, hurricanes, and extreme weather, all inflicting compounding damage to American lives during the pandemic. As a result, the incoming Biden Administration has set defeating COVID-19, fostering economic recovery, addressing racial inequality, and combating climate change as its top four priorities for Day One.[3] To aid in addressing these Day One priorities, the next administration should establish a National Bioeconomy Manufacturing and Innovation Initiative to invest in the U.S. bioeconomy and America's future prosperity.

Advances in biotechnology have led to some of the fastest vaccine candidates developed in history. In less than a year from the start of the COVID-19 pandemic, multiple vaccine candidates have been developed and shown >90% efficacy in Phase III clinical trials. However,

[1] Bioeconomy Capital (2018). Available at http://www.bioeconomycapital.com/bioeconomy-dashboard.
[2] Engineering Biology Research Consortium (2020). Technical Roadmaps. https://roadmap.ebrc.org/.
[3] Biden-Harris Transition (2020). Available at https://buildbackbetter.gov/priorities/

manufacturing and distributing millions of doses of vaccines remains a non-trivial hurdle to ending the pandemic.

In addition, the U.S. bioeconomy comprises a diverse group of industries that collectively contribute an estimated 2% of U.S. GDP,[4] and are expected to contribute an even greater fraction in the coming decade. Recent advances in biological engineering have opened immense opportunities for the United States to grow and sustain a globally leading bioeconomy and to play a leadership role in international collaborations, standards, and security. In a post-COVID era, investing in the U.S. bioeconomy across the areas of biomanufacturing and innovation will be paramount to economic recovery, long-term growth, and national security.

The bioeconomy also provides opportunities to develop sustainable domestic technology and manufacturing processes that will aid in creating jobs and combating climate change by reducing U.S. dependence on petroleum-based products and by building a growing class of biomanufacturing jobs. Bioeconomy jobs will create new technical and trade career fields and will enable U.S.-based manufacturing and production of American products, made in all corners of America.

To realize these benefits, the United States must invest in cross-cutting research and development (R&D) initiatives across the areas of healthcare, food & agriculture, energy, environment, and industry[5]. The Department of Defense has taken steps towards these efforts by establishing biotechnology as a defense modernization priority, and the United States currently funds three biomanufacturing innovation institutes.[6]

The R&D initiatives proposed and described herein will enhance and accelerate ongoing work to build the U.S. bioeconomy. These initiatives can be broadly grouped into three pillars: (1) cutting-edge R&D, (2) development of fundamental and publicly available tools (e.g., for cellular modeling), and (3) biomanufacturing. The latter should include infrastructure investments to build biomanufacturing capacity at the small, medium, and industrial scales, as well to improve national DNA sequencing and synthesis capabilities and coordination, storage, and protection of national data resources.

All initiatives should be coordinated in accordance with a national strategy standpoint, and should build in biosecurity, biosafety, and biodefense considerations from the ground up.

Our nation's international partners and allies also maintain strong bioeconomy innovation programs, many with particular emphasis on the environmental and climate benefits of biomanufacturing and a bio-based economy. The United States should develop bioeconomy partnerships with Canada, the European Union, the United Kingdom, Singapore, Australia, and

[4] Bioeconomy Capital (2018).
[5] Engineering Biology Research Consortium (2020).
[6] These are the Advanced Regenerative Manufacturing Institute (ARMI), the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL), and the Bioindustrial Manufacturing and Design Ecosystem (BioMADE).

other nations, focusing on bioeconomic benefits to global health security, pandemic prevention, and the environment.

To achieve and sustain global leadership in the bioeconomy, policy changes are required. The United States must track and measure the bioeconomy through mechanisms such as:

- NAICS codes for bioeconomy industries.[7]
- A national stance on biodefense that includes natural, unintentional, and intentional biological threats.
- Consideration of domestic biomanufacturing as a viable route for production, especially as a way to avoid offshoring of manufacturing programs.
- Designation of bioeconomy-related infrastructure as critical infrastructure.
- Appointment of a senior leader at each federal agency responsible for implementing bioeconomy modernization. An example of an existing position on which new positions at other agencies could be modeled is the Principal Director for Biotechnology position at the Department of Defense.
- Creation of innovative R&D programs focusing on the bioeconomy at key federal research agencies such as the National Science Foundation (NSF) and the Departments of Defense, Energy, Healthy and Human Services, and Agriculture (DOD, DOE, HHS, and USDA).
- Creation of mission-specific bioeconomy programs in healthcare, food & agriculture, energy, environment, and industrial applications at appropriate federal agencies.

Plan of Action

The U.S. bioeconomy is central to a strong recovery and growth in a post-COVID economy, and every community in America can help build the future of the U.S. bioeconomy. The recommended actions below are designed to help the U.S. bioeconomy reach its full potential.

Due to the immense nature of the U.S. bioeconomy, a National Bioeconomy Coordination Office (NBCO) should be established within the White House. The NBCO should be a joint mandate of the National Security Council (NSC) and the White House Office of Science and Technology Policy (OSTP) to work with federal agencies on bioeconomy priorities through a "National Bioeconomy Manufacturing and Innovation Initiative". A bioeconomy leader should be identified at both the NSC and OSTP. These leaders should co-chair the NBCO, together responsible for coordinating efforts to promote and protect the U.S. bioeconomy.

[7] Per the United States Census Bureau: "The North American Industry Classification System (NAICS) is the standard used by Federal statistical agencies in classifying business establishments for the purpose of collecting, analyzing, and publishing statistical data related to the U.S. business economy." See: United States Census Bureau (2020). Introduction to NAICS. https://www.census.gov/eos/www/naics/.

Nearly every U.S. federal agency has some responsibility for and equity in the U.S. bioeconomy. In the table below, we briefly describe the bioeconomy interests of a representative group of federal agencies. We also suggest key roles that each agency could play in a new "National Bioeconomy Manufacturing and Innovation Initiative". Additional detail is provided in the subsequent Research & Development, Infrastructure Investments, International Partnerships, and Policy Considerations sections.

Agency	Role
Department of Defense (DOD)	The DOD has a broad mandate and large investments in innovation.[8] In 2019, the DOD established biotechnology as a modernization priority, and appointed a Principal Director for Biotechnology to oversee the investment strategy for biotechnology. The DOD should be the principal agency for investments in biomanufacturing. The ability to produce defense-relevant products in an operationally relevant timeframe is crucial to military readiness. These investments would enhance the entire U.S. biomanufacturing industry and supply chain resiliency. DOD should also be the principal agency to lead the National Sequencing Network.
Department of Health and Human Services (HHS)	HHS and related agencies[9] should remain the principal agencies responsible for healthcare and public health. HHS would benefit from an appointed leader to develop a cohesive biotechnology-related investment strategy. HHS should be the principal agency for investments in cutting-edge R&D. These investments will enhance the healthcare and public-health mission as well as drive underlying innovation in fundamental techniques in biological engineering.
Department of Energy (DOE)	The DOE has a long history of technology development and innovations in computing and tools. As such, DOE should be the principal agency for investments in development of fundamental tools. DOE should also be the principal agency to lead the National Biological Data Collective.
Department of Labor (DOL)	The DOL is the principal agency for workforce and labor, and as such should be the principal agency to lead the development and establishment of biomanufacturing training and reskilling programs.
Department of Commerce (DOC)	As the principal agency for economic considerations, the DOC should be the principal agency for tracking and measuring the U.S. bioeconomy. In addition, the National Institute of Standards and Technology (NIST) should be the principal agency for standardization of measurements and tool development across the bioeconomy.
Department of Homeland Security (DHS)	DHS should be the principal agency responsible for establishing and protecting bioeconomy-related critical infrastructure.
Department of State (DOS)	DOS should be the principal agency for leading the establishment of a Global Biosurveillance Innovation Network (see below), as well as for overseeing biomanufacturing and supply-chain resiliency programs globally.

[8] E.g., through the Office of the Secretary of Defense (OSD), the U.S. Army, Navy, and Air Force, and the Defense Advanced Research Projects Agency (DARPA).

[9] E.g., the National Institutes of Health (NIH), the Food and Drug Administration (FDA), the Centers for Disease Control and Prevention (CDC), and the Biomedical Advanced Research and Development Authority (BARDA).

National Science Foundation (NSF)	The NSF should be the principal agency for investments in programs investigating the fundamental nature of biological engineering techniques.
Advanced Research Projects Agency for Health (ARPA-H; to be established)	ARPA-H should be established and set as the principal agency for bioeconomy-related innovation at the intersection of biological engineering and healthcare, with investments complementary to other advanced research projects agencies.[10]

Research & Development

The United States is a global leader in life sciences and pharmaceutical research and development. Recent advances in biological engineering have opened new applications of biotechnology and life sciences across healthcare, food and agriculture, clean energy, the environment, and industrial applications—the bioeconomy. A major benefit of biotechnology and engineered biology is the cross-cutting nature of technology development. Innovation in the fundamental understanding of biological engineering and its applications will impact all areas of the economy.

Due to the cross-cutting nature of biotechnology and the life sciences, investments should be structured to address three crucial pillars of innovation. These pillars are (1) cutting-edge R&D for scientific discovery, (2) development of foundational and publicly available tools for biological engineering (e.g., for cellular modeling), and (3) biomanufacturing.

Pillar 1: Cutting-edge R&D

Investments in fundamental science should be made to advance the state of measurement and control/manipulation of biology. Regarding the former, most modern sensors and measurement techniques destroy the biological sample being analyzed. Non-destructive measurement techniques will accelerate the ability to understand biology. Regarding the latter, investments in new techniques in genome editing as well as DNA sequencing and synthesis will accelerate the ability to design, engineer, and manufacture new products and capabilities at scale.

All investments in R&D should include biodefense and health-security considerations. By building security considerations into development plans, biotechnology will be co-developed alongside mitigation, control, and containment techniques.

Pillar 2: Foundational, publicly available tools for biological engineering

Modern biological engineering is a young field. Much innovation in biological engineering currently comes from academia and a culture of open-source development or a few emerging companies with bespoke tools developed in-house. To establish biological engineering as a robust and reliable engineering discipline akin to electrical or mechanical engineering, investments need to be made in the development of high-quality tools. These tools, such as

[10] E.g., DARPA, BARDA, the Intelligence Advanced Research Projects Agency (IARPA), and the Advanced Research Projects—Energy (ARPA-E).

standardized measurement techniques, biological design software, and data-analysis pipelines, will empower small and medium sized businesses that lack the personnel or capital to develop bespoke tools in-house. In short, these tools will provide the foundation upon which the U.S. bioeconomy will thrive.

Pillar 3: Biomanufacturing

The ability to manufacture new products and capabilities that come from engineered biology requires a new class of manufacturing techniques. Investments should be made in advancing U.S. leadership in biomanufacturing through three federally-funded biomanufacturing innovation institutes: NIIMBL, ARMI, and BioMADE. These institutes and organizations collectively bring together hundreds of industry and academic partners as well as hundreds of millions of dollars of private sector cost-share to enhance federal investment in biomanufacturing. These institutes focus on innovation in the foundation of biomanufacturing technologies and are designed to enhance the entire U.S. bioeconomy. In addition, investments should be made in partnerships with leading commercial biomanufacturing organizations.

Initiatives to Accelerate Innovation

To accelerate and achieve a globally leading bioeconomy based on modern biological engineering and life sciences, several national initiatives should be implemented.

Initiative 1: Regional Bioinnovation Hubs

All 50 states—as well as leading universities, companies, and nonprofits—have equities in the bioeconomy. To accelerate innovation in the bioeconomy and harness the talent and expertise of regions outside of the Northeast U.S. and the San Francisco Bay Area, regional innovation hubs should be established with region-specific technology foci. For example, coastal bioinnovation hubs would focus on aquatic applications of engineered biology, while midwestern hubs would focus on applications in food and agriculture.

Initiative 2: Innovative graduate and post-graduate training programs

Modern biological engineering requires expertise from a wide range of disciplines, but current training programs do not incentivize such cross-training. Innovative graduate and post-graduate programs should be implemented to incentivize and support cross-training of biologists and engineers. For example, a graduate and postdoctoral training program should be implemented to support graduate students from life sciences in pursuing postdoctoral training in engineering, and vice versa. This program could be modeled on the F99/K00 pilot training program from the NIH and National Cancer Institute (NCI).

Initiative 3: Biomanufacturing training and reskilling

The heart of American innovation lies within American workers. While novel discoveries are often first made at university or industry labs, the true impact stems from the women and men who turn those discoveries into reality. Investments should be made into biomanufacturing training

and reskilling programs that will open new job opportunities and career tracks for the U.S. manufacturing workforce. In addition, biological technician training programs should be developed alongside mechanic, electrician, and other post-high-school training programs.

Infrastructure Investments

The United States currently lacks the requisite infrastructure to accelerate and maintain and globally leading bioeconomy. To achieve a robust modern bioeconomy, investments must be made across sequencing, data, and manufacturing infrastructure.

Infrastructure investment 1: National Sequencing Network

DNA sequencing and DNA synthesis are the two techniques most foundational to the modern bioeconomy based on biological engineering. DNA sequencing must become a commodity, akin to public utilities, to achieve a cost-competitive bioeconomy. Investments in a National Sequencing Network to provide access to high-throughput and low-cost DNA sequencing facilities would enable DNA sequencing to become a fundamental tool in U.S. bioeconomic leadership.

Infrastructure investment 2: National Biological Data Collective

Data is central to progress in artificial intelligence. The United States collects massive amounts of biological data each year, but these informational resources are disjointed and not stored in a manner conducive to progress. Investments in a National Biological Data Collective should be made to provide a resource from which small- and medium-sized businesses applying the tools of artificial intelligence can draw to develop new products, therapies, and capabilities for the bioeconomy.

Infrastructure investment 3: Domestic biomanufacturing capacity

The United States currently lacks sufficient biomanufacturing capacity and thus offshores such production to countries around the world (such as Brazil). This delays product innovation due to slow turnaround time and means that other countries reap the economic benefits of American biomanufacturing business. To address this problem, investments must be made in biomanufacturing at the small, medium, and industrial scales.

International Partnerships

Many international partners and allies of the United States are making robust bioeconomy investments. Many of these investments are focused on enhancing a bio-based economy and environmental considerations. The United States should leverage these investments by establishing stronger innovation, manufacturing, and health-security partnerships around the world.

Global Biosurveillance Innovation Network

The post-COVID era will require finely tuned biosurveillance capabilities to prevent another global pandemic from occurring. The United States should establish partnerships with allies around the world—including but not limited to Canada, the United Kingdom, Australia, Singapore, Germany, France, Mexico, and Brazil—to enhance global biosurveillance capacity. In addition to investing in a biosurveillance network, investments in biomanufacturing resilience and innovation should be made with these same international partners to build domestic and international supply chains that are resilient to disruption due to conflict or natural disaster, such as any future pandemics.

Policy Considerations

There are several policy changes that can readily enhance the U.S. bioeconomy. First, there does not currently exist a specific set of NAICS code for tracking and measuring the U.S. bioeconomy. Such a code should be developed.

Second, the 2018 National Biodefense Strategy defined biodefense as defense against natural, unintentional, or intentional biological threats.[11] However, the strategy left it up to individual agencies to determine the precise contours of biodefense in practice. This has created a divide in organizational authorities between intentional and natural biological threats in some federal agencies (such as the Department of Defense). The divide often occurs in appropriation language, as well as at the agency policy level. A detailed and consistent government-wide policy is needed to explain what constitutes biodefense. Such a policy would, for instance, enable a more fluid and robust response to future pandemics.

Third, enhancing domestic biomanufacturing capabilities requires market incentives or mandates that encourage companies to manufacture domestically. Companies that benefit from federal investments in the bioeconomy should be required to consider domestic biomanufacturing first, and only move to offshore biomanufacturing if domestic biomanufacturing is clearly infeasible.

Fourth and finally, bioeconomy-related infrastructure should be designated as "critical infrastructure" by DHS. This would allow security, response, and resiliency investments to be prioritized towards the bioeconomy and would mitigate future supply-chain failures.

[11] National Biodefense Strategy (2018) Available at https://www.whitehouse.gov/wp-content/uploads/2018/09/National-Biodefense-Strategy.pdf

Budget Proposal

The "National Bioeconomy Manufacturing and Innovation Initiative" includes investments, programs, and policies across a range of application areas. As 2% of the U.S. economy, commensurate investments in driving the bioeconomy forward are outlined below.

	Budget ($B)			
Initiative component	2021	2022	2023	2024
Cutting-edge R&D	$3.3	$3.7	$4.1	$4.1
Foundational tool development	$1.7	$1.9	$2.3	$2.2
Biomanufacturing	$0.7	$1.2	$1.1	$1.3
Bioinnovation hubs	$0.5	$0.9	$1.3	$1.6
Education & workforce	$0.4	$0.7	$0.9	$0.9
National Sequencing Network	$0.3	$0.9	$1.1	$1.7
National Data Collective	$0.5	$0.8	$1.1	$1.5
Domestic biomanufacturing capacity	$1.3	$2.1	$2.5	$1.7
International partnerships	$0.3	$0.3	$0.3	$0.3
Total	***$9.0***	***$12.5***	***$14.7***	***$15.3***

Conclusion

The U.S. bioeconomy comprises over 2% of GDP and is continuing to grow. In a post-COVID era, our nation's ability to leverage biotechnology and the life sciences for the health, safety, and security of the American people will be more important than ever. Investments in manufacturing and innovation programs to accelerate the U.S. bioeconomy will provide economic growth, international partnerships, and jobs for millions of Americans. These investments will also be central to combating climate change, confronting infectious disease, and other critical priorities. Finally, investments in the U.S. bioeconomy are essential for growing and maintaining U.S. global leadership and maintaining the strength of American innovation. The bioeconomy is paramount to the future of all Americans and must continue to build on what all of America has to offer.

Frequently Asked Questions

What challenges might the next administration encounter from industry in launching this initiative?

The U.S. bioeconomy comprises a large number of companies, universities, and government agencies. The bioeconomy also includes applications in healthcare, agriculture, energy, environment, and industrial products, among many others. As such, working with each bioeconomy-subindustry to develop specific solutions to promote and protect the U.S. bioeconomy will be essential. In addition, much of the bioeconomy is highly regulated and care will need to be taken when approaching changes.

A large portion of the emerging bioeconomy is based on relatively new technologies (e.g., synthetic biology and CRISPR). As such, the majority of companies in these sectors are small, privately held startups. In addition to industry-specific initiatives, there will need to be a focus on serving different-size companies to foster American innovation from small, medium, and large businesses across all geographies.

How can the next administration build the bipartisan support necessary to secure the funding for a National Bioeconomy Manufacturing and Innovation Initiative?

The U.S. bioeconomy encompasses every geography in America, from the established biotechnology innovation hubs found in New England and on the West Coast, to the heart of American farmland. The key to developing bipartisan support is to demonstrate that solutions can be developed to support industries ranging from agriculture to healthcare, from industrial synthetic biology to designer high-value chemicals. Biomanufacturing is also an emerging source of domestic manufacturing jobs in red and blue states alike. The American bioeconomy can help produce cutting edge and competitive products domestically, and across all of America.

About the Author

Alexander Titus is a technologist serving at the intersection of industry, government, and academia. He is the Chief Strategy Officer at the Advanced Regenerative Manufacturing Institute (ARMI), the Founder of Bioeconomy.XYZ, and an Adjunct Assistant Professor of Biotechnology at the University of New Hampshire. Prior to his role at ARMI, Alexander was the inaugural Assistant Director for Biotechnology at the Department of Defense (DoD), where he led the DoD's biotechnology modernization efforts. Alexander is a biomedical data scientist by training and holds a Ph.D. in Quantitative Biomedical Sciences from Dartmouth College as well as a B.S. in Biochemistry and a B.A. in Biology from the University of Puget Sound. The views expressed herein solely reflect those of Alexander Titus and not of any private or public business or agency.

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