REPORT TO THE PRESIDENT

Biomanufacturing to Advance the Bioeconomy

Executive Office of the President

President's Council of Advisors on Science and Technology

December 2022

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EXECUTIVE OFFICE OF THE PRESIDENT
PRESIDENT'S COUNCIL OF ADVISORS ON SCIENCE AND TECHNOLOGY
WASHINGTON, D.C. 20502

President Joseph R. Biden, Jr.
The White House
Washington, D.C.

Dear Mr. President,

We are on the cusp of a new industrial revolution—a revolution emerging from astounding advancements in biotechnology, such as the RNA-based vaccines that are now saving countless lives around the world. Biotechnology will soon provide us with the ability to program our own cells to cure disease, harvest meat without the worries of climate impact, engineer microbes to break down plastic in landfills, and use biomass—in place of petrochemicals—to make the materials and chemicals we use in our daily lives. Many of these scientific developments and innovations were seeded by Federal R&D funding provided over the past two decades, accelerated by the policies of the Obama-Biden Administration. In a recent report, the National Academies of Sciences, Engineering, and Medicine estimated the value of the direct economic inputs from the U.S. bioeconomy to be approximately $402 billion in 2016; when including indirect and induced effects, they estimated the total economic impact to be $959 billion. As companies continue to shift to biologically based processes or develop novel bioproducts, the bioeconomy is poised for enormous growth over the coming decades.

With this revolution comes great opportunity: desirable new jobs for skilled workers, a reduced carbon footprint, and new products that will expand U.S. manufacturing and accelerate our economy, all with the potential to enhance access to these benefits in underserved regions of the country. Indeed, critical discoveries in biological science and biotechnology, such as gene editing and cell engineering, were developed in the United States. If we act now, we have the chance to leverage these and other scientific and engineering advances to achieve your goal that biotechnologies invented in America lead to products that are made in America. Inaction could carry significant costs that include impeding the ability of the United States to reach its climate goals, continuing the loss of manufacturing jobs, curbing usage of innovative biotechnology, and increasing reliance on imported products.

The Biden Administration's recent Executive Order (EO) 14081, *Advancing Biotechnology and Biomanufacturing Innovation for a Sustainable, Safe, and Secure American Bioeconomy*, sets in motion numerous new policies and actions in support of American competitiveness in this fast-developing sector. With our report, we are pleased to fulfill the charge in EO 14081 for PCAST to deliver a report on "how to maintain United States competitiveness in the global bioeconomy." Our recommendations synergize with, but are distinct from, the actions described in EO 14081. We hope that our recommendations will establish a systematic approach to investment and engagement in the bioeconomy while enabling equity and access across the country, transitioning to climate-friendly manufacturing platforms, and fostering strong economic growth. Specifically, PCAST has identified **three key gaps that are slowing the country's progress and must be addressed** if we are to realize this enormous potential and remain in the forefront of global markets: **insufficient manufacturing capacity**, **regulatory uncertainty**, and an **outdated national strategy**.

The first and biggest gap—insufficient biomanufacturing capacity—has been emphasized by key stakeholders in every sector of the bioeconomy. Too often companies encounter a bottleneck when searching for available biomanufacturing facilities and trained workforce needed to expand production to market scale. This bottleneck leads some companies to move to Europe or Asia where manufacturing facilities and trained workforce are more readily available. Much like the American semiconductor industry turned to countries in Asia to bring their products to commercial scale, China is rapidly becoming a leader in biobased production and a source of manufacturing expertise and assistance. Federal investment is critical now to create large, shared, and scalable facilities that can be utilized by American product developers at transitional stages of growth. **Biomanufacturing infrastructure hubs could provide these critical facilities in locations across America, advancing manufacturing methods for complex new bioproducts[1] and providing training opportunities for skilled workers.** These hubs should be public-private partnerships, established in geographically diverse regions of the United States, and catalyzed by a Federal investment on the order of $50 million per hub. The hubs would expand equitable access to job opportunities and enable better utilization of the unique natural resources and industrial capabilities located in different parts of the country. Investing in this infrastructure would spur the growth of companies and lead to good-paying jobs making needed medicines, consumer goods, and materials across all regions of the country.

The second key gap is regulatory uncertainty. The regulatory approval process can be a significant hurdle for companies with novel, complex, and often transformative ideas and products. Primary regulatory responsibilities are assigned to three agencies, and all three may be involved in approving a new product before it goes to market. In this report, **we recommend the creation of more clear and transparent pathways for evaluating new bioproducts**. Streamlined regulatory paths and cross-trained, rapid response regulatory experts would provide more consistent, efficient, agile, and timely product evaluations while still ensuring consumer safety.

The third key gap is that we need an updated national strategy for the bioeconomy. The *National Bioeconomy Blueprint*, published in 2012 by the Obama-Biden Administration, helped to launch us on a path of vigorous innovation that created many new products and companies. However, in the past 10 years much has changed. **Therefore, we recommend that the National Science and Technology Council develop a new, long-term, data-driven plan to secure our Nation's future leadership in the expanding bioeconomy**. The plan should provide a clear vision for improvements in safety, access and affordability, and ethical issues; improving national security; and strengthening the bioeconomy supply chain. To keep up with the rapid changes in this field, we need a quantitative, fact-based means of measuring the key drivers in this field and a coordinated means of adapting our approach to secure America's competitive advantage as the biotechnology industrial revolution sweeps the globe.

Sincerely,

The President's Council of Advisors on Science and Technology

[1] Products produced using biological systems and/or often derived from biobased precursors.

The President's Council of Advisors on Science and Technology

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Executive Summary

Advances in biotechnology over the past decade have led to an explosion of innovative new products that touch many aspects of American life, from novel RNA vaccines and cell-based medicines, to engineered meats and plants, to fuels and chemicals made from renewable resources, and much more. Science and engineering continue to unveil new ways of leveraging biological resources and biological processes to create innovative products in America for the benefit of the American people. The potential for enormous growth in this sector over the coming decades is widely recognized, as companies shift to biologically based processes or develop novel bioproducts.[2] The United States has been the source of key advances that launched biotechnology and the bioeconomy—but we need to take action now to ensure the benefits of these advances are reaped at home.

Biomanufacturing is the engine by which the innovative products of the bioeconomy are brought to commercial scale. It is integral to the solutions for many of our national and global challenges, including resource utilization, climate change, economic stability, and environmental justice. The newly released Executive Order (EO) 14081, *Advancing Biotechnology and Biomanufacturing Innovation for a Sustainable, Safe, and Secure American Bioeconomy*,[3] and the CHIPS and Science Act[4] could bolster the bioeconomy, support a diverse domestic workforce, and catalyze the country's scientific and technological pursuits. Combined with accelerating private sector activity across all areas of the bioeconomy, these historic efforts by the Federal Government will help ensure that the research performed in America is translated into products made in America. Over the last decade, government and private sector efforts have spawned hundreds of new businesses and product innovations. Without these strategic investments, the United States will not be able to make the necessary growth to fully capitalize on our current global leadership in the biological sciences and bioengineering.

As a part of a whole-of-government effort to advance biomanufacturing and in turn advance the bioeconomy, PCAST has identified three key challenges that must be addressed to ensure the United States maintains its competitive edge and maximizes the benefits of the bioeconomy: 1) *U.S. biomanufacturing capacity and workforce* are not keeping pace with the bioproducts in development nor with the emerging biomanufacturing approaches that can expeditiously move new ideas and discoveries to commercial scale products; 2) the *regulatory review and approval process* for many new cross-cutting bioproducts, particularly those emerging from new companies with innovative technologies, is complex and uncertain, which can delay or even stop the commercialization process; and 3) *an integrated and overarching bioeconomy strategy* is needed to help guide Federal agencies in managing the development and transfer of these powerful biotechnologies toward social and economic advancements. This strategy should establish achievable objectives, provide options for adapting the strategy to a continually evolving bioeconomy landscape, and identify data and metrics that will be used to monitor progress and reorient programs and funding.

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[2] Products produced using biological systems and/or often derived from biobased precursors

[3] Executive Order 14081: Advancing Biotechnology and Biomanufacturing Innovation for a Sustainable, Safe, and Secure American Bioeconomy (2022). https://www.federalregister.gov/documents/2022/09/15/2022-20167/advancing-biotechnology-and-biomanufacturing-innovation-for-a-sustainable-safe-and-secure-american

[4] Division A ("CHIPS Act of 2022") of Public Law 117-167 (commonly known, and referred to herein, as the "CHIPS and Science Act").

PCAST's recommendations to address these three critical issues are synergistic with, but distinct from actions and policies set forth in EO 14081, and leverage the provisions of the CHIPS and Science Act as well as coordination among our science and regulatory agencies to implement a long-term vision for advancing biomanufacturing in support of our growing bioeconomy.

Recommendations

Recommendation 1: Biomanufacturing Infrastructure Hubs

1.1 The Secretary of Commerce should establish biomanufacturing infrastructure hubs[5] with the authorities and resources necessary to successfully scale up from prototype components in a production relevant environment (Manufacturing Readiness Level [MRL] 6) to low-rate production capability (MRL 8) by expanding the capability and capacity of the Manufacturing USA Institutes and leveraging the Regional Technology Hubs authorized in the CHIPS and Science Act.

1.2 The Office of Science and Technology Policy (OSTP) Director and the Secretary of Commerce, in consultation with the Secretary of Defense, the Director of the National Science Foundation (NSF), and the Secretary of Energy, should develop a plan that A) includes a competitive process for determining biomanufacturing infrastructure hubs' specific foci, funding allocations, and geographic locations and B) directs the creation of a network that connects the hubs established via any of the available innovation hub programs, including the Manufacturing USA Institutes, the Department of Commerce Regional Technology Hubs, the Department of Defense (DOD) biomanufacturing initiatives, Department of Energy (DOE) Agile BioFoundry Consortium, and the NSF Regional Innovation Engines. The plan should be completed within 180 days of the publication of this report.

1.3 NSF, DOD, DOE, the Food and Drug Administration (FDA), the National Institutes of Health (NIH), the United States Department of Agriculture (USDA), and other relevant agencies should form partnerships and establish funding opportunities with local university and research institutions that coordinate with the biomanufacturing infrastructure hubs. These partnerships should focus on bioprocessing and biomanufacturing, establish advanced biomanufacturing research opportunities that leverage or expand the biomanufacturing infrastructure hub network and facilities, and support programs across the spectrum of postsecondary training opportunities in this area.

Recommendation 2: Regulatory Approval Process

2.1 The Environmental Protection Agency (EPA) Administrator, Secretary of Agriculture, and FDA Commissioner should establish a standing Rapid Response Team of key agency representatives that meets regularly to vet new, cross-cutting products and provide recommended regulatory routes for bioproducts to developers. This team should be involved with the continued development of the Unified Website for Biotechnology Regulation that is required by EO 14081. The Rapid Response Team should provide opportunities to cross-train

[5] Consistent with the criteria for hubs established in the CHIPS and Science Act, biomanufacturing infrastructure hubs at MRLs 6 to 8 will help to fill a number of important roles in supporting the growth of the bioeconomy, including physical facilities, continuing education and hands-on training, research and development related to bioproducts/bioprocessing, and touchpoints between regulators and industry.

regulatory staff members as guides that would reside within each agency to support the review of bioproducts.

2.2 EPA, FDA, and USDA should develop streamlined and model pathways for regulatory review and approval of emergent bioproducts of similar type by either: a) drawing from the evolution of pathways as a result of past product review processes, and/or b) creating an open access, searchable library of previously determined routes or pathways for new bioproducts as they are established.

2.3 EPA, FDA, and USDA should create a training and information network that links across the biomanufacturing infrastructure hubs and existing or future federally funded advanced biomanufacturing centers (e.g., BioMade, BioFAB, NIIMBL, and other relevant centers), and to assign regulatory scientists as affiliates to the biomanufacturing infrastructure hubs.

Recommendation 3: A New, Data-Based Strategy for the Bioeconomy

3.1 The National Science and Technology Council (NSTC) should prepare a long-term (10-year) strategy for the bioeconomy. This strategy should be informed by the reports required by the CHIPS and Science Act and EO 14081. The strategy should be completed and delivered within 18 months to the OSTP Director. The strategy must consider the long-term economic, environmental, and societal benefits and liabilities of the proposed actions and policies as well as national security implications.

3.2 The OSTP Director should include research needs of the bioeconomy as a key component of the National Biotechnology and Biomanufacturing Initiative outlined in EO 14081, and the National Engineering Biology Research and Development Initiative and the 5-year coordinated research report designated by the CHIPS and Science Act to be delivered in 2023. These plans should emphasize the fundamental and translational research needed to accelerate the growth of the bioeconomy and other key objectives for international competitiveness.

3.3 The Secretary of Commerce should direct the Bureau of Economic Analysis to establish a satellite account for the bioeconomy as soon as possible and no later than FY 2024. Federal statistical agencies should plan to provide data for the strategy's established metrics and request the resources necessary to do so in their budget requests for FY 2025. The plan should provide the data necessary for the metrics defined by the NSTC strategy and with the cadence necessary to track the bioeconomy.

Biomanufacturing to Advance the Bioeconomy

Introduction to the Bioeconomy

Biotechnological advances over the past decade have led to a wealth of innovative new products that touch all aspects of American life. Innovations such as novel RNA vaccines are helping to prevent the next pandemic. Cell-based medicines are on the cusp of transforming tissue repair and curing cancers.[6] Development of bio-based materials will reduce global dependence on petrochemicals. Meat and leather that do not come from animals, plant-based proteins, and crops that need far less water and synthetic fertilizers will significantly reduce greenhouse gas emissions and environmental harms.[7] Biomanufacturing has the potential to address key national and global challenges, including optimizing the use of limited natural resources, mitigating climate change, increasing economic stability, and accelerating environmental justice.

Exciting new bioproducts are driving innovation in the use of biological resources and biological processes, giving rise to **the bioeconomy—an emerging and rapidly expanding economic sector that represents the portion of the economy based on products, processes, tools, and services derived from biological resources.**[8] The bioeconomy encompasses an enormous diversity of products, from foods to pharmaceuticals and fuels to consumer products. They are unified through their shared reliance on biological organisms in some phase of their production. Although the size of the bioeconomy is challenging to measure because of its impact throughout the economy—including agricultural, bioindustrial, and biomedical sectors—a recent National Academies study estimated

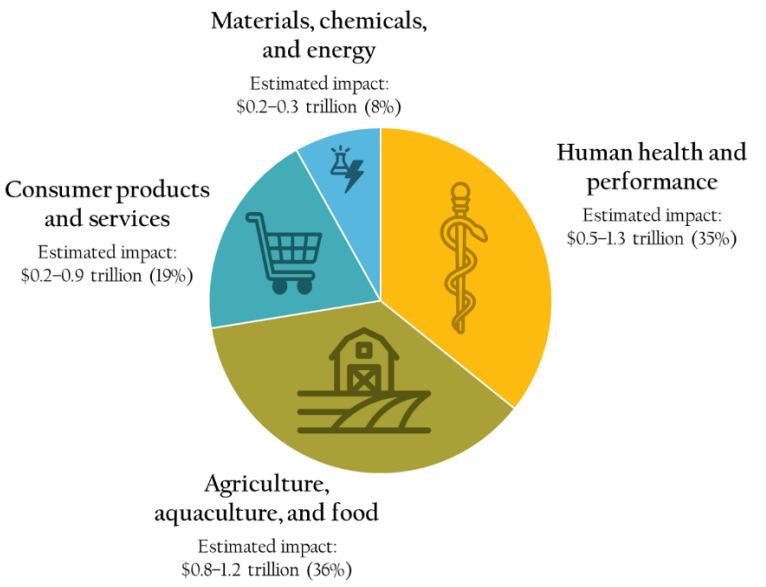

Figure 1. Estimated ranges of the potential annual direct economic impact on global economy in 2030–2040.

Source: *Adapted from Exhibit E5, McKinsey Global Institute (2020). The Bio Revolution: Innovations transforming economies, societies, and our lives.*

[6] Larson, R. C., & Maus, M. V. (2021). Recent advances and discoveries in the mechanisms and functions of CAR T cells. *Nature reviews. Cancer*, *21*(3), 145–161. https://doi.org/10.1038/s41568-020-00323-z

[7] Morach, B., Clausen, M., Rogg, J., Brigl, M., Schulze, U., Dehnert, N., Hepp, M., Yang, V., Kurth, T., Koeller, E. von, Burchardt, J., Witte, B., Obloj, P., Koktenturk, S., Grosse-holz, F., & Meinl, O. S. (2022). *The Untapped Climate Opportunity in Alternative Proteins. BCG Global*. https://www.bcg.com/publications/2022/combating-climate-crisis-with-alternative-protein

[8] Gallo, M. E. (2022). *The Bioeconomy: A Primer.* Congressional Research Service. https://crsreports.congress.gov/product/pdf/R/R46881

the direct economic value of the U.S. bioeconomy to be $402.5 billion[9] in 2016; when including indirect and induced effects, they estimated the total economic impact to be $959.2 billion.[10] A 2020 McKinsey Global Institute report[11] emphasizes that because of the rapid changes in this field, projections are subject to a great deal of uncertainty. Within the context of this uncertainty, the report estimates that by 2030–2040 the global bioeconomy could create approximately $2 trillion to $4 trillion in direct annual economic impacts.[12] Figure 1[13] demonstrates the potential contributions by sector during the same time period.

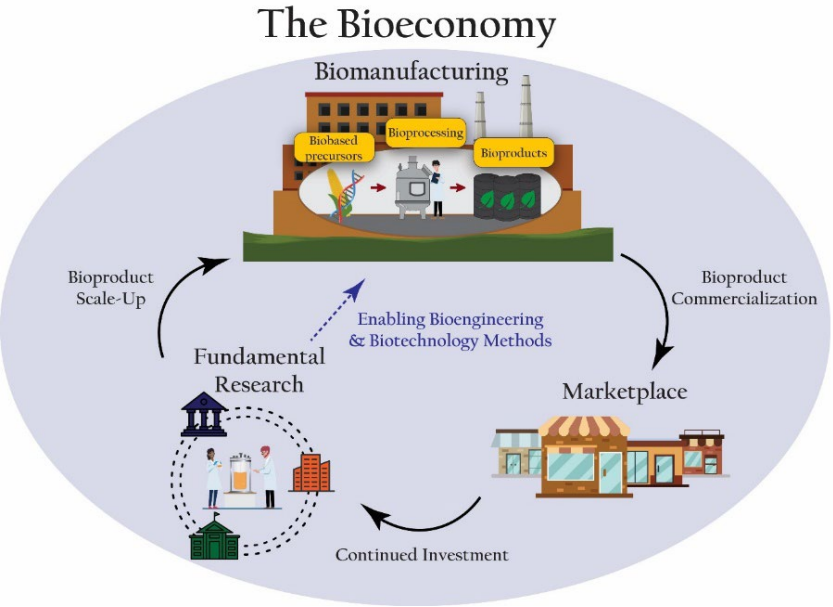

Figure 2. The Bioeconomy: from fundamental research to marketplace

Biomanufacturing[14] is the engine by which innovative bioproducts are brought to commercial scale (see Figure 2). Recent transformative advances in fundamental biotechnology, including gene editing, CAR-T[15] and other cell therapies, metabolic engineering and synthetic biology, and RNA vaccines—many pioneered in the United States.[16,17]—are creating

[9] National Academies of Sciences, Engineering, and Medicine. (2020). *Safeguarding the Bioeconomy: Finding Strategies for Understanding, Evaluating, and Protecting the Bioeconomy while Sustaining Innovation and Growth*. https://www.nationalacademies.org/our-work/safeguarding-the-bioeconomy-finding-strategies-for-understanding-evaluating-and-protecting-the-bioeconomy-while-sustaining-innovation-and-growth. See Table 3-2 for details on direct impacts and Table 3-3 for details on total impacts.

[10] Ibid.

[11] McKinsey Global Institute. (2020). *The Bio Revolution: Innovations transforming economies, societies, and our lives*. https://www.mckinsey.com/industries/life-sciences/our-insights/the-bio-revolution-innovations-transforming-economies-societies-and-our-lives

[12] The McKinsey Global Institute study defined "direct economic impact" as the adoption volume and value game of a product or technology. The drivers of value game that were considered were the reduced disease burden translated to economic productivity, proved quality as expressed through greater willingness to pay, because productivity such as the incremental cost savings to make products, and environmental health such as reduced greenhouse gas emissions.

[13] Figures may not sum to 100% because of rounding that is no longer in the report.

[14] Zhang, Y.-H. P., Sun, J., & Ma, Y. (2017). Biomanufacturing: History and perspective. *Journal of Industrial Microbiology & Biotechnology*, *44*(4-5), 773–784. https://doi.org/10.1007/s10295-016-1863-2

[15] Larson, R. C., & Maus, M. V. (2021). Recent advances and discoveries in the mechanisms and functions of CAR T cells. *Nature reviews. Cancer*, *21*(3), 145–161. https://doi.org/10.1038/s41568-020-00323-z

[16] Jinek, M., Chylinski, K., Fonfara, I., Hauer, M., Doudna, J. A., & Charpentier, E. (2012). A programmable dual-RNA-guided DNA endonuclease in adaptive bacterial immunity. *Science*, *337*(6096), 816–821. https://doi.org/10.1126/science.1225829

[17] Cohen, S. N., Chang, A. C., Boyer, H. W., & Helling, R. B. (1973). Construction of biologically functional bacterial plasmids in vitro. *Proceedings of the National Academy of Sciences of the United States of America*,

enormous new opportunities to grow the bioeconomy. However, past experience has shown[18] that bringing new bioproducts to market can be as challenging as inventing them in the first place, sometimes requiring whole new biomanufacturing paradigms.

Opportunities for the United States from Biomanufacturing

Biomanufacturing will be a critical component of the future U.S. economy, as researchers, entrepreneurs, and other stakeholders across industry unlock the next generation of biotechnology innovations. Biomanufacturing will have significant impacts on carbon emissions, jobs and economic opportunities, and national security.

1. **Reduced dependence on fossil fuels and lower greenhouse gas emissions.** Efforts in this area will help the United States meet its climate goals and emission targets.[19,20] The use of renewable biological ingredients in existing products, petrochemical-free biomanufacturing methods, and innovative new products made from biomass feedstocks will reduce our dependence on fossil fuels and their extracted petrochemicals.[21] Similarly, agricultural bioproducts could require less fertilizer or water, improve soil health, and remove more CO_2 from the atmosphere when compared with traditional crops.[22]

2. **More job opportunities for Americans at all educational levels.** A thriving U.S. bioeconomy will require expanded production systems in order to grow, harvest, transport, and process large volumes of biomass, as well as continual development and adaption of technologies to convert biomass to bioproducts. These growing demands are already creating employment opportunities that require significant technical skills in areas such as bioprocessing. Jobs like these—those that require STEM skills—are better paying than non-STEM jobs at all degree levels.[23]

70(11), 3240–3244. https://doi.org/10.1073/pnas.70.11.3240[18] Paul, M. J., Thangaraj, H., & Ma, J.K.C. (2015) Commercialization of new biotechnology: A systematic review of 16 commercial case studies in a novel manufacturing sector. *Plant Biotechnology Journal, 13(8),* 1209-1220

[18] Paul, M. J., Thangaraj, H., & Ma, J.K.C. (2015) Commercialization of new biotechnology: A systematic review of 16 commercial case studies in a novel manufacturing sector. *Plant Biotechnology Journal, 13(8),* 1209-1220

[19] The White House (2021, April 22). *President Biden Sets 2030 Greenhouse Gas Pollution Reduction Target Aimed at Creating Good-Paying Union Jobs and Securing U.S. Leadership on Clean Energy Technologies [Fact Sheet]*. https://www.whitehouse.gov/briefing-room/statements-releases/2021/04/22/fact-sheet-president-biden-sets-2030-greenhouse-gas-pollution-reduction-target-aimed-at-creating-good-paying-union-jobs-and-securing-u-s-leadership-on-clean-energy-technologies/

[20] Scown, C. D. (2022). Prospects for carbon-negative biomanufacturing. Trends in Biotechnology. *Trends in Biotechnology, 40(12),* 1415-1424. https://doi.org/10.1016/j.tibtech.2022.09.004

[21] Feedstocks refer to the raw materials used to supply an industrial process, for example cellulosic biomass (the fibrous part of plants) that can be converted to biofuels (see Glossary).

[22] Schmidt Futures. (2022). *The U.S. Bioeconomy: Charting a Course for a Resilient and Competitive Future*. https://www.schmidtfutures.com/wp-content/uploads/2022/04/Bioeconomy-Task-Force-Strategy-4.14.22.pdf

[23] Okrent, A., & Burke, A. (2021). Science & Engineering Indicators 2022: The STEM Labor Force of Today: Scientists, Engineers, and Skilled Technical Workers. STEM Labor Market and the Economy. National Science Board. https://ncses.nsf.gov/pubs/nsb20212/stem-labor-market-conditions-and-the-economy

3. **Expanding economic opportunity across the country:** As discussed at the White House Summit on Biotechnology and Biomanufacturing,[24] equitable access to the many opportunities afforded by an expanded biomanufacturing sector will be critical to maximizing America's advantage in the global bioeconomy. Some companies and regional biomanufacturing partnerships have prioritized working with their local communities and underserved populations.[25,26,27] Further, co-locating[28] biomass and biomanufacturing facilities has the potential to revitalize rural economies and create new opportunities in economically disadvantaged areas.[29,30] (See Appendix C for examples of additional bioproducts, bioeconomy development, and educational opportunities.) PCAST supports these efforts, and believes much more is needed and achievable so that Americans in every corner of the Nation and from all demographic groups can take advantage of employment opportunities in this emerging technological sector.

4. **Strengthened national security position:** Federal investment to accelerate growth across the bioeconomy, particularly around developing robust domestic supply chains and onshoring manufacturing capacity, will have advantages for our national security. These benefits include ensuring access to essential products (e.g., biofuels and pharmaceuticals), supporting the development of defense-related products, protecting U.S. intellectual property, reducing dependence on foreign energy producers, and enhancing U.S. leadership by promoting beneficial applications of biotechnology and developing and enforcing standards to inhibit nefarious use.[31] (For more information on national security, see Appendix D.)

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[24] The White House (2022, September 14). *The United States Announces New Investments and Resources to Advance President Biden's National Biotechnology and Biomanufacturing Initiative [Fact Sheet]*. https://www.whitehouse.gov/briefing-room/statements-releases/2022/09/14/fact-sheet-the-united-states-announces-new-investments-and-resources-to-advance-president-bidens-national-biotechnology-and-biomanufacturing-initiative/

[25] Lyles-Williams, T. (2022, September 14). LucasPye Bio Opening Statement. White House Summit on Biotechnology and Biomanufacturing. https://www.youtube.com/watch?v=LcP9zPNuUh4&ab_channel=TheWhiteHouse

[26] Oklahoma City Economic Development Foundation. (2022). Build Back Better Regional Challenge - Coalition Overarching Narrative. https://eda.gov/files/arpa/build-back-better/finalists/narratives/Oklahoma_Biotech_Innovation_Cluster_Initiative.pdf

[27] MacDougall, A. (2022, April 20). BioConnects creates partnership for life sciences racial, gender equity. *Worcester Business Journal*. https://www.wbjournal.com/article/bioconnects-creates-partnership-for-life-sciences-racial-gender-equity

[28] Co-location is a manufacturing concept of physically locating product resources and processing facilities in the same area, for example placing feedstocks near their fermentation facilities to produce biofuels (see Glossary).

[29] Schmidt Futures. (2022). *The U.S. Bioeconomy: Charting a Course for a Resilient and Competitive Future*. https://www.schmidtfutures.com/wp-content/uploads/2022/04/Bioeconomy-Task-Force-Strategy-4.14.22.pdf

[30] National Institute of Food and Agriculture. (n.d.). Bioeconomy, Bioenergy, and Bioproducts (B3) Programs. https://www.nifa.usda.gov/grants/programs/bioeconomy-bioenergy-bioproducts-b3-programs

[31] National Academies of Sciences, Engineering, and Medicine. (2020). *Safeguarding the Bioeconomy: Finding Strategies for Understanding, Evaluating, and Protecting the Bioeconomy while Sustaining Innovation and Growth*. https://www.nationalacademies.org/our-work/safeguarding-the-bioeconomy-finding-strategies-for-understanding-evaluating-and-protecting-the-bioeconomy-while-sustaining-innovation-and-growth

If the United States does not take steps to capitalize on the Federal support of fundamental and translational research that has created these opportunities, we put our future economic growth and national security at risk.

Challenges Facing U.S. Biomanufacturing

Recent actions by the Biden Administration outline a whole-of-government approach to accelerate progress in the burgeoning U.S. bioeconomy. Executive Order (EO) 14081, *Advancing Biotechnology and Biomanufacturing Innovation for a Sustainable, Safe, and Secure American Bioeconomy*,[32] and the CHIPS and Science Act, position the United States to maintain its leadership in biomanufacturing by bolstering infrastructure for the bioeconomy, supporting a diverse domestic workforce, and catalyzing the country's scientific and technological pursuits—all of which are essential to translate U.S.-funded research into U.S.-manufactured products. PCAST enthusiastically supports these efforts to advance U.S. leadership in the global bioeconomy. Toward that same end, our recommendations complement these new policies and programs, and are intended to assist Federal science and regulatory agencies in implementing a long-term vision for advancing biomanufacturing to navigate the challenges in growing the bioeconomy.

We focus on three key challenges: capacity, regulation, and strategy.

First, U.S. biomanufacturing capacity is not keeping pace in terms of both the workforce needed to meet the demand to scale up new bioproducts and the biomanufacturing infrastructure[33] necessary to move products to pilot scale production. This has led some entrepreneurs and companies to move to Europe or Asia to begin scaling up production. Without a robust and technologically advanced biomanufacturing sector, the move to produce American-designed products overseas could increase and the American people will not reap the full benefits of the growing global bioeconomy.

Second, in many cases the current regulatory review and approval processes are not applicable to novel, complex bioproducts, particularly those developed using innovative technologies and biomanufacturing techniques. The U.S. regulatory system is viewed, in many respects, as the "gold standard" by entrepreneurs and companies. However, the complexity and length of the regulatory process is burdensome when it involves more than one agency, slowing the pace at which innovations can move to market.[34] Meanwhile, many other countries[35] are actively trying to improve their regulatory systems to remove obstacles and speed up their processes. If actions are not taken soon

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[32] Executive Order 14081: Advancing Biotechnology and Biomanufacturing Innovation for a Sustainable, Safe, and Secure American Bioeconomy (2022). https://www.federalregister.gov/documents/2022/09/15/2022-20167/advancing-biotechnology-and-biomanufacturing-innovation-for-a-sustainable-safe-and-secure-american

[33] Manufacturing infrastructure includes the facilities with the required tools and instrumentation for the prototyping, testing, demonstration, maturation and scale-up manufacturing of technology.

[34] Challener, C. (2018). Managing Uncertainty in Continuous Biomanufacturing. *BioPharm International*. https://www.biopharminternational.com/view/managing-uncertainty-continuous-biomanufacturing

[35] Belder, T. de. (2021). *Biotechnology and Other New Production Technologies Annual*. United States Department of Agriculture Foreign Agricultural Service; Global Agricultural Information Network.https://apps.fas.usda.gov/newgainapi/api/Report/DownloadReportByFileName?fileName=Biotechnology%20and%20Other%20New%20Production%20Technologies%20Annual_Brussels%20USEU_European%20Union_11-20-2021.pdf

to improve and streamline regulatory review and approval processes here in the United States, we could be at a competitive disadvantage in the near future.

Third, major advances in biotechnology have been made in the last decade, and as a result, the current national strategy,[36] written in 2012, is now outdated. Furthermore, this strategy was largely qualitative, at least in part because neither metrics to assess the bioeconomy nor measurable strategic goals had been established. To maintain U.S. competitiveness in the rapidly expanding global bioeconomy, the Nation needs an integrated, data-informed strategy that is robust and adaptive, sets clear strategic goals, and incorporates data and metrics to monitor progress towards achieving those goals. The CHIPS and Science Act, EO 14081, and the National Advanced Manufacturing Strategy[37] have initiated multiple efforts that will produce a series of near-term reports to capture the current state of the U.S. bioeconomy. These reports will be essential input for the development of an overarching, long-term strategy.

In this report, PCAST is focused on the key issues that have been identified by stakeholders as impacting our Nation's competitive advantage. Addressing these issues will require coordinated partnerships between government, industry, and scientific and educational institutions to achieve goals that are too difficult for any particular sector alone. The U.S. bioeconomy also faces additional challenges, such as the need for economic policies that drive sustainable technology development, the maintenance of critical supply chains, the need for predictive techno-economic models to guide the direction of large scale bioindustrial manufacturing, and the management and protection of intellectual property that further incentivizes and advances innovation. We believe these aspects and others will ultimately be addressed by other ongoing efforts. Thus, we have decided to emphasize the critical gaps outlined above.

Biomanufacturing Infrastructure Hubs

Limited Manufacturing Capacity and Infrastructure

Although the United States has been the source of many key advances that launched the global bioeconomy, growth in U.S. biomanufacturing capacity has not matched product and process development in this sector. In 2011, PCAST recommended ways to ensure that the United States maintained its leadership in advanced manufacturing.[38] Those recommendations formed the basis for the Advanced Manufacturing Partnership and the Manufacturing USA program.[39] There are three biomanufacturing centers in the Manufacturing USA program: BioFab, which focuses on regenerative medicine;[40] BioMade, which specializes in bioindustrial manufacturing;[41] and the National Institute

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[36] The White House. (2012). *National Bioeconomy Blueprint*. https://obamawhitehouse.archives.gov/sites/default/files/microsites/ostp/national_bioeconomy_blueprint_april_2012.pdf

[37] Subcommittee on Advanced Manufacturing, & National Science and Technology Council. (2022). *National Strategy for Advanced Manufacturing*. https://www.whitehouse.gov/wp-content/uploads/2022/10/National-Strategy-for-Advanced-Manufacturing-10072022.pdf

[38] President's Council of Advisors on Science and Technology. (2011). *Report to the President on Ensuring American Leadership in Advanced Manufacturing*. https://obamawhitehouse.archives.gov/sites/default/files/microsites/ostp/pcast-advanced-manufacturing-june2011.pdf

[39] Revitalize American Manufacturing and Innovation Act of 2014, H.R. 2996, 113th Cong. (2014, December 16). https://www.congress.gov/bill/113th-congress/house-bill/2996

[40] BioFabUSA. (2022). https://www.armiusa.org/biofabusa/

[41] BioMADE. (2022). https://www.biomade.org/

for Innovation in Manufacturing Biopharmaceuticals (NIIMBL), which develops biologic drugs such as proteins, peptides, RNA, and DNA.[42] These centers have made significant advances in each of their fields, but as currently constituted, they are not able to support product development at the point of transition from prototyping to pilot scale manufacturing. They also do not have the requisite authorities or biomanufacturing capacity and capabilities to support the increasingly wide range of bioproducts currently in the development pipeline. This creates a major impediment to growing the biomanufacturing capacity needed to develop and scale bioproducts.

Indeed, many bioproduct developers have found the limited biomanufacturing infrastructure and the high cost of launching new products in the United States to be a significant impediment to bringing their products to commercial scale. As a result, some developers have moved their biomanufacturing to countries that have established manufacturing infrastructure and technical expertise or that provide co-location of biomanufacturing facilities with biological crops and other resources—options that help to contain manufacturing costs (for more information see Appendix D).

The challenges in biomanufacturing will continue to grow with the increased diversity, complexity, and sophistication of bioproducts and biomanufacturing processes, heightened global competition, and great demand associated with surges in the sheer number of products in the development pipeline (see Figure 3). For well-known biological processes, like fermentation, a large capital expense is required to begin production. Furthermore, in some cases, entirely new biobased manufacturing processes for which there are no standardized production methods will be needed. Developing these methods requires even greater effort than scaling known processes. Federal and private research and development (R&D) efforts coordinated with existing and future

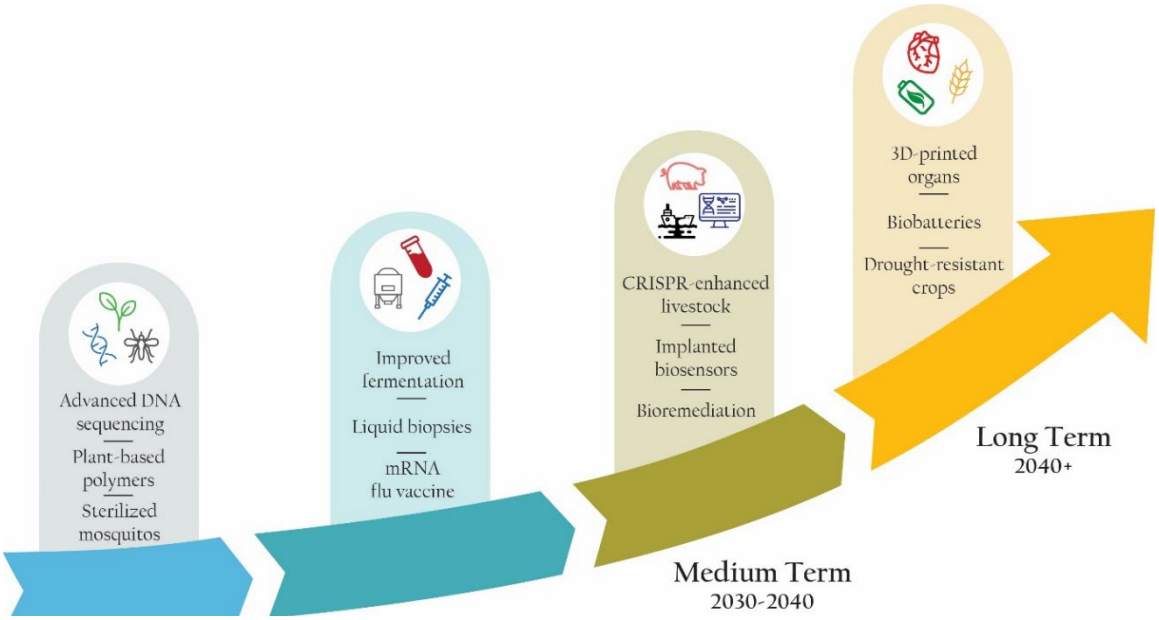

Figure 3. An estimated prospective timeline for development of example bioproducts

Source: Adapted from Exhibit E5, *McKinsey Global Institute (2020). The Bio Revolution: Innovations transforming economies, societies, and our lives.*

[42] NIIMBL. (2022). https://niimbl.force.com/s/

biomanufacturing infrastructure hubs will help to leverage state-of-the-art knowledge to advance these new manufacturing processes.

Ultimately, the ability to translate the many promising biotechnologies from lab to a manufacturing-relevant scale requires:

- a strong and technically advanced biomanufacturing base that aligns with industrial growth in biotechnology, including the design and operation of pilot scale facilities capable of developing new biomanufacturing approaches (e.g., the purification of bioproducts);
- a skilled and diverse workforce at every level, from equipment operators to advanced process engineering and development; and
- shared infrastructure that can support development of different bioprocesses and products to efficiently advance innovation through each phase of scale up—from fundamental research to manufacturing-relevant production.[43]

Recommendation 1.1:

The Secretary of Commerce should establish biomanufacturing infrastructure hubs with the authorities and resources necessary to successfully scale up from prototype components in a production relevant environment (Manufacturing Readiness Level [MRL] 6) to low-rate production capability (MRL 8) by expanding the capability and capacity of the Manufacturing USA Institutes and leveraging the Regional Technology Hubs authorized in the CHIPS and Science Act.

Recommendation 1.2:

The OSTP Director and the Secretary of Commerce, in consultation with the Secretary of Defense, the Director of NSF, and the Secretary of Energy, should develop a plan that A) includes a competitive process for determining biomanufacturing infrastructure hubs' specific foci, funding allocations, and geographic locations and B) directs the creation of a network that connects the hubs established via any of the available innovation hub programs, including the Manufacturing USA Institutes, the Department of Commerce Regional Technology Hubs, the Department of Defense biomanufacturing initiatives, Department of Energy Agile BioFoundry Consortium, and the National Science Foundation Regional Innovation Engines. The plan should be completed within 180 days of the publication of this report.

These recommended biomanufacturing infrastructure hubs at MRLs 6–8 will help to fill a number of important roles in supporting the growth of the bioeconomy, including physical facilities, continuing education and hands-on training, R&D for bioproducts/bioprocessing, and touchpoints between regulators and industry.

To meet the critical demand for pilot scale manufacturing that is flexible and adaptive, the hubs should contain the facilities, equipment, and staff needed to transition a prototype product from low-level laboratory production to low-rate initial production in a manufacturing-relevant environment.

[43] National Academies of Sciences, Engineering, and Medicine. (2015). *Industrialization of Biology: A Roadmap to Accelerate the Advanced Manufacturing of Chemicals*. https://nap.nationalacademies.org/catalog/19001/industrialization-of-biology-a-roadmap-to-accelerate-the-advanced-manufacturing

Further, the hub facilities should be designed for modularity and adaptability for a range of new bioproducts. The hubs will also serve as integrated technological centers distributed across the Nation at locations selected to leverage regional biological and agricultural resources, train skilled workers, and enhance geographic diversity.[44]

Symbiotic Supplements

Many farmers supplement their soil with synthetic fertilizers and manure, which, when used in excess, can negatively affect the environment by increasing greenhouse gas emissions, thinning the ozone, contaminating drinking water sources, and harming aquatic life.[45,46] California-based Pivot Bio created new fertilization technology that harnesses the natural relationship between crops and microbes. The company modifies microbes that attach themselves to the root of the plants, feed on sugars, and convert atmospheric nitrogen into beneficial ammonia for the crops, facilitating plant growth.[47] While the microbes are removed after harvesting, their ability to attach directly to roots makes them more resilient against removal by rainwater compared to typical synthetic nitrogen. This new method has proven successful; according to Pivot Bio, their microbes increased corn plant biomass by 6.5%. Farmers and investors have taken notice: Pivot Bio has tripled its revenue in 2021 and has reached a nearly $2 billion valuation.[48] An expanded biomanufacturing infrastructure system in the United States would catalyze the development of more companies like Pivot Bio, bolstering the agricultural sector through sustainable, technologically advanced means.

Source: Pivot Bio

The funding for these biomanufacturing infrastructure hubs should originate from public-private partnerships, and a substantial portion of the funding for the hubs should come from private industry. We anticipate that each hub facility could be catalyzed with a Federal investment on the order of $50 million. Federal funding can serve as an important signal to State and local governments and the private sector about priorities within this area, which can lead to increased overall

[44] Ensuring the geographic diversity of the hubs aligns with the CHIPS and Science Act, which requires consideration of geographic diversity in the selection of new Manufacturing USA institutes and Regional Technology and Innovation Hubs.

[45] University of Minnesota Extension. (2021). Understanding nitrogen in soils. https://extension.umn.edu/nitrogen/understanding-nitrogen-soils

[46] United States Environmental Protection Agency. (2021). *Understanding the Impacts of Synthetic Nitrogen on Air and Water Quality Using Integrated Models.* https://www.epa.gov/sciencematters/understanding-impacts-synthetic-nitrogen-air-and-water-quality-using-integrated

[47] Pivot Bio. (2022). https://www.pivotbio.com/product-proven

[48] Feldman, A. (2021, July). Pivot Bio Nears $2 Billion Valuation As It Raises Whopping $430 Million To Replace Synthetic Fertilizers On Corn And Wheat. *Forbes.* https://www.forbes.com/sites/amyfeldman/2021/07/19/pivot-bio-nears-2-billion-valuation-as-it-raises-whopping-430-million-to-replace-synthetic-fertilizers-on-corn-and-wheat-sustainability/?sh=237eb87d2273

investment. The Federal portion of the funding for these hubs could be obtained through programs authorized in the CHIPS and Science Act—such as the Department of Commerce Regional Technology and Innovation Hubs or NSF's Regional Innovation Engines—from other relevant new or existing programs, or alternatively through budgetary discussions with the Office of Management and Budget (OMB).

Integration across the regional biomanufacturing infrastructure hubs is crucial. As an integrated network, the hubs would have the ability to share science and expertise across different biotechnology and biomanufacturing areas. This structure provides a means to create deep expertise in specific areas of the bioeconomy within a single hub, while establishing a network to share information and methods across hubs in different manufacturing areas.

Integrated Biomanufacturing Ecosystems

Consistent with the Manufacturing USA program, the biomanufacturing infrastructure hubs will be private-public partnerships that engage industry to form integrated networks across regions of the country based on advantageous bioeconomic drivers (biological feedstock, commercial advantage, availability of trainable workforce). The hubs will also engage local universities, startup companies, and other nearby research institutions and/or national labs to accelerate R&D and speed the translation and pace of new discoveries to practical applications.

Recommendation 1.3:

NSF, DOD, DOE, FDA, NIH, USDA, and other relevant agencies should form partnerships and establish funding opportunities with local university and research institutions that coordinate with the biomanufacturing infrastructure hubs. These partnerships should focus on bioprocessing and biomanufacturing, establish advanced biomanufacturing research opportunities that leverage or expand the biomanufacturing infrastructure hub network and facilities, and support programs across the spectrum of postsecondary training opportunities in this area.

These partnerships with key science and engineering agencies enable the development of the new and more advanced methods needed to improve and expand biomanufacturing approaches and address some of the challenges of current bioprocess and manufacturing methods. Partnerships should provide training opportunities for doctoral students and increase the workforce for expertise at the bachelors and doctoral level through university research funding. For example, partnerships with graduate degree-granting institutions could also include doctoral students, whose work will contribute to the advancement of innovative biomanufacturing research at universities through collaborative efforts with industry partners that leverage the hub facilities.

Furthermore, the biomanufacturing infrastructure hubs should provide hands-on training for skilled workforce development and should engage community colleges, universities, and technical education programs to develop training curricula for bioprocess operations, manufacturing design principles, and bioethics. The recommended partnerships will play an important role in supporting programs across the spectrum of post-secondary training opportunities, in particular providing apprenticeship programs to train workers. The proposed hubs should engage both 2-year and 4-year institutions of higher education to include training platforms and internships to promote on-the-job training. In this way, individuals with high school or associate's degrees might be introduced to training opportunities geared toward the operational aspects of bioprocesses or other technical skills

that could be acquired as part of a community college degree or with adult education certificates. Ultimately, the jobs generated by these manufacturing facilities and the companies that service and supply them will create greater economic opportunities for low- and middle-income Americans at a variety of skill and training levels.

This report highlights a few of the critical needs the hubs can fulfill, but it is not exhaustive. In fulfilling these needs and others not specified here, the recommended hubs should align with the activities of the National Biotechnology and Biomanufacturing Initiative outlined in the CHIPS and Science Act, which specifically calls for the development of interdisciplinary research centers to progress and scale up biomanufacturing.

Educating an Appropriately Skilled Workforce

According to USDA's recent report on the biobased products industry—which includes agriculture and forestry; biobased chemicals; biobased plastic bottles and packaging; biorefining; enzymes; forest products; and textiles—over four million Americans were employed in this sector in 2017.[49] Based on prior USDA data, researchers estimate that these sections of the bioeconomy alone could see an additional one million jobs added by 2030.[50]

However, in order to realize this potential to create new jobs for American workers and support the growth of new companies, more educational and training opportunities are needed. Indeed, the size and skillset of the U.S. biomanufacturing workforce has not kept up with the needs of U.S. biomanufacturing companies. In its *Safeguarding the Bioeconomy* report,[51] the National Academies notes that insufficient Federal funding for university bioeconomy training programs threatens the Nation's capacity to build and retain the needed technical workforce. Biotechnology and biomanufacturing require educational programs that combine fundamental engineering and manufacturing science principles with an experiential component that can be difficult to replicate in typical university labs.

At this time, only a small number of universities have launched bioprocessing-focused programs that provide instruction on how to manage reactor design, product flow, and scale up from pilot to large scale facilities. Currently, most universities provide biotechnology and bioprocessing education only in chemical or biological engineering or industrial/process engineering departments (see examples of relevant programs in Appendix B). As a result, there is a shortage of scientists and engineers who have the deep knowledge of biological processes, chemical and systems engineering, machine learning, and process design that are necessary to develop new manufacturing processes.[52] Undergraduate programs are needed to train bioprocess engineers in foundational concepts, and

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[49] U.S. Department of Agriculture. (2019). *An Economic Impact Analysis of the U.S. Biobased Products Industry*. https://www.rd.usda.gov/sites/default/files/usda_rd_economic_impact_analysis_us_biobased_products_industry.pdf

[50] Rogers, J. N., Stokes, B., Dunn, J., Cai, H., Wu, M., Haq, Z., & Baumes, H. (2017). An assessment of the potential products and economic and environmental impacts resulting from a billion ton bioeconomy. *Biofuels, Bioproducts and Biorefining*, *11*(1), 110–128. https://doi.org/10.1002/bbb.1728

[51] National Academies of Sciences, Engineering, and Medicine. (2020). *Safeguarding the Bioeconomy: Finding Strategies for Understanding, Evaluating, and Protecting the Bioeconomy while Sustaining Innovation and Growth*. https://www.nationalacademies.org/our-work/safeguarding-the-bioeconomy-finding-strategies-for-understanding-evaluating-and-protecting-the-bioeconomy-while-sustaining-innovation-and-growth

[52] Ibid.

master's degree programs are needed to provide opportunities for students to focus foundational skills on bioprocess design and management.

Additionally, there is a paucity of experiential training opportunities across the country,[53] and a strong need for hands-on learning in the operation of biomanufacturing facilities—from reactor maintenance to product quality assurance. PCAST found only three apprenticeship programs created explicitly for biomanufacturing in the United States. Segments of the biomanufacturing industry have begun to form education partnerships[54] with States and local governments, community colleges and universities, certificate and degree programs, and apprenticeships that blend industry biomanufacturing needs with existing educational programs; this is a good start, but such partnerships are few compared to industry needs (see "Model of a Modern Major-Apprentice" vignette below and "Partnerships Make Perfect" vignette in Appendix C).

Model of a Modern Major-Apprentice

Source: MassBioEd

Behind every bioproduct, from cancer therapy treatments to alternative meat products, there is a long line of scientists, manufacturers, line workers, assemblers, and engineers involved in the production process. These workers make it possible for bioproducts to be created and delivered to the American people, but there need to be enough workers with these skills to meet employer demand. That is why organizations like MassBioEd and the North Carolina Community College System are pairing with private industry to offer biomanufacturing apprenticeships in the United States at major companies. These apprenticeships serve as a pathway for good-paying, stable jobs for many Americans without the need for an advanced degree—all while tapping into the diverse workforce available right here in the United States. For example, at MassBioEd's Biomanufacturing Technical Apprenticeship, apprentices range in age from 19 to 63, of which two-thirds are women and 60% are people of color, with backgrounds in chemistry, architecture, education, and retail.[55] These types of programs, which would be mirrored and expanded upon in the new biomanufacturing infrastructure hubs, are paving the path for many Americans to begin new careers.

[53] U.S. Department of Labor. (2022). *APPRENTICESHIPUSA*. Accessed June 13, 2022. https://www.apprenticeship.gov/?utm_source=dol_gov_agencies_eta_apprenticeship&utm_medium=text&utm_campaign=apprenticeship_homepage.

[54] Blois, M. (2022, February 7). "Help wanted in biomanufacturing." *Chemical & Engineering News.* https://cen.acs.org/education/Help-wanted-biomanufacturing/100/i5

[55] Talanian, K. (2022, March 24). An Update on the MassBioEd Life Sciences Apprenticeship Program. MassBioEd. https://www.massbio.org/news/recent-news/an-update-on-the-massbioed-life-sciences-apprenticeship-program/

Regulatory Approval Process

Regulatory Uncertainty

Public confidence in novel products and processing methods depends on rigorous health, safety, and environmental regulatory review. Many Federal regulations require new products to undergo safety testing to prevent harmful effects to the health of the public and the environment. For many bioproducts, and especially for those that are novel or cross-cutting, the country will need to invest in new regulatory processes that maintain the same rigor, but increase the pace at which these products can move through the review and approval process. Additionally, regulatory uncertainty can lead to long review times, which can hamper business development. Economic research shows that regulatory uncertainty contributes to reductions in industrial output, investment, consumption, and hiring—and creates a competitive disadvantage if other countries streamline their regulatory processes more effectively and faster than the United States.[56] This disadvantage is compounded for biotechnology, which produces novel and innovative bioproducts across multiple regulatory domains. Indeed, bioproducts often do not align well with pre-existing authorities.[57]

The regulatory approval pathway is clearer for medicines than for other bioproducts. For example, if a new bioproduct is intended to be a drug for human use, it falls under FDA's regulatory authority and is assessed for its safety and efficacy. On the other hand, if it is a food for human consumption, it may require review by both USDA (if it is a meat, poultry, or egg product) and/or FDA (for all other foods) for safety. If it is a pesticide that will be applied to food that will be eaten by humans, it would undergo review by the EPA and/or USDA and/or FDA. The organism(s) in the bioprocess, as well as the final products, may be reviewed by USDA and EPA for their ecological risks should they be released into the environment, and by the Occupational Safety and Health Administration (OSHA) for worker safety.

EPA, FDA, and USDA published the U.S. Coordinated Framework for Biotechnology Products in 1986[58] and, given the increasing number of bioproducts and their increasing complexity, the agencies updated the framework in 2017.[59] The framework provides an outline of regulations that may apply to biotechnology products and guidance to navigate the regulatory process within each agency. However, many new bioproducts do not align with a single regulatory process entry point or pathway. Therefore, bioproducts may not fit neatly within agency jurisdictions under existing statutes, and the framework does not have guidance to help companies determine which agency or agencies have jurisdiction over their product or components of their product. For some products, this situation may necessitate regulatory filings to multiple agencies, possibly requiring different datasets and different formats for each agency to demonstrate safety and efficacy. All of this can lead to potentially wasted time and effort for both regulators and product developers.

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[56] Xie, Z. (2022). *Comparing Regulatory Uncertainty with Other Policy Uncertainty Measures*. The George Washington University Regulatory Studies Center. https://regulatorystudies.columbian.gwu.edu/sites/g/files/zaxdzs4751/files/2022-06/gw-reg-studies-comparing-regulatory-uncertainty-with-other-policy-measures-zxie.pdf

[57] National Academies of Sciences, Engineering, and Medicine. (2017). *Preparing for Future Products of Biotechnology*. https://www.ncbi.nlm.nih.gov/books/NBK442204/

[58] Ibid.

[59] United States Environmental Protection Agency. (2017). *Modernizing the Regulatory System for Biotechnology Products: Final Version of the 2017 Update to the Coordinated Framework for the Regulation of Biotechnology*. https://usbiotechnologyregulation.mrp.usda.gov/2017_coordinated_framework_update.pdf

Recommendation 2.1:

The EPA Administrator, Secretary of Agriculture, and FDA Commissioner should establish a standing Rapid Response Team of key agency representatives that meets regularly and frequently to vet new, cross-cutting products and provide recommended regulatory routes for bioproducts to developers. This team should be involved with the continued development of the Unified Website for Biotechnology Regulation that is required by EO 14081. The Rapid Response Team should provide opportunities to cross-train regulatory staff members as guides that would reside within each agency to support the review of bioproducts.

The Rapid Response Team (RRT) should be composed of bioproducts regulatory experts who are familiar with FDA, EPA, USDA regulations and able to respond rapidly to industry inquiries about regulatory requirements for bioproducts. The RRT should cross-train additional regulatory staff in the responsibilities of two or more of the key regulatory agencies so that more regulatory staff are equipped to effectively guide inquiries about regulation of new cross-cutting bioproducts.[63] The RRT, working with regulatory agency leadership, will chart and vet anticipated regulatory pathways for

Comfortable in My Own Bioskin

Source: Mallinckrodt Pharmaceuticals

In 2020 alone, more than 1,000 firefighters sustained burn injuries while at the fireground.[60] In the most severe cases, injured firefighters are often treated by autografts—transplants of the patient's healthy skin to the wound area. This process of collecting skin for the transplant can cause pain, infection, or scarring. To replace this traditional method, researchers at Mallinckrodt Pharmaceuticals have invented StrataGraft, a biobased synthetic skin that can be applied at the site of injury to promote the patient's own skin cells to grow over the injury site. In clinical trials, StrataGraft-treated wounds were 25 times less likely to need a follow-up treatment compared to traditional autograft-treated wounds.[61] Following these successes, in 2021, StrataGraft was approved by the FDA for treatment of adult patients with thermal burns, potentially revolutionizing the way that severe burns are treated.[62] With streamlined regulatory approval pathways, it will be easier for more paradigm-shifting products like StrataGraft to come to market, revolutionizing the way that first responders and everyday Americans receive treatment.

[60] Campbell, R., & Evarts, B. (2021). United States Firefighter Injuries in 2020. *National Fire Protection Association*. https://www.nfpa.org/-/media/Files/News-and-Research/Fire-statistics-and-reports/Emergency-responders/osffinjuries.pdf

[61] Kuehn, B. (2021, August 3). FDA Approves Skin Graft Alternative for Thermal Burns. *JAMA Network*. https://jamanetwork.com/journals/jama/fullarticle/2782661

[62] United States Food and Drug Administration. (2021, June 15). FDA Approves StrataGraft for the Treatment of Adults with Thermal Burns [Press release]. https://www.fda.gov/news-events/press-announcements/fda-approves-stratagraft-treatment-adults-thermal-burns

[63] EPA, FDA, and USDA have primary responsibility for regulating biotechnology products and have several efforts designed to clarify bioproduct regulation.

novel bioproducts. The Director of OMB should identify additional funding required to implement this approach, including additional personnel and training resources.[64]

Model Pathways and Coordinated Information Sharing

Responding to private sector concerns about lengthy approval times[65] and lack of clarity of the regulatory process for bioproducts, the regulatory agencies developed a Unified Website for Biotechnology Regulation to explain agency responsibilities and the authorities from relevant legislation.[66] While establishing the website was an important step in the right direction, it currently lacks the information (e.g., decision trees) developers need to understand the agency specific processes applicable to their bioproducts. Further efforts are needed to harmonize regulatory processes and requirements, eliminate redundancies and duplications of effort, and deliver the appropriate information on navigating these processes directly to developers.

Making the Unified Website for Biotechnology Regulation fully operational will require ongoing technical support and a dedicated team of knowledgeable, experienced regulatory scientists. As a part of this effort, the RRT could provide the expertise required to develop model bioproduct review pathways and disseminate them through the site to make the review process more predictable and shorten time from submission to approval. These efforts could also be coupled with the creation and dissemination of other changes that facilitate the effective review of bioproducts such as updated guidance on risk assessments.

Recommendation 2.2:

FDA, EPA, and USDA should develop streamlined and model pathways for regulatory review and approval of emergent bioproducts of similar type by either a) drawing from the evolution of pathways as a result of past product review processes, and/or b) creating an open access, searchable library of previously determined routes or pathways for new bioproducts as they are established.

The creation of a Bioproducts Interagency Working Group (BIWG) is a mechanism that could develop these streamlined and model regulatory pathways and act as a vehicle for sharing promising practices across agencies. For example, FDA could provide information on its expedited approval process for advanced manufacturing.[67] USDA could share its recently revised biotechnology regulatory process.[68] In the latter case, the agency updated its regulations related to biotechnology in 2021. The initial results of the updated regulations appear to hold promise for supporting the expanding bioeconomy: Since their launch, USDA has seen an increase in the diversity of new crop

[64] EO 14081 recognizes the complexity of regulatory review and approval of new products of biotechnology and biomanufacturing and sets out a number of steps the regulatory agencies undertake to "clarify and streamline regulations in service of a science- and risk-based, predictable, efficient, and transparent system to support the safe use of products of biotechnology."

[65] There is anecdotal information about companies' experiences with regulatory review of novel bioproducts but little hard data about whether a prolonged regulatory review led companies to stop development of novel products or processing approaches.

[66] See: https://usbiotechnologyregulation.mrp.usda.gov/biotechnologygov/home/

[67] See: https://www.fda.gov/industry/prescription-drug-user-fee-amendments/pdufa-vii-fiscal-years-2023-2027

[68] Croft, G., & Cowan, T. (2020). *USDA's SECURE Rule to Regulate Agricultural Biotechnology.* CRS In Focus. Congressional Research Service. https://crsreports.congress.gov/product/pdf/IF/IF11573/2

types, an increase in applications from small businesses, and a dramatic increase in the number of first-time petitioners.

BIWG members could be selected from each of the three regulatory agencies with their respective divisions responsible for review of bioproducts. The BIWG could report to the heads of the agencies (the FDA Commissioner, USDA Secretary, and EPA Administrator) and be guided by the NSTC Executive Director, the NSF Director, and the Secretary of the Department of Commerce.

Investing in Federal Scientists

Federal scientists working in regulatory agencies have been constrained in their ability to remain up-to-date with science and technology trends over the last decade, missing opportunities to learn about the novel technologies and products that ultimately require their review. Opportunities for participating in scientific conferences and other educational opportunities are very limited for the Federal scientific community, yet these opportunities provide an important platform for brainstorming and information exchange, and developing new initiatives and innovative approaches to regulation.[69,70] Cross-cutting, high quality research and innovation are often a result of collaborations developed at scientific meetings.[71] To best fulfill their agency's science-based mission, Federal scientists need the opportunity and resources to engage in professional development activities.[72]

Recommendation 2.3:

FDA, USDA, and EPA should create a training and information network that links across the biomanufacturing infrastructure hubs and existing or future federally funded advanced biomanufacturing centers (e.g., BioMade, BioFAB, NIIMBL, and other relevant centers) and assigns regulatory scientists as affiliates to the biomanufacturing infrastructure hubs.

The network should be designed to connect regulatory scientists with emergent products and their biomanufacturing processes, enable regulatory staff to remain current with emerging technologies, and provide insights as manufacturing processes are implemented and expanded. The hubs described in the previous section could provide opportunities for Federal regulatory scientists to keep abreast of emerging technologies through participation in the biomanufacturing infrastructure hubs as liaisons to various development and training programs, while still maintaining protocols to allow for an independent regulatory review of bioproducts.

Creating this network could lead to several beneficial outcomes. First, this type of participation could lead to better coordination among the regulatory agencies reviewing new bioproducts and technologies and enable more cross-regulatory conferencing between agencies at early-stage development. Second, access to the novel processes and products could help the regulatory agencies to better anticipate the necessary measures and regulatory pathways for new products. This can help

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[69] Ibid.
[70] Oester, S., Cigliano, J. A., Hind-Ozan, E. J., & Parsons, E. C. M. (2017). Why Conferences Matter—An Illustration from the International Marine Conservation Congress. *Frontiers in Marine Science*, *4*(257), 257. https://doi.org/10.3389/fmars.2017.00257
[71] Union of Concerned Scientists. (2018). *DOI Restricts Scientists From Attending Scientific Conferences*. https://www.ucsusa.org/resources/attacks-on-science/doi-restricts-scientists-attending-scientific-conferences
[72] Ibid.

shorten the time for review and encourage developers to move together toward review rather than waiting to be a "fast second."

Additionally, this network could enable regulatory scientists to attend scientific presentations and shared science activities, and to engage virtually and on-site with bioproduct and bioprocess developers as new products evolve at the hubs. Early engagement with innovative bioprocesses could prepare Federal regulatory scientists to better provide guidance to companies seeking regulatory approval. For example, if an emerging manufacturing process is sufficiently well described, it may be able to be reviewed independent of any particular product, which would allow developers to scale development of novel products safely and expeditiously during emergencies. Lastly, this network could serve as an important pipeline for recruiting regulatory scientists by enabling scientists to interact with and mentor students and young professionals who may be interested in regulatory science.

A New, Data-Based Strategy for the Bioeconomy

To remain competitive in the global marketplace, the United States needs a whole-of-government strategy to guide agency efforts—one that is attuned to the evolving ethical, social, and legal issues as well as the science and technology. Much has been accomplished under the *National Bioeconomy Blueprint,*[73] but much has changed in 10 years since it was published. A new action plan is urgently needed and strongly recommended to chart a course for the next decade with a long view based on current needs and technologies and the latest thinking on the future of this rapidly evolving field.

The breadth and complexity of the bioeconomy, the integrated and multi-disciplinary nature of science and engineering, and the distribution of responsibilities for the bioeconomy among multiple Federal agencies make it difficult for the United States to maximize benefit for the American people and remain internationally competitive. The passage of the CHIPS and Science Act has launched new Federal R&D initiatives with direct implications for biomanufacturing nd the bioeconomy in several agencies (e.g., NSF, DOC, DOE, and DOD); however, these initiatives are not biomanufacturing and bioeconomy-specific and their efforts to advance the bioeconomy are not informed by an overarching national bioeconomy strategy. A coherent guiding strategy and metrics to assess progress in achieving national goals will significantly strengthen U.S. competitiveness in the global bioeconomy.

Recommendation 3.1:

The National Science and Technology Council (NSTC) should prepare a long-term (10-year) strategy for the bioeconomy. This strategy should be informed by the reports required by the CHIPS and Science Act and EO 14081. The strategy should be completed and delivered within 18 months to the OSTP Director. The strategy must consider the long-term economic, environmental, and societal benefits and liabilities of the proposed actions and policies as well as national security implications.

The national strategy should address key facets of the bioeconomy including:

- workforce development;
- infrastructure needs;

[73] The White House. (2012) *National Bioeconomy Blueprint*. https://obamawhitehouse.archives.gov/sites/default/files/microsites/ostp/national_bioeconomy_blueprint_april_2012.pdf

- data and information sharing and management;
- ethical, legal, and societal issues;
- sustainability, environmental, and climate goals;
- national security;
- privacy; and
- metrics for assessing growth in the bioeconomy.

The strategy should clearly define the process for measuring the scope of the bioeconomy, and statistical agencies should collect data on the key strategy elements to chart progress and initiate data-driven course corrections.

Developing a new long-term national bioeconomy strategy will be challenging. The strategy will need to include clear, achievable objectives, options to adapt the strategy to a continually evolving bioeconomy landscape, and measures to determine progress and reorient programs and funding. Formal data collection and analysis methods to assess progress in achieving strategic objectives are essential but not yet identified, nor are there adequate mechanisms to collect data to monitor the growth of this economic sector. The ultimate measure of success would be that products of the bioeconomy are accessible and affordable to all.

In EO 14081, President Biden set a new course for the bioeconomy by bringing multiple programs administered in five Federal agencies together in a concerted strategy to maintain U.S. leadership in biotechnology research, its translation into new bioproducts and, ultimately, a thriving bioeconomy. Supporting this work, the Secretary of Commerce is charged with developing a lexicon to inform the development of measurements of the bioeconomy and the Chief Statistician is charged with coordinating statistical agencies' data collection related to the bioeconomy, including providing recommendations related to the 2027 revision of the North American Industry Classification System (NAICS).

Using provisions of the CHIPS and Science Act, the President can continue setting a new course for the bioeconomy to maintain U.S. leadership in research, biotechnology, and the translation of these into new bioproducts and a thriving bioeconomy. The Act authorizes several new programs and funding that are important building blocks for biomanufacturing and the Nation's longer-term bioeconomy, along with a coordination mechanism and reports to Congress. These programs and reports are necessary inputs to any long-term strategy.

Societal Implications

Bioeconomy policies must be sensitive to civil society's concerns and contribute to communities' long-term welfare, especially underserved communities. The CHIPS and Science Act launched new research programs to examine the ethical, legal, environmental, and social considerations related to growing the bioeconomy. Previously, little investment has been made in the research needed to understand these evolving viewpoints. The national strategy should consider how to coordinate resource investments ethically and equitably across communities. Bioeconomy policies must consider the ethical implementations of new technologies and societal impacts including environmental sustainability and environmental justice. The national strategy should also consider how to develop best practices for effective engagement with the public to encourage an informed perspectives of bioproducts and their associated risks and benefits.

The innovations that drive the bioeconomy have the potential for both beneficial and nefarious applications. For example, inexpensive and accessible methods for gene editing facilitate novel research. However, this accessibility also creates an opportunity for malicious actors to use the technology to create dangerous viruses or for citizen scientists to perform science experiments that have unintended adverse consequences.[74,75] Use of individual genetic information that is stored in large database generates concerns about privacy and confidentiality.[76] There may also be unintended negative consequences to growing the bioeconomy. In some cases, the additional pressure on a region's biological resources could have negative effects on the sustainability of those resources. The inclusion of a process to develop evidence-based ethical guidelines that consider individual, cultural, and national practices, combat malicious actors, and minimize unintended consequences in this national bioeconomy strategy is critical to the healthy expansion of the bioeconomy.

Recommendation 3.2:

The OSTP Director should include research needs of the bioeconomy as a key component of the National Biotechnology and Biomanufacturing Initiative outlined in EO 14081; and the National Engineering Biology Research and Development Initiative and the 5-year coordinated research report designated by the CHIPS and Science Act to be delivered in 2023. These plans should emphasize the fundamental and translational research needed to accelerate the growth of the bioeconomy and other key objectives for international competitiveness.

The CHIPS and Science Act authorizes new bioeconomy-related R&D initiatives, grant programs, hubs, centers and user facilities to be administered by three different Federal departments and coordinated by the NSTC. Because so many of these programs provide the research base and facilities necessary for the biomanufacturing infrastructure hubs recommended above, the preparation of a new national bioeconomy strategy should be integral to the interagency work on a National Engineering Biology Research and Development Initiative and the OSTP-led 4-year national science and technology strategy. The past decade has made clear several key gaps in the original strategy, particularly as they relate to later stages in R&D; workforce development; manufacturing challenges and capacity; lack of information about this sector of the economy; and little consideration of its social, ethical, and legal dimensions. The national strategy should focus on incentives for biomanufacturing and the broader bioeconomy to reap climate risk reduction and equitable economic development goals in ways that are broadly accepted by Americans.

Data Management and Sharing

Standards are lacking for sharing data among researchers and developers that would allow them to access and use pre-competitive information relevant to new product formulations and mechanisms for bringing products to scale. Scientific information that is the base for biomanufacturing encompasses genomics, synthetic biology, biochemistry, bioprocessing, and the performance of

[74] McKinsey Global Institute. (2020). *The Bio Revolution: Innovations transforming economies, societies, and our lives*. https://www.mckinsey.com/industries/life-sciences/our-insights/the-bio-revolution-innovations-transforming-economies-societies-and-our-lives

[75] Baumgaertner, E. (2018, May 14). As D.I.Y. Gene Editing Gains Popularity, 'Someone Is Going to Get Hurt'. *The New York Times*. https://www.nytimes.com/2018/05/14/science/biohackers-gene-editing-virus.html

[76] McKinsey Global Institute. (2020). *The Bio Revolution: Innovations transforming economies, societies, and our lives*. https://www.mckinsey.com/industries/life-sciences/our-insights/the-bio-revolution-innovations-transforming-economies-societies-and-our-lives

specific organisms and enzymes under different environmental conditions. Considering how challenging the identification and management of relevant data can be, the NSTC could play a pivotal role in accelerating the bioeconomy by developing ways to share data securely based on successful models that enabled microfabrication and integrated circuit industries in the 1980s—and more recently, examples such as the National Cancer Institute's Nanotechnology Characterization Laboratory, the collaboration of 10 pharmaceutical companies on the Machine Learning Ledger Orchestration for Drug Discovery project, and the National Microbiome Data Collaborative.[77]

Recommendation 3.3:

The Secretary of Commerce should direct the Bureau of Economic Analysis to establish a satellite account[78] for the bioeconomy as soon as possible and no later than FY 2024. Federal statistical agencies should plan to provide data for the strategy's established metrics and request the resources necessary to do so in their budget requests for FY 2025. The plan should provide the data necessary for the metrics defined by the NSTC strategy and with the cadence necessary to track the bioeconomy.

Metrics

Measuring the bioeconomy's contribution to the larger U.S. economy is difficult because definitions of the bioeconomy vary widely, there are substantial gaps in data on the bioeconomy, and the bioeconomy spans several economic sectors. In their 2020 report on the bioeconomy, the National Academies developed a targeted and specialized framework for analyzing the value of the bioeconomy across six segments: genetically modified crops; biobased industrial materials; biopharmaceuticals; biotechnology consumer products; biotechnology R&D business service; and design of biological data-driven patient health care solutions. Their estimate of the value of the bioeconomy, $959 billion, is based on this framework.[79] However, there is currently no means of regularly updating these economic estimates. A satellite account would help the country to understand much better the real economic impacts of this sector and make realistic assessments about future growth, rather than the current projections from one-off studies.

Metrics about the status of the emerging bioeconomy and the key data supporting their generation need to be identified, and existing metrics, such as the Bureau of Labor Statistic's Quarterly Census of Employment and Wages program, could be expanded to track the development of the bioeconomy workforce.[80] EO 14081 calls on the Chief Statistician "to improve and enhance federal statistical data collection designed to characterize the economic value of the United States bioeconomy." As agencies coordinate gathering metrics, regular updates should be provided to the NSTC to enhance the ability to track progress on the national strategy, identify bottlenecks inhibiting progress, and distill key

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[77] Schmidt Futures. (2022). *The U.S. Bioeconomy: Charting a Course for a Resilient and Competitive Future*. https://www.schmidtfutures.com/wp-content/uploads/2022/04/Bioeconomy-Task-Force-Strategy-4.14.22.pdf

[78] The statistics in the Bureau of Economic Analysis' (BEA) satellite accounts take a close look at a part of the economy, such as outdoor recreation, health care, or marine-related activities. For more information see this BEA one-pager.

[79] National Academies of Sciences, Engineering, and Medicine. (2020). *Safeguarding the Bioeconomy: Finding Strategies for Understanding, Evaluating, and Protecting the Bioeconomy while Sustaining Innovation and Growth*. https://www.nationalacademies.org/our-work/safeguarding-the-bioeconomy-finding-strategies-for-understanding-evaluating-and-protecting-the-bioeconomy-while-sustaining-innovation-and-growth

[80] United States Bureau of Labor Statistics. (2022). *Quarterly Census of Employment and Wages*. https://www.bls.gov/cew/

elements contributing to the growth of the bioeconomy. The long-term strategy will be better informed by having regular, well-defined information on the progress of the bioeconomy, such as gross national product attributed to bioproducts, the number and education level/type of training required for bioeconomy jobs, as well as regional and national economic growth attributed to the bioeconomy.

Conclusion

The technological advances and fundamental research that launched the bioeconomy were achieved through the application of engineering principles to biological systems and new capabilities in genetics, computing, and information sciences. The convergence of these sciences under the rubric *biotechnology* produced innovations in consumer products across our national priorities for energy, agriculture, food, pharmaceuticals, and national security. Recognizing biotechnology's potential for economic growth and environmental and societal benefits, the Obama-Biden Administration published the *National Bioeconomy Blueprint* in 2012 and identified the emerging bioeconomy as a national priority.[81] Biotechnology has since evolved into an essential component of solutions to critical societal challenges and serves as the scientific basis for our bioeconomy; however, national efforts to promote biotechnology, biomanufacturing, and the bioeconomy have since become disjointed.[82]

PCAST recommends that the three key gaps identified in this report be addressed to strengthen our competitive advantage in this critically important and growing economic sector. The limited biomanufacturing capacity needed for translational efforts to launch new products and train the workforce can be addressed through the establishment of biomanufacturing infrastructure hubs that result from industry-government-academic partnerships. The regulatory processes for new bioproducts must become streamlined and more transparent and efficient. Finally, a data-informed and integrated national strategy that provides a broad 10-year vision for the bioeconomy will enable the country to take maximum advantage of programs authorized in EO 14081 and the CHIPS and Science Act and seize opportunities crucial to our competitive advantage and global leadership. When combined with accelerating private sector activity across the bioeconomy, these efforts will help to ensure that the cutting-edge research performed in America is translated into new and improved products that are made in America.

[81] The White House. (2012). *National Bioeconomy Blueprint*. https://obamawhitehouse.archives.gov/sites/default/files/microsites/ostp/national_bioeconomy_blueprint_april_2012.pdf

[82] For example, the 2012 National Bioeconomy Blueprint describes strategic objectives to help realize the full potential of the U.S. bioeconomy and highlights early achievements toward those objectives. In the 2020 CARES Act (HR 748), Federal investments are made to prevent, prepare for, and respond to coronavirus, domestically or internationally, by supporting continuity of operations, including biomanufacturing. In the 2022 National Defense Authorization Act (HR 4350), the Act establishes the National Security Commission on Emerging Biotechnology that will conduct a review of biotechnology and biomanufacturing.

Acknowledgments

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Glossary of Terms

Bioeconomy: economic activity that is derived from research and innovation in the life sciences to create and manufacture new products, processes, and services for economic, environmental, and societal benefit and for national security

Bioengineering: application of engineering design principles and practices to biological systems, including molecular and cellular systems, to advance fundamental understandings of complex natural systems and to enable or optimize functions, capabilities, or products; also called engineering biology

Biomanufacturing: manufacturing of bioproducts at scale using naturally occurring or synthetically derived biological systems

Biomass: renewable organic material that comes from plants or animals that is used as fuel

Bioprocessing: manufacturing process that involves the use of microbial, plant, or animal cells, or their constituent parts, for the production of desired compounds or products; also called bioprocess engineering

Bioproducts: products produced using biological systems and/or often derived from biobased precursors

Bioreactor: an apparatus used for growing organisms under controlled conditions, often used in industrial processes to produce pharmaceuticals and to convert biomass into ethanol

Biotechnology: technologies and methodologies derived from the understanding of genetics that enables manipulation of biological-based systems to produce desired outcomes and products

Co-location: a manufacturing concept of physically locating product input and processing facilities in the same area

Feedstock: raw material used to supply an industrial process

Appendix A. External Experts Consulted

PCAST sought input from a diverse group of additional experts and stakeholders. PCAST expresses its gratitude to those listed here who shared their expertise. They did not review drafts of the report, and their willingness to engage with PCAST on specific points does not imply endorsement of the views expressed herein. Responsibility for the opinions, findings, and recommendations in this report and for any errors of fact or interpretation rests solely with PCAST.

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Appendix B. Bioprocessing and Bioprocessing-Related Degree Programs

Using job titles and associated degree programs derived from the Bureau of Labor Statistics, we identified 27 bioprocessing and bioprocessing-related programs at U.S. postsecondary institutions.[83] Of these programs, only nine (four universities and five community colleges) had independent bioprocessing specific degree programs (Table 1).

Table 1. Institutions Identified in This Survey That Offer Bioprocessing Degree Programs

Institution	State	Program	Degrees Awarded
UC Berkeley	CA	Bioprocess Engineering	Master's
University of Illinois Urbana-Champaign	IL	Bioprocessing and Bioenergy	Master's
State University of New York	NY	Bioprocess Engineering	Bachelor's
North Carolina State University	NC	Bioprocessing Science	Bachelor's
Central Carolina Community College	NC	Bioprocess Technology	Certificate, Associate's, Diploma
Johnston Community College	NC	Bioprocess Technology	AAS*
Vance-Granville Community College	NC	Bioprocess Technology	AAS
Frederick Community College	MD	Bioprocess Technology	AAS, Certificate
Howard Community College	MD	Bioprocessing Technology	AAS

*AAS is an Associate's Degree in Applied Science.

Most universities and community colleges do not have bioprocessing-specific programs. There are four engineering programs that are more common across academic institutions and applicable to the bioprocessing workforce: industrial engineering, biomedical engineering, biosystems engineering, and biotechnology engineering. These data from the Bureau of Labor Statistics are supplemented by

[83] Universities and community colleges that were identified by our search terms but did not have bioprocessing-specific degree programs were University of North Carolina, Thomas Jefferson University, University of Georgia, Keck Graduate Institute, Cecil College, University of Minnesota, Albany College of Pharmacy and Health Sciences, Florida Agricultural and Mechanical University, Trine University, University of Wisconsin Madison, University of Nebraska Lincoln, Clemson University, Auburn University, University of Iowa, Iowa State University, East Carolina University, Virginia Tech, and University of Massachusetts Lowell.

other degree programs that may, in some of their specialty concentrations, incorporate the engineering of biological systems to create products or that may be relevant to the bioprocessing workforce in specific industrial sectors. These degree programs include chemical engineering and agricultural engineering.

a. Industrial Engineering

Industrial Engineering (IE) degrees prepare students to design, improve, install, and operate integrated systems of people, materials, and facilities needed for manufacturing. The typical IE curriculum leading to a bachelor's or graduate degree combines four key areas: product and production process design, work analysis, decision sciences, and engineering-management sciences. Specialized areas of focus in IE may vary, but most students take two years of foundational courses in basic sciences, engineering science, mathematics, the humanities, and social sciences, and they finish the remaining years developing skills in statistics, operations research, information systems, systems analysis, organizational management, manufacturing, and industrial engineering methods.

b. Biomedical Engineering

Biomedical Engineering (BE) combines biological sciences with engineering design. BE curriculum includes 12 months of mathematics and basic sciences, 6 months of humanities and social sciences, and 18 months of core engineering topics. Core engineering topics include biomechanics, biotransport, biothermodynamics, biomaterials, bioinstrumentation, biofluids, systems physiology, and biosignal analysis. Most universities offer undergraduate to graduate degrees in BE, and a graduate degree is typically necessary for faculty and R&D BE positions.[84]

c. Biosystems Engineering

Biosystems Engineering (BSEN) is defined as the analysis, design, and control of biologically-based systems for the sustainable production and processing of food and biological materials and the efficient use of natural and renewable resources in order to align human health and the environment. BSEN curriculum combines engineering science and design with applied biological, environmental, and agricultural sciences. To date, no consensus has been reached about degree requirements, and they vary by institution.

d. Biotechnology Engineering

Biotechnology Engineering (BTE) curriculum combines biology and technology for programs such as gene therapy, protein and tissue engineering, and tissue remediation. Degree requirements vary widely by institution. At Tufts University, BTE doctoral students focus research-oriented coursework on topics such as cell and microbe cultivation, biochemistry and cellular metabolism, protein purification, molecular biology, and biochemical engineering. Conversely, BTE certificate students can be trained as electrical engineers in the medical uses of diagnostic imaging instrumentation, using tissue engineering to develop tissue implants, and as mechanical engineers that are well-versed in biomaterials. At UCLA, BTE Certificate students gain knowledge in biotechnology fundamentals, manufacturing techniques, European and FDA regulatory approval requirements and quality engineering, and other theoretical and practical knowledge.

[84] Reaser, A. (2002). Jobs in Biotechnology: Applying Old Sciences to New Discoveries. *Occupational Outlook Quarterly*, *46*(3), 26-35.

e. Chemical Engineering

Chemical Engineering (CE) involves the use of chemical processes—such as mixing, compounding, and processing—for the production and manufacturing of products. Core CE curriculum includes thermodynamics and physical chemistry, fluid mechanics/transport phenomena, unit operations, chemical reaction engineering, and process dynamics and control.[85] An understanding of organic chemistry, biotechnology, biochemistry, and microbiology are increasingly important as the applications of chemical engineering increase for biotechnology and life sciences.[86] Chemical engineers are able to enter the workforce with a bachelor's degree and can further specialize through graduate education, which allows them to work in R&D or in academia.

f. Agricultural Engineering

Agricultural engineering, also called biosystems engineering, combines agricultural and biological studies to develop practical solutions for the food and pharmaceutical industries, among others. Degrees are awarded at the bachelor's, master's, and doctoral levels. The interdisciplinarity of these programs is highlighted by a variety of undergraduate majors such as agricultural engineering, agricultural systems technology, industrial technology, and biological systems engineering, the latter of which includes a focus on food and bioprocessing engineering concentration. Courses at Iowa State University, Purdue, and UC Davis offer similar programs that include biological thermodynamics, biosystem engineering, microbiology, food chemistry, and process design. Degrees in agricultural-related machinery or resource management are also typically offered in these same departments.

[85] Gillett, John E. (2001). "Chemical Engineering Education in the Next Century," *Chemical Engineering Technology.* 24, no. 6: 561-570. https://doi.org/10.1002/1521-4125(200106)24:6<561::AID-CEAT561>3.0.CO;2-X

[86] Ibid.

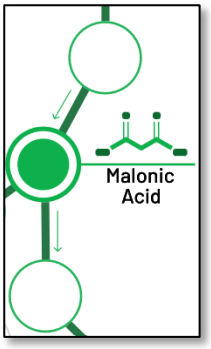
Appendix C. Biomanufacturing Vignettes

The Road Less Carboned

Source: BioMason

If cement production were its own country, it would rank third as the largest carbon emitter in the world, behind China and the United States.[87,88] Aiming to substantially reduce concrete carbon emissions, North Carolina-based BioMason has developed environmentally friendly yet structurally sound building materials by combining bacteria, carbon, and calcium to produce a "biologically formed limestone material," eliminating the need for high heat and fossil fuels required for traditional concrete production.[89] The company has already seen success in scaled up production: clothing retailer H&M has partnered with BioMason to outfit new stores and retrofit older stores with their commercially available biobricks, Biolith, which are also now available for purchase by the public.[90] By establishing more domestic biomanufacturing facilities, companies will be able to more rapidly translate their products, just like BioMason, to the market.

Move Over Petroleum: Malonic Acid Is In



Source: Lygos

From artificial turf to artificial limbs, hula hoops to hearing aids, petroleum plays a crucial role as a chemical precursor in over 6,000 everyday products in addition to use for transportation fuel and heating.[91] Researchers and Federal laboratories are developing sustainable alternatives to petroleum. In 2015, researchers at Lygos, Inc. and Lawrence Berkeley National Lab teamed up to develop a scaled up, environmentally and economically viable process to produce malonic acid, a critical chemical that is traditionally derived from petroleum.[92] The fermentation-based process uses a biomass-derived sugar as an alternative to petroleum to create the malonic acid. Lygos has successfully

[87] Lucy Rodgers (2018, December 16). Climate change: The massive CO2 emitter you may not know about. *BBC News*. https://www.bbc.com/news/science-environment-46455844

[88] Lehne, J., & Preston, F. (2018). *Making Concrete Change: Innovation in Low-carbon Cement and Concrete.* Chatham House. https://www.chathamhouse.org/2018/06/making-concrete-change-innovation-low-carbon-cement-and-concrete

[89] BioMason. (2022). https://biomason.com/faq

[90] Amy Feldman. (2021, June). Startup BioMason Makes Biocement Tiles, Retailer H&M Group Plans To Outfit Its Stores' Floors With Them. *Forbes*. https://www.forbes.com/sites/amyfeldman/2021/06/14/startup-biomason-makes-bio-cement-tiles-retailer-hm-group-plans-to-outfit-its-stores-floors-with-them/?sh=51cb001157c9

[91] Department of Energy. (n.d.) *Products Made From Oil and Natural Gas*. Department of Energy (DOE). https://www.energy.gov/sites/prod/files/2019/11/f68/Products%20Made%20From%20Oil%20and%20Natural%20Gas%20Infographic.pdf

[92] Advanced Biofuels and Bioproducts Process Development Unit. (2015, March 2). *First Bioprocess Pilot Production of Malonic Acid From Renewables [Press release]*. https://abpdu.lbl.gov/news/first-bioprocess-pilot-production-of-malonic-acid-from-renewables/

scaled the process out of the lab and onto the production floor, diversifying the global supply chain of malonic acid.

Students Burning the Midnight Renewable Oil

As new jobs and opportunities are established in the growing bioeconomy, academic institutions are moving to prepare students to enter into this modern workforce. Universities and community colleges are increasingly offering degree programs, from associate to doctoral, focused on biomanufacturing and bioprocessing. Community colleges in Maryland and North Carolina offer accessible and affordable associate degrees and certificates in bioprocess technology, positioning graduates to enter the biotechnology industry. Agricultural engineering programs in Iowa and Indiana are training the next generation of 21st century farmers, who will be able to harness the power of the latest biotechnology to deliver food from the farm to the dinner tables of all Americans. And biotechnology engineering programs in California and Massachusetts are tapping into the latest gene-editing technologies to create next generation therapeutics. These programs have already seen successes: alumni have gone on to lead agricultural research companies, open biotech startups, and invent new, effective water quality practices.[93, 94, 95]

Source: Iowa State University – Institutional Research

Future Fabrication of Foam, Pharmaceuticals, and Fuel

Biomanufacturing using engineered E. coli is becoming increasingly recognized as a sustainable and efficient process for large scale manufacturing of 1,2,4-butanetriol (BT), a versatile chemical precursor used in many fields.[96] For example, BT is a precursor for many commercial applications, including polyurethane foams used in bedding, furniture, carpet underlays, car interiors, and

[93] Hays, S. (2021, December 22). ABE Alum Accepts Lead Role in Largest Agricultural Research Company in Latin America. *Iowa State University - College of Engineering News*. https://news.engineering.iastate.edu/2021/12/22/abe-alum-accepts-lead-role-in-largest-agricultural-research-company-in-latin-america/

[94] Purdue University. (2018). 2018 Outstanding Agricultural & Biological Engineering Alumni. https://engineering.purdue.edu/ABE/foryou/alums/AlumniAwards

[95] Hays, S. (2022, August 31). Providing solutions through water quality practices: A glimpse into ABE alum Bethany Brittenham's career 5 years after graduation - College of Engineering News. *Iowa State University - College of Engineering News*. https://news.engineering.iastate.edu/2022/08/31/providing-solutions-through-water-quality-practices-a-glimpse-into-abe-alum-bethany-brittenhams-career-5-years-after-graduation/

[96] Cao, Y., Niu, W., Guo, J., Xian, M., & Liu, H. (2015). Biotechnological production of 1,2,4-butanetriol: An efficient process to synthesize energetic material precursor from renewable biomass. *Scientific Reports*, 5, 18149. https://doi.org/10.1038/srep18149

packaging.[97] BT can also be used as a potential building block for cholesterol-lowering pharmaceutical drugs like Crestor and Zetia.[98] Furthermore, BT is the direct precursor to butanetriol trinitrate, which is used by the military as missile fuel. Biomanufacturing of BT using a renewable biomass, such as E. coli, is more sustainable and efficient than current chemical production, which is inefficient, costly, and creates environmental pollution.[99] Researchers at the U.S. Army's Combat Capabilities Development Command Chemical Biological Center (DEVCOM CBC) have already begun large scale biomanufacturing efforts to produce BT, diversifying the supply chain of this critical process that is currently limited to a single domestic supplier.[100]

Source: U.S. Army DEVCOM CBC

Partnerships Make Perfect

The United States has a wealth of resources, expertise, and infrastructure that are distributed across industry, academia, and local communities. Partnerships between the three can drive innovation and promote collaboration while strengthening the local workforce and economy. Biomanufacturing partnerships are particularly beneficial for establishing new connections between educators, industry professionals, and students. In California, public-private partnerships through the Engineering Biology Research Consortium (EBRC) provide students with internship and mentorship opportunities as well as workshops and short-courses on a range of synthetic biology topics.[101] Students can benefit from partnership opportunities by learning about biomanufacturing career paths and getting hands-on experience in the field. Some students who participate in this program end up working in the field.

Source: BioBuilder

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[97] American Chemistry Council. (n.d.) Polyurethane Applications. https://www.americanchemistry.com/industry-groups/center-for-the-polyurethanes-industry-cpi/applications-benefits/polyurethane-applications

[98] Cao, Y., Niu, W., Guo, J., Xian, M., & Liu, H. (2015). Biotechnological production of 1,2,4-butanetriol: An efficient process to synthesize energetic material precursor from renewable biomass. *Scientific Reports*, 5, 18149. https://doi.org/10.1038/srep18149

[99] Hu, S., Gao, Q., Wang, X., Yang, J., Xu, N., Chen, K., Xu, S., & Ouyang, P. (2018). Efficient production of d-1,2,4-butanetriol from d-xylose by engineered Escherichia coli whole-cell biocatalysts. *Frontiers of Chemical Science and Engineering*, *12*(4), 772–779. https://doi.org/10.1007/s11705-018-1731-x

[100] Feeney, B. (2021). Army seeks to establish self sufficiency through biomanufacturing. U.S. Army. https://www.army.mil/article/246234/army_seeks_to_establish_self_sufficiency_through_biomanufacturing#:~:text=Biomanufacturing%20is%20a%20manufacturing%20revolution,the%20organisms%20that%20make%20them

[101] EBRC. (2022). https://ebrc.org/

For example, an alumnus of the program is among the researchers who developed one of the first COVID-19 vaccines. These types of partnerships could be bolstered by a revitalized national strategy, where stakeholders across the U.S. bioeconomy can coordinate and optimize their diverse efforts and expertise.

Alternative Food for Thought

Source: Vegconomist

The livestock industry currently imposes significant stress on the global environment, contributing between 12–18% of total greenhouse gas emissions in addition to causing water pollution and water scarcity.[102] This impact is felt most in the rural communities where livestock is raised. Companies such as Beyond Meat,[103] Nature's Fynd,[104] Impossible Foods,[105] and Morning Star Farms[106] are developing biobased proteins as a greener alternative and rely heavily on clear regulatory guidelines. These companies create sustainable bioproducts, made from resilient biobased precursors like protein-rich mushrooms, spanning the livestock industry from dairy to meat products. Studies have shown that one biobased alternative required 18 times less land, 9 times less fuel, and 10–12 times less fertilizer and pesticides per 1 kg of protein compared to traditional beef.[107] Moreover, these companies are stimulating local economies right here in the United States: startup company Nature's Fynd is growing and processing their fungi-based meat substitutes in Chicago. The company also takes advantage of the benefits of co-location by reducing carbon emissions needed to travel between closer production sites while generating new jobs for the local area.[108,109]

Navigating the Regulatory Labyrinth

Pests cause approximately 35% of farming yield loss, demonstrating the need for innovative pest control technologies that can boost farmers' livelihoods and create more resilient food supplies.[110] Companies such as Marrone Bio are creating novel, biobased pest control technologies that use the

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[102] González, N., Marquès, M., Nadal, M., & Domingo, J. L. (2020). Meat consumption: Which are the current global risks? A review of recent (2010-2020) evidences. *Food Research International*, 137, 109341. https://doi.org/10.1016/j.foodres.2020.109341

[103] Beyond Meat. (2022). https://www.beyondmeat.com/en-US/

[104] Nature's Fynd. (2022). https://www.naturesfynd.com/fy-protein

[105] Impossible. (2022). https://impossiblefoods.com/

[106] MorningStar Farms. (2022). https://www.morningstarfarms.com/en_US/home.html

[107] González, N., Marquès, M., Nadal, M., & Domingo, J. L. (2020). Meat consumption: Which are the current global risks? A review of recent (2010-2020) evidences. *Food Research International*, 137, 109341. https://doi.org/10.1016/j.foodres.2020.109341

[108] Watson, E. (2020, March 24). Nature's Fynd (formerly Sustainable Bioproducts) raises $80m to grow food from microbes. *FoodNavigator-USA.* https://www.foodnavigator-usa.com/Article/2020/03/24/Nature-s-Fynd-formerly-Sustainable-Bioproducts-raises-80m-to-grow-food-from-microbes

[109] Nature's Fynd. (2022). https://www.naturesfynd.com/

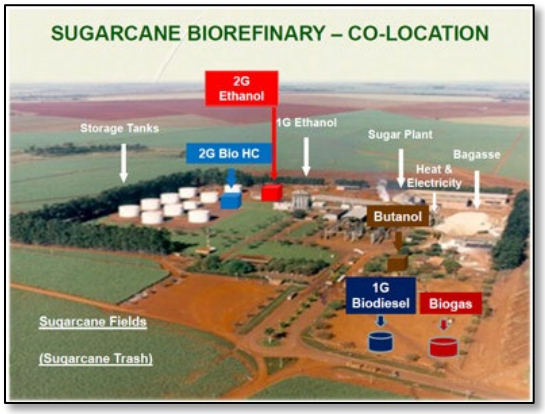
[110] European Commission. (2020, March 13). *Biopesticides can boost global food supplies, making agriculture greener, safer and more efficient*. https://cordis.europa.eu/article/id/415443-biopesticides

latest advances in agricultural science to make them more effective and environmentally friendly.[111] However, the U.S. regulatory landscape for these agricultural products is constantly changing with numerous requirements both at the Federal and State levels. Startups and small family companies are forced to dedicate significant resources to stay on top of these complicated regulations that likely span across multiple jurisdictions. For example, crop protection chemicals are regulated at the Federal level by EPA, but separate registration is required in each State and territory where the active substance will be marketed.[112] Companies like Marrone Bio were able to bring products to market only after early key investments allowed them to overcome regulatory hurdles. Their products have helped farmers increase their plant health and bolster crop yields all while reducing negative environmental impacts.[113] By standardizing and demystifying the regulatory landscape, more companies can leverage the latest biotechnologies, benefitting both the American farmer and the American bioeconomy.

Source: Marrone Bio Innovations

Co-location Makes Good Neighbors

Co-locating bioprocessing facilities with their biomass feedstocks provides an opportunity to rethink how the Nation produces and builds integrated production facilities.[114] Co-location is a manufacturing concept of physically locating product input and processing facilities in the same area. For example, cereal grain mills and sugarcane biorefineries produce intermediate and end products that are used in the production of a range of bioproducts from food to biofuels. Several industry leaders have already adopted the co-location model: companies including Cargill and Eddyville have placed starch-based feedstocks near their fermentation facilities in Nebraska and Iowa, respectively,



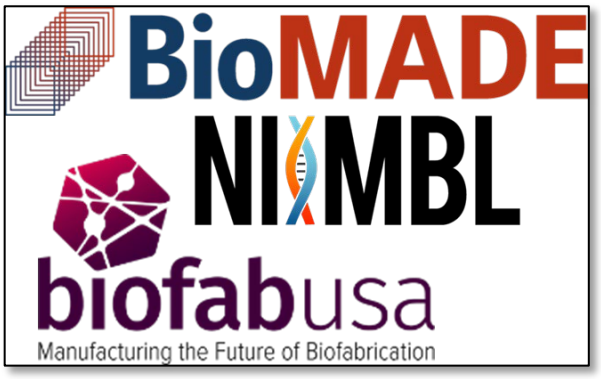
Source: ETIP Bioenergy

[111] Marrone Bio Innovations. (n.d.). https://marronebio.com/about/
[112] Labcorp Drug Development. (2022, February 15). TSCA and US state legislation: navigating your chemical or agrochemical through the federal and state regulatory landscape in the USA. https://ddblog.labcorp.com/2022/02/tsca-and-us-state-legislation-navigating-your-chemical-or-agrochemical-through-the-federal-and-state-regulatory-landscape-in-the-usa/
[113] Marrone Bio Innovations. (n.d.). https://marronebio.com/sustainability-esg/
[114] Schmidt Futures. (2022). *The U.S. Bioeconomy: Charting a Course for a Resilient and Competitive Future*. https://www.schmidtfutures.com/wp-content/uploads/2022/04/Bioeconomy-Task-Force-Strategy-4.14.22.pdf

to produce ethanol, a common biofuel.[115,116] Moreover, the production of bioproducts within the United States would be a strategic asset for national security, as it would strengthen the Nation against future supply shocks.[117] By removing the need to transport biomass to bioprocessing facilities across long distances, these companies are supporting and growing rural workforces and local communities all while reducing their carbon footprint.

Made in the USA

Manufacturing USA Institutes work to accelerate the commercialization of novel technological products through advanced manufacturing and workforce development.[118] Three of these institutes contribute to the bioeconomy: the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL),[119] BioMade,[120] and BioFabUSA,[121] respectively specializing in biopharmaceutical innovation, bioindustrial manufacturing, and the biofabrication industry. These institutes are public-private partnerships with members representing industry, academia, government, and nonprofit organizations. The institutes reduce barriers to scale up and commercialization and provide critical technical support. For example, NIIMBL's bioproducts are used to treat some of the most common and debilitating diseases, and BioFabUSA addresses the medical needs of injured soldiers and people living with incapacitating health conditions through manufacturing cells, tissues, and organs. BioMade accelerates the bioindustrial manufacturing industry by investing in the commercialization of innovative bioproducts. Manufacturing USA institutes are a model that can be applied to the multitude of applications of advanced biotechnology and biomanufacturing to enable a sustainable, safe, and secure bioeconomy.



Source: BioMade, NIIMBL, BiofabUSA

Refueling Coal-Dependent Economies

As the United States invests in a greener, biotechnology-driven economy powered by renewable energy, biomanufacturing has the potential to bolster States whose economies were formerly dependent on oil and coal production. By retooling and reskilling their existing facilities and

[115] Jolie, R., Troostembergh, J.-C. de, Aristidou, A., Bregola, M., & Black, E. (2016). Colocation as Model for Production of Bio-Based Chemicals from Starch. In F. Cavani, S. Albonetti, F. Basile, & A. Gandini (Eds.), Chemicals and fuels from bio-based building blocks (pp. 549–568). https://doi.org/10.1002/9783527698202.ch21

[116] Ou, L., Brown, T., Thilakaratne, R., Hu, G., & Brown, R. (2014). Techno-economic Analys of Co-located Corn Grain and Corn Stover Ethanol Plants. *Biofuels, Bioproducts and Biorefining*, 8: 412-422. https://dr.lib.iastate.edu/server/api/core/bitstreams/57ac1ee3-ba32-4dbf-a4e8-2fe8ad36dfe4/content

[117] Clomburg, J. M., Crumbley, A. M., & Gonzalez, R. (2017). Industrial biomanufacturing: The future of chemical production. *Science*, *355*(6320). https://doi.org/10.1126/science.aag0804

[118] Manufacturing USA. https://www.manufacturingusa.com/institutes

[119] NIIMBL. (2022). https://niimbl.force.com/s/about-niimbl

[120] BioMADE. (2022). https://www.biomade.org/about-biomade

[121] BioFabUSA. (2022). https://www.armiusa.org/biofabusa/

workforce, States such as West Virginia and Ohio can leverage their preexisting expertise in manufacturing to support U.S. biomanufacturing capabilities while revitalizing their economies.

Source: Steve Allen Adams, The Parkersburg News and Sentinel

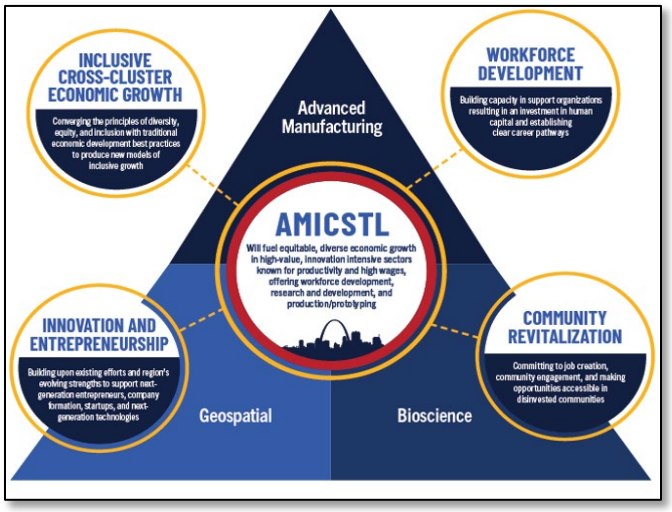
Various recent Federal investments have already begun to lay this foundation. For instance, the Appalachian Climate Technologies Initiative of West Virginia was awarded $62.8 billion through the Department of Commerce's Build Back Better Regional Challenge to create a "hub of clean energy and green economy jobs."[122] Additionally, the CHIPS and Science Act includes provisions to boost localities formerly dependent on coal including by establishing carbon material research centers in major coal-producing regions of the United States and encouraging these regions to create Regional Technology and Innovation Hubs. Private industry is also making large investments: ElevateBio and University of Pittsburgh[123] announced a $500 million biomanufacturing facility in Pittsburgh, and BHE Renewables has invested $500 million in retrofitting an abandoned aluminum manufacturing plant into a new manufacturing site that runs on 100% renewable energy.[124] These initiatives demonstrate U.S. commitment to curbing the effects of climate change while ensuring that all States are ready to evolve with the latest biotechnological advances.

[122] United States Economic Development Administration. (2022). *Coalfield Development - Build Back Better Regional Challenge Winners [Press release]*. https://eda.gov/arpa/build-back-better/finalists/Coalfield-Development.htm

[123] ElevateBio. (2022, August 25). *ElevateBio and the University of Pittsburgh Announce Creation of Pitt BioForge BioManufacturing Center at Hazelwood Green to Accelerate Cell and Gene Therapy Innovation [Press release]*. https://www.elevate.bio/press-releases/elevatebio-and-the-university-of-pittsburgh-announce-creation-of-pitt-bioforge-biomanufacturing-center-at-hazelwood-green-to-accelerate-cell-and-gene-therapy-innovation

[124] Adams, S. A. (2022, September 14). Diversifying: Berkshire Hathaway to build new plant on Century Aluminum site. *The Parkersburg News and Sentinel*. https://www.newsandsentinel.com/news/business/2022/09/diversifying-berkshire-hathaway-to-build-new-plant-on-century-aluminum-site/

An Overarching Effort



Source: STLPartnership

The integrative nature of the bioeconomy has served as a unique initiative that weaves community stakeholders together, strengthening local economies. In St. Louis, MO, State government, academia, investors, and private industry have joined forces to bolster the local biotechnology and biomanufacturing economies. The St. Louis Tech Triangle, recently awarded $25 million by the Department of Commerce, integrates the region's biosciences, geospatial, and advanced manufacturing capabilities to accelerate innovation and entrepreneurship, all supported by industry, labor organizations, educational institutions, and community-based organizations.[125] Large pharmaceutical companies, like Bayer AG and Pfizer, in addition to hundreds of biotech startups, have located their headquarters or research and commercialization facilities in St. Louis. Moreover, universities and colleges located in the Midwest at-large are collaborating with these biotech and pharmaceutical companies while helping to train the local workforce for new industries. Academic institutions including Washington University in St. Louis, University of Missouri, University of Illinois, and Harris Stowe State University make up an expansive research network to boost the regional research capabilities. By convening stakeholders and leveraging their unique capabilities, cities across the United States can strengthen their local institutions and industries all while boosting the national economy.

Biotech State of Mind

Source: Chemical and Engineering News

New York City is positioning itself as a leader in the biotechnology industry by strategically investing in biopharmaceutical, device and diagnostic research, and development and manufacturing to facilitate novel healthcare solutions. There has been an influx of funding from both private and public sources working to spur innovation and economic activity in the biotech sector. Led by the city, LifeSci NYC is a $1 billion initiative that is investing holistically in the cycle of technology innovation, funding $530 million in lab and incubator space construction, $20 million to support a diverse workforce

[125] United States Economic Development Administration. (2022, September 14). *Greater St. Louis, Inc. - Build Back Better Regional Challenge Winners [Press release]*. https://eda.gov/arpa/build-back-better/finalists/Greater-St-Louis.htm

pipeline, and $450 million to advance new research.[126] The initiative includes partnering with biopharmaceutical companies to create innovative solutions to address Lyme disease, one of the fastest growing infectious diseases in the country. In addition, Empire State Development's Western New York office was awarded $25 million as part of Build Back Better's regional challenge program.[127] The investment aims to bolster the regional industry while promoting economic equity, creating good-paying jobs, and strengthening U.S. competitiveness. The projects will work on scaling up existing advanced manufacturing processes to facilitate the transition of products to market.[128] New York City's investments demonstrate the various facets of societal benefits the industry can provide, from technical health solutions to a strong economy and the opportunity to support a diverse and equitable workforce.

[126] LifeSci. (2022). https://lifesci.nyc/

[127] New York State. (2022, September 1). *Governor Hochul Announces Empire State Development's Regional Western New York Office $25 Million Winner of Federal Build Back Better Regional Challenge [Press release]*. https://www.governor.ny.gov/news/governor-hochul-announces-empire-state-developments-regional-western-new-york-office-25

[128] Empire State Development. (2016). Biotech and Life Sciences. https://esd.ny.gov/industries/biotech-and-life-sciences?tid_cc_startup%5B0%5D=1&page=207&tid_cd_region=All&tid_cd_industry=All&tid_cc_startup%5B%5D=1&utm_source=Bing&utm_medium=CPC&utm_campaign=StartUpNY

Appendix D. International Competition & National Security Concerns

In anticipation of a potential superpower manufacturing technology race, other nations are increasing their biomanufacturing capacity and workforce at a faster rate than the United States.[129] China, the United Kingdom (UK), and the European Union (EU) are ramping up their biomanufacturing capacity through research, policy, and infrastructure strategies. China is rapidly closing the gap between its biotechnology industry and that of the United States through increased R&D investment, top-down government directives in its 2015 *Made in China 2025* plan,[130] and a national workforce strategy.[131] China has been aggressive in attracting and nurturing STEM (science, technology, engineering, and math) talent, building domestic R&D capabilities, and offering attractive R&D incentives to foreign companies.[132,133] There are currently few areas in which Chinese firms are globally competitive, but there is evidence that the country's investment in building its biotechnology sector is changing the global dynamic. For example, 5 of the 10 largest biotechnology firms that published initial public offerings (IPOs) in 2019 were based in China, and Western companies are acquiring stakes in Chinese biotech firms.[134]

Countries in Europe have also already established strong biotechnology sectors, with half of today's biotechnology companies located in France, Germany, and the UK.[135] In the UK alone, bioscience clusters at Research and Innovation Campuses support over 4,100 jobs and host more than 200

[129] Deloitte. (2015). *Advanced Technologies Initiative: Manufacturing & Innovation*. https://www2.deloitte.com/content/dam/Deloitte/us/Documents/manufacturing/us-indprod-deloitte-and-council-on-competitiveness-advanced-tech-report.pdf

[130] Center for Security and Emerging Technology. (2022). *Translation of Notice of the State Council on the Publication of "Made in China 2025"*. https://cset.georgetown.edu/wp-content/uploads/t0432_made_in_china_2025_EN.pdf

[131] Dileo, J., Rambhia, K., Downs, M., Rowell, J., & Kennedy, C. (2022). *Maintaining US Leadership in Advanced Biotechnology & Growing the Bioeconomy*. MITRE Center for Data-Driven Policy. https://www.mitre.org/sites/default/files/2022-05/pr-22-00151-01-maintaining-us-leadership-in-advanced-biotechnology-growing-the-bioeconomy.pdf

[132] Deloitte. (2015). *Advanced Technologies Initiative: Manufacturing & Innovation*. https://www2.deloitte.com/content/dam/Deloitte/us/Documents/manufacturing/us-indprod-deloitte-and-council-on-competitiveness-advanced-tech-report.pdf

[133] Cao, F. F. (2015). *Global Survey of R&D Incentives- China*. https://www2.deloitte.com/content/dam/Deloitte/us/Documents/Tax/us-tax-countrypage-china.pdf

[134] Moore, S. (2020). *China's Role in the Global Biotechnology Sector and Implications for U.S. Policy. Global China*. Brookings Institution. https://www.brookings.edu/wp-content/uploads/2020/04/FP_20200427_china_biotechnology_moore.pdf

[135] Le Deu, F., & Da Santos Silva, J. (2019). *Biotech in Europe: A strong foundation for growth and innovation*. McKinsey & Company. https://www.mckinsey.com/industries/life-sciences/our-insights/biotech-in-europe-a-strong-foundation-for-growth-and-innovation

companies.[136] In 2021, approximately $4.5 billion in public and private funding for biotechnology and life science companies was raised in the UK.[137]

Europe is actively expanding its bioeconomy. In 2022, the EU updated their Bioeconomy Strategy Action Plan, emphasizing the importance of the biotechnology sector to strengthen national and regional bioeconomies.[138] The plan also reports that the original €100 million investment in the European Circular Bioeconomy Fund to fill a financing gap in the bioeconomy sector has grown to €206 million after four rounds of investment. As of September 2022, 10 EU Member States have developed dedicated bioeconomy strategies and 7 EU Member States are in the process of developing their strategies.[139] Similarly, the UK has developed a 2022–2025 biotechnology strategic plan that will launch a strategic investment to catalyze and expand research, innovation, and commercialization in sustainable biomanufacturing across the country.[140]

South America has also made investments in the bioeconomy. Argentina is producing the third largest share of the world's biotechnology crops (14%), behind the United States and Brazil, and is experiencing rapid expansion in its biotechnology sector with more than 200 firms earning over $2 billion across multiple sectors such as human health, animal health, food processing, and agriculture. Brazil produces the second-largest amount of ethanol biomass in the world, accounting for about 30% of global output. [141] U.S. startups are offshoring their bioproduct development to South America to take advantage of scientific expertise and significantly lower costs for laboratory space.[142] For example, to take advantage of Brazil's resources, U.S.-based Amyris opened a production facility in Brazil co-located with sugar mills that supply precursors to their products.[143]

Despite our strengths in research and innovation, manufacturing of pharmaceuticals and medicines in the United States dropped by nearly a third between 2009 and 2018, and our biopharmaceutical trade deficit worsened over the past decade.[144] Expanding U.S. biomanufacturing capacity across all economic sectors would contribute to future national prosperity through domestic investments in R&D, domestic production of biological resources, and by dissuading industrial offshoring in

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[136] UKRI Biotechnology and Biological Sciences Research Council. (2022). *Strategic Delivery Plan 2022-2025*. UK Research and Innovation. https://www.ukri.org/wp-content/uploads/2022/09/BBSRC-010922-StrategicDeliveryPlan2022.pdf

[137] UK BioIndustry Association, & Clarivate. (2022). *UK biotech financing in 2021*. https://www.bioindustry.org/static/971705d9-651c-4db3-b563b39ba4f49d17/91c3d748-048d-4ab3-b6717fc3dcbfbc04/BIA-report-UK-biotech-financing-in-2021.pdf

[138] Directorate-General for Research and Innovation. (2022). *EU Bioeconomy Strategy Progress Report: European Bioeconomy Policy: Stocktaking and future developments*. European Commission. https://op.europa.eu/en/publication-detail/-/publication/ae0a36d3-eac3-11ec-a534-01aa75ed71a1

[139] Ibid.

[140] UKRI Biotechnology and Biological Sciences Research Council. (2022). *Strategic Delivery Plan 2022-2025*. UK Research and Innovation. https://www.ukri.org/wp-content/uploads/2022/09/BBSRC-010922-StrategicDeliveryPlan2022.pdf

[141] U.S. Department of Energy. (2021). *Alternative Fuels Data Center: Maps and Data - Global Ethanol Production by Country or Region*. https://afdc.energy.gov/data/10331

[142] Haar, J. (2017). *Ecosystems of Innovation: The Case of Biotechnology in America*. Wilson Center. https://www.wilsoncenter.org/sites/default/files/media/documents/misc/biotechnology_in_arg_haar.pdf

[143] Oils & Fats International (2022). Amyris starts squalene production at plant in Brazil. https://www.ofimagazine.com/news/amyris-starts-squalene-production-at-plant-in-brazil

[144] Ezell, S. (2020) *Ensuring U.S. Biopharmaceutical Competitiveness*. Information Technology & Innovation Foundation (ITIF). https://www2.itif.org/2020-biopharma-competitiveness.pdf

countries with established biomanufacturing infrastructure.[145] Expanding initiatives such as USDA's BioPreferred program, which requires the Federal Government and its contractors to purchase domestically manufactured bioproducts, would foster and catalyze entrepreneurial growth among domestic biomanufacturers.[146]

National Security Concerns

In addition to biotechnology and biomanufacturing providing many defense-related products critical to national security, a fragmented national biomanufacturing and regulatory infrastructure leaves the United States vulnerable to offshoring of critical technologies and products. Reliance on imported raw materials and foreign manufacturing weakens domestic biomanufacturing capacity and leaves the United States vulnerable to critical supply chain failures, putting access to essential products such as biofuels and pharmaceuticals at risk for all Americans.

Domestic biomanufacturing will also be crucial in protecting U.S. intellectual property from foreign adversaries. Without adequate manufacturing infrastructure at home, American entrepreneurs are at risk of having their product designs and production details exploited by foreign competitors.[147] For example, China has positioned itself to become a leader in biobased production, and companies are turning to them for biomanufacturing capacity and expertise. China's increasing influence on the global bioeconomy threatens critical U.S. manufacturing capabilities and U.S. national security.[148] The biotechnology revolution and the burgeoning bioeconomy is transforming global relationships, potentially disrupting traditional industrial technology and trade practices.

Moreover, biotechnology has the potential for both beneficial and nefarious applications. U.S. global leadership in biobased research, product development, and biomanufacturing would position the United States to lead in the creation of evidence-based, ethically-informed global norms and standards that reflect American values. Increased biotechnology infrastructure will provide an opportunity for U.S. science, technology, and policy leaders to remain at the forefront of bioprocess and bioproducts development to ensure U.S. participation in national and international standards-setting bodies. Without ethical guidelines, adverse actors may harness the vast capabilities of bioprocessing in ways that are at odds with national security and societal practices.

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[145] National Academies of Sciences, Engineering, and Medicine. (2020). *Safeguarding the Bioeconomy: Finding Strategies for Understanding, Evaluating, and Protecting the Bioeconomy while Sustaining Innovation and Growth*. https://www.nationalacademies.org/our-work/safeguarding-the-bioeconomy-finding-strategies-for-understanding-evaluating-and-protecting-the-bioeconomy-while-sustaining-innovation-and-growth

[146] See: https://www.biopreferred.gov/BioPreferred/

[147] Platzer, M., Sargent, J., & Sutter, K. (2020). *Semiconductors: U.S. Industry, Global Competition, and Federal Policy*. (CRS Report No. R46581) Congressional Research Service. https://crsreports.congress.gov/product/pdf/R/R46581

[148] Dileo, J., Rambhia, K., Downs, M., Rowell, J., & Kennedy, C. (2022). *Maintaining US Leadership in Advanced Biotechnology & Growing the Bioeconomy*. MITRE Center for Data-Driven Policy. https://www.mitre.org/sites/default/files/2022-05/pr-22-00151-01-maintaining-us-leadership-in-advanced-biotechnology-growing-the-bioeconomy.pdf