BUILDING A VIBRANT DOMESTIC BIOMANUFACTURING ECOSYSTEM

A Report by the

BIOMANUFACTURING INTERAGENCY WORKING GROUP

November 2024

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About this Report

In September 2022, President Biden signed Executive Order 14081 on Advancing Biotechnology and Biomanufacturing Innovation for a Sustainable, Safe, and Secure American Bioeconomy. The executive order directs federal departments and agencies to develop a strategy that identifies policy recommendations to expand domestic biomanufacturing capacity for products spanning the health, energy, agriculture, and industrial sectors, with a focus on advancing equity, improving biomanufacturing processes, and connecting relevant infrastructure. Toward this mandate, this report provides a strategic direction and recommended actions to be considered by a whole-of-government effort to address persistent gaps in United States biomanufacturing capacity, which were identified through stakeholder engagement.

About the Biomanufacturing Interagency Working Group

The Biomanufacturing Interagency Working Group—with representatives from the Department of Defense, Department of Energy, Department of Commerce, Department of Agriculture, Department of Health and Human Services, National Science Foundation, Department of State, the National Security Council, the Office of Science and Technology Policy, and the National Aeronautics and Space Administration—convened to respond to the Executive Order 14081 on Advancing Biotechnology and Biomanufacturing Innovation for a Sustainable, Safe, and Secure American Bioeconomy direction to establish a strategic direction for domestic biomanufacturing capacity expansion in the United States.

Stakeholder Engagement

Public stakeholders were engaged in the development of this plan through a Request for Information (RFI) and several agency-led listening sessions. Input from this outreach informed the proposed actions described herein.

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Abbreviations and Acronyms

ASPR	Administration for Strategic Preparedness and Response
DOC	Department of Commerce
DOD	Department of Defense
DOE	Department of Energy
DOS	Department of State
EDA	Economic Development Administration
EPA	Environmental Protection Agency
HHS	Department of Health and Human Services
NASA	National Aeronautics and Space Administration
NBBI	National Biotechnology and Biomanufacturing Initiative
NIST	National Institute of Standards and Technology
NSC	National Security Council
NSF	National Science Foundation
NSTC	National Science and Technology Council
OMB	Office of Management and Budget
OSTP	Office of Science and Technology Policy
R&D	research and development
USDA	United States Department of Agriculture
VA	Department of Veteran's Affairs

Executive Summary

The United States bioeconomy is economic activity derived from the life sciences, particularly in the areas of biotechnology and biomanufacturing, including industries, products, services, and the workforce.[1] Biomanufacturing is the use of biological systems to produce goods and services at commercial scale. Biomanufacturing enables biological conversion of plants, waste materials, and even industrial off-gas into molecules that form the building blocks of everyday consumer products, medicines, fuels, and more. Increasing biomanufacturing capacity in the United States, i.e., the quantity of product that can be produced with the infrastructure and operational resources within a given facility, group of facilities, region, or industry, is the key to growing the bioeconomy and applying biotechnology to help achieve societal goals, such as reducing U.S. reliance on fossil fuels.

In September 2022, President Biden signed Executive Order 14081 on Advancing Biotechnology and Biomanufacturing Innovation for a Sustainable, Safe, and Secure American Bioeconomy.[2] Amongst the many mandates in the Executive Order (the Bioeconomy EO) was the establishment of the National Biotechnology and Biomanufacturing Initiative (NBBI),[3] a whole-of-government effort to strengthen America's bioeconomy. The NBBI has already spurred significant action to expand the U.S. bioeconomy by putting forward reports that describe bioeconomy workforce and data initiatives, promoting American leadership by establishing Bold Goals[4] for biotechnology and biomanufacturing research and development, and ensuring that biotechnology is developed and utilized responsibly. The Bioeconomy EO is part of the Biden-Harris Administration's broader modern industrial strategy where the Investing in America agenda[5] is catalyzing once-in-a-generation investments in building a net-zero and equitable economy of the future. These investments, across a suite of historic legislation including the Bipartisan Infrastructure Law,[6] CHIPS and Science Act,[7] and Inflation Reduction Act,[8] support President Biden's climate and clean energy goals, build stronger supply chains, reshore American manufacturing, and advance American leadership around the globe.

The Biden-Harris Administration recognized the specific role of biomanufacturing in growing the bioeconomy, and through the Bioeconomy EO, directed federal departments and agencies to develop a plan to expand biomanufacturing capacity for health, energy, agriculture, and industrial sectors. In responding to the Bioeconomy EO, this report describes the current state of U.S. biomanufacturing

[1] NIST. 2022. "NIST Bioeconomy Lexicon." Last updated Dec. 9, 2022. https://www.nist.gov/bioscience/nist-bioeconomy-lexicon

[2] The White House. "Executive Order on Advancing Biotechnology and Biomanufacturing Innovation for a Sustainable, Safe, and Secure American Bioeconomy." September 2022. https://www.whitehouse.gov/briefing-room/presidential-actions/2022/09/12/executive-order-on-advancing-biotechnology-and-biomanufacturing-innovation-for-a-sustainable-safe-and-secure-american-bioeconomy/

[3] The White House. "White House Fact Sheet: President Biden to launch a National Biotechnology and Biomanufacturing initiative." (2022). https://www.whitehouse.gov/briefing-room/statements-releases/2022/09/12/fact-sheet-president-biden-to-launch-a-national-biotechnology-and-biomanufacturing-initiative/#:~:text=Today%2C%20President%20Biden%20signed%20an,lower%20prices%20for%20American%20families

[4] The White House. "Bold Goals for U.S. Biotechnology and Biomanufacturing: Harnessing Research and Development to Further Societal Goals." March 2023. https://www.whitehouse.gov/wp-content/uploads/2023/03/Bold-Goals-for-U.S.-Biotechnology-and-Biomanufacturing-Harnessing-Research-and-Development-To-Further-Societal-Goals-FINAL.pdf

[5] The White House. "Investing in America." October 2024. https://www.whitehouse.gov/invest/

[6] H.R.3684 - 117th Congress (2021-2022): Infrastructure Investment and Jobs Act. (2021, November 15). https://www.congress.gov/bill/117th-congress/house-bill/3684

[7] H.R.4346 - 117th Congress (2021-2022): CHIPS and Science Act. (2022, August 9). https://www.congress.gov/bill/117th-congress/house-bill/4346

[8] Text - H.R.5376 - 117th Congress (2021-2022): Inflation Reduction Act of 2022. (2022, August 16). https://www.congress.gov/bill/117th-congress/house-bill/5376/text

capacity and identifies key factors driving growth. Eleven actions were identified through stakeholder engagement that the federal government could consider in order to continue increasing U.S. biomanufacturing capacity. They are:

1. Further leverage federal procurement programs and incentives to increase the U.S. market share of biobased and biotechnology-derived products and services, and ensure tools are in place to accurately measure resulting economic growth.
2. Create right-sized federal incentives to accommodate the range of sizes of biotechnology and biomanufacturing companies.
3. Engage in international partnerships to address cross-border challenges that otherwise limit the global footprint of U.S. biomanufacturing, such as intellectual property protection and enforcement, barriers to market entry abroad, and international market competitiveness.
4. Enable further technology advances by supporting research and development and initiatives that improve biomanufacturing scale-up efficiency.
5. Encourage further development and utilization of a diverse and sustainable biomanufacturing feedstock supply chain as input material for biomanufacturing.
6. Encourage biomanufacturing industry adoption of established corporate manufacturing best practices that minimize environmental impacts and conserve energy to lower operational costs and speed production output timelines.
7. Continue to expand the availability of U.S. biomanufacturing scale-up infrastructure through a distributed network.
8. Further integrate the emerging U.S. bioeconomy with the clean energy economy to enable a sustainable commercial biomanufacturing ecosystem.
9. Advance U.S. biological risk management for biotechnology and biomanufacturing research and development.
10. Continue to modernize biomanufacturing digital infrastructure to meet ecosystem informatics needs.
11. Further expand and diversify the U.S. talent pool for biotechnology and biomanufacturing jobs and careers to promote innovation and advance equity.

Following this report, the next step is to coordinate efforts across government to address these proposed actions, such as through the National Bioeconomy Board. This could be accomplished by aligning current investments within federal agencies to support the above actions further outlined herein, establishing priorities, and identifying funding gaps in order to inform future budget requests. Full implementation of the proposed actions is subject to the annual President's Budget process and the availability of appropriations.

Introduction

President Biden's Executive Order 14081 on Advancing Biotechnology and Biomanufacturing Innovation for a Sustainable, Safe, and Secure American Bioeconomy lays the foundation for a robust U.S. biomanufacturing ecosystem. Section 5 of the Bioeconomy EO calls on federal departments and agencies to develop a plan and provide strategic direction to "expand domestic biomanufacturing capacity for products spanning the health, energy, agriculture, and industrial sectors, with a focus on advancing equity, improving biomanufacturing processes, and connecting relevant infrastructure." This section of the report defines biomanufacturing and describes the potential of biomanufacturing to contribute to U.S. economic growth.

Biomanufacturing – Background

Biomanufacturing is the use of biological systems, including plants and microbes such as bacteria, yeast, and algae, or the molecular components thereof, to produce products at relevant commercial scale.[9] For example, since the 1980s, scientists have been using living microbes to convert sugar from plants into insulin in industrial size fermenters, forming the basis of medication for diabetes. This technology was only possible because scientists advanced biotechnology—they programed microbes using DNA, essentially turning the microbes into microscopic factories.

In 2012, the Obama Administration released the National Bioeconomy Blueprint,[10] which laid out the initial framework to grow the U.S. bioeconomy and resulted in a number of key advances in biomanufacturing that now impact the everyday lives of Americans. The technology is now available to biologically produce 1,4-butanediol (BDO) at an industrial scale,[11] an intermediate to a wide array of products in the electronics, automotive, and apparel industries. A facility in Blair, Nebraska,[12] can transform corn into polylactic acid, a bioplastic used in additive manufacturing, food containers, landscaping, agriculture, and medical products, at industrial scale[13] using a process that generates substantially fewer greenhouse gas emissions than petroleum-based plastic manufacturing. Countless examples exist across many diverse sectors of the economy (Table 1), including biotechnology and

[9] NIST. 2022. "NIST Bioeconomy Lexicon." Last updated Dec. 9, 2022. https://www.nist.gov/bioscience/nist-bioeconomy-lexicon

[10] The White House. "National Bioeconomy Blueprint." 2012. https://obamawhitehouse.archives.gov/administration/eop/ostp/library/bioeconomy

[11] Burgard, A., et al., "Development of a commercial scale process for production of 1,4-butanediol from sugar." *Current Opinion in Biotechnology*, 2016. **42**: 118-125. https://www.sciencedirect.com/science/article/abs/pii/S0958166916301240

[12] Nebraska Corn Board. "Bioplastics." https://nebraskacorn.gov/cornstalk/research/bioplastics/

[13] Castro-Aguirre, E., et al., "Poly(lactic acid)—Mass production, processing, industrial applications, and end of life." *Advanced Drug Delivery Reviews*, 2016. **107**: 333-366. https://www.sciencedirect.com/science/article/abs/pii/S0169409X16300965

biomanufacturing for producing lubricants,[14] durable fibers,[15,16] sustainable aviation fuels,[17] food products,[18] growable cement,[19] crop protection solutions,[20] and biopharmaceuticals.[21]

Table 1. Example Bioeconomy Sectors and Product or Technology Categories[22,23]

	Bioeconomy Sector			
Product/Technology Category	**Human Health and Performance**	**Materials, Chemicals, and Energy**	**Agriculture, Aquaculture, and Food**	**Products and Services**
	• Monoclonal antibodies/protein-based therapeutics • Gene therapy • Cell therapy • Regenerative medicine • mRNA vaccines • Subunit vaccines • Small-molecule pharmaceuticals	• Industrial Chemicals (Commodity, Specialty, and Fine) • Lubricants • Plastics • Durable fibers and textiles • Biorefining to produce fuels (bioethanol, sustainable aviation fuel, and chemicals) • CO_2 sequestration • Biomining/biorecovery • Cement/building products	• Precision-fermented chemicals and proteins • Biomass feedstocks • Food, feed, fiber • Genetically engineered plants, animals, and microbes	• Cosmetics • Fragrances • DNA sequencing • Wellness and fitness

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

[15] Bhattacharyya, G., et al., "Large scale production of synthetic spider silk proteins in Escherichia coli." *Protein Expression and Purification*, 2021. **183**. https://doi.org/10.1016/j.pep.2021.105839

[16] Pena-Francesch, A., et al., "Biosynthetic self-healing materials for soft machines," *Nature Materials*, 2020. **19**: 1230-1235. https://www.nature.com/articles/s41563-020-0736-2

[17] DOE Bioenergy Technologies Office. "Sustainable Aviation Fuels." https://www.energy.gov/eere/bioenergy/sustainable-aviation-fuels

[18] Banks, M., et al. "Industrial production of microbial protein products." *Current Opinion in Biotechnology*, 2022. **75**. https://doi.org/10.1016/j.copbio.2022.102707

[19] Air Force Research Laboratory. "Biocement for Agile Infrastructure." https://afresearchlab.com/technology/biocement-for-agile-infrastructure/

[20] Sparks, T.C., et al. "Natural Product-Based Crop Protection Compounds—Origins and Future Prospects." *Journal of Agricultural and Food Chemistry*, 2023. https://doi.org/10.1021/acs.jafc.2c06938

[21] Szkodny, A.C. and K.H. Lee. "Biopharmaceutical Manufacturing: Historical Perspectives and Future Directions." *Annual Review of Chemical and Biomolecular Engineering*, 2022. **13**: 141-165. https://doi.org/10.1146/annurev-chembioeng-092220-125832

[22] The White House. "Report to the President: Biomanufacturing to Advance the Bioeconomy." President's Council of Advisors on Science and Technology. 2022. https://www.whitehouse.gov/wp-content/uploads/2022/12/PCAST_Biomanufacturing-Report_Dec2022_Letter-ExecSumm.pdf

[23] National Academies of Sciences, Engineering, and Medicine. "Safeguarding the Bioeconomy." 2020. https://doi.org/10.17226/25525

U.S. Biomanufacturing Landscape and Potential for Economic Growth

The U.S. bioeconomy is currently estimated to be worth hundreds of billions in direct economic value add,[23, 24, 25, 26, 27] primarily derived from the biopharmaceutical and health care industries. When indirect contributions[28] are accounted for, this value is estimated at almost $1 trillion. According to industry and private sector reports, the bioeconomy is expected to grow significantly over the next 15-25 years due to advances in foundational tools in such fields as synthetic biology.[29] Nascent biomanufacturing sectors, including specialty chemicals (e.g., key ingredients for critical medicines), food, and chemical precursors, are currently reported to make up only a small percentage of the bioeconomy. A 2023 industry report that focused specifically on U.S. bioindustrial manufacturing estimated that the direct value add of the non-health and non-agricultural sectors of the bioeconomy was $14.9 billion.[30] Though still emerging, these sectors have some of the greatest potential for growth, where a separate industry report predicts that an increase in biomanufacturing capacity will result in a seven-fold increase in their global market share by 2040 to $200 billion.[31]

Global Biomanufacturing Landscape

Globally, the current total value of the bioeconomy is estimated to be $4 trillion, and is projected to grow to $30 trillion by 2050.[28] U.S. allies and partners, as well as strategic adversaries, have well-developed bioeconomy strategies and are making key investments in research and development (R&D) and scale-up. China has indicated biotechnology and biomanufacturing are a top national priority starting with the 13th Five Year Plan and continuing into the 14th Five Year Plan with an emphasis on biomedicine and health, agriculture, industrial biotechnology, and frontier biotechnology, which includes synthetic biology and brain science. The European Union updated its bioeconomy strategy in 2018 and is reported to be investing nearly $12 billion between 2021 and 2027.[32]

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[24] *Direct economic value add*, also referred to as GDP by industry, is the market value it adds in production, or the difference between the price at which it sells its products and the cost of the inputs it purchases from other industries. For example, when a baker makes and sells a cake, the baker's value added is the market price of the cake minus the cost of the ingredients that the baker uses. https://www.bea.gov/resources/learning-center/what-to-know-industries

[25] Carlson, R. "Estimating the biotech sector's contribution to the US economy." *Nature Biotechnology*, 2016. **34**(3):247-55. https://doi.org/10.1038/nbt.3491

[26] Planetary Technologies. "Bioeconomy Dashboard." 2023. https://www.planetarytech.earth/bioeconomy-dashboard-1

[27] Golden, J.S., et al. "An Economic Impact Analysis of the U.S. Biobased Products Industry: 2023 Update." A Joint Publication of the Dynamic Sustainability Lab at Syracuse University and the Supply Chain Resource Cooperative at North Carolina State University. 2024. Volume V. https://www.rd.usda.gov/media/file/download/usda-rd-economic-impact-analysis-us-biobased-products-industry-2023-508.pdf

[28] *Indirect economic contribution*, also known as the multiplier effect, is the economic activity generated throughout the supply chain of an industry, encompassing the jobs, income, and GDP created when one industry buys inputs from another to produce its goods or services. This is often estimated using input-output tables. https://www.bea.gov/resources/learning-center/what-to-know-industries

[29] Chui, M., et al. "The Bio Revolution: Innovations Transforming Economies, Societies, and Our Lives." McKinsey Global. 2020. https://www.mckinsey.com/mgi/overview

[30] Teconomy Partners LLC. "The Economic Impact of the U.S. Bioeconomy." 2024. https://content.presspage.com/uploads/2544/4f7314e2-c45e-4e26-86be-70580565812b/economicimpactofu.s.industrialbioeconomy.v6.6.pdf

[31] Bobier, J.-F., et al. "Breaking the Cost Barrier in Biomanufacturing." Boston Consulting Group and Synonym. 2024. https://www.bcg.com/publications/2024/breaking-the-cost-barrier-on-biomanufacturing

[32] Congressional Research Service. "The Bioeconomy: A Primer." September 2022. https://crsreports.congress.gov/product/pdf/R/R46881

Without sustained U.S. investment, there is a risk of geographically concentrating biomanufacturing capacity in locations that could lead to supply chain vulnerabilities in times of geopolitical tension, resulting in costly disruptions that could have dramatic societal implications. As an example, in the agricultural sector, one report states that over 85% of certain amino acids used to supplement animal feed are now biomanufactured in China due to lower prices, which is impacting domestic production and has the potential to cost American jobs and economic activity.[33]

Goal of this Report

In December, 2022, OSTP conducted a Request for Information (RFI)[34] to seek public input on, among other topics, how biomanufacturing can help achieve societal goals and support a strong American bioeconomy. Input received as part of the RFI indicated that, to fully realize the economic benefits of biomanufacturing in the United States, businesses must be able to efficiently and predictably produce cost competitive biobased and biotechnology-derived products in America. The intent of this report is to provide strategic direction for a whole-of-government effort to grow U.S. biomanufacturing capacity based on this input and additional stakeholder engagement. Recent federal investments are highlighted, and specific actions are put forward to sustain momentum for growing capacity. As with other priority actions from the Bioeconomy EO, this report identifies international cooperation in biomanufacturing with like-minded partners to be an important component toward accelerating progress to promote and protect the U.S. and global bioeconomies.

[33] Brannon, I., and Kashian, R. "The Impact of the Amino Acids Industry on the U.S. Economy." *SSRN*, 2021. https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3894589

[34] The White House. "Request for Information; National Biotechnology and Biomanufacturing Initiative." Federal Register 2022-27600 (87 FR 77901). https://www.federalregister.gov/documents/2022/12/20/2022-27600/request-for-information-national-biotechnology-and-biomanufacturing-initiative

Key Terms

Bioeconomy: Economic activity derived from the life sciences, particularly in the areas of biotechnology and biomanufacturing, including industries, products, services, and the workforce.[a,b]

Biomanufacturing: The use of biological systems to produce goods and services at commercial scale.[a]

Biomanufacturing capacity: The quantity of product that can be produced with the infrastructure and operational resources available within a given facility, group of facilities, region, or industry sector.

Biomass: Any material of biological origin that is available on a renewable or recurring basis, for example, plants, trees, algae, and waste material such as crop residue, wood waste, animal waste and byproducts, food waste, and yard waste.[a]

Biological (biomass) feedstock: Biomass intended for use as a starting material or an intermediate ingredient to be converted to another material through biomanufacturing or another manufacturing process.[a]

Sustainability: The aspiration to meet current needs while maintaining capacity for future generations to meet their needs and while considering economic, social, and environmental impacts.[c,d]

Bioproduct: A product determined by the Secretary of Agriculture to be a commercial or industrial product (other than food or feed) that is—(A) composed, in whole or in significant part, of biological products, including renewable domestic agricultural materials, renewable chemicals, and forestry materials; or (B) an intermediate ingredient or feedstock. Synonymous with a biobased product.

Biobased product: Synonymous with bioproduct.[a]

Biotechnology: Technology that applies to and/or is enabled by life sciences innovation or product development.[a]

[a] NIST Bioeconomy Lexicon | National Institute of Standards and Technology
[b] Within the scope of this report, bioeconomy includes the share of the economy based on products, services, and processes derived from biological resources (e.g., plants and microorganisms) and encompasses multiple sectors, in whole or in part (e.g., agriculture, textiles, chemicals, and energy). The Bioeconomy: A Primer | Congressional Research Service
[c] Terms of Reference | AIM for Climate
[d] Definitions: Sustainability and Food Systems | U.S. Department of Agriculture

Biomanufacturing Capacity – Drivers and Current Investments

Biomanufacturing capacity is the quantity of product that can be produced with the infrastructure and operational resources available within a given facility, group of facilities, region, or industry sector. This definition is inclusive of all bioprocesses, such as fermentation and cell-free biosynthesis. This section of the report describes biomanufacturing capacity drivers that were identified through stakeholder feedback and engagement. Current investments stimulated by the Bioeconomy EO that bolster these drivers are also summarized.

Biomanufacturing Capacity Drivers

Four key drivers of biomanufacturing capacity were identified and include economic factors, technological advancements, infrastructure, and workforce availability. Drivers are sector agnostic, although product-specific requirements will dictate which have the greatest influence over the biomanufacturing development and commercialization pipeline. This pipeline includes the processes and decision points for biobased and biotechnology-derived products from ideation through product launch and commercialization and is described further in Appendix A. The pipeline can generally be broken into three phases that align with specific manufacturing readiness levels (MRLs): 1) proof of concept, 2) pilot-scale development and product testing, and 3) commercialization and production-scale manufacturing. While most products made by biomanufacturing will proceed through these three phases, the specific capacity needs at each phase can vary significantly by product or technology category. Drivers are described in more detail below and were used to inform the proposed actions in the section that follows.

Economic. Economic drivers include a diverse set of factors that impact the likelihood that a biomanufacturing company will be successful. These may include access to financing, demand for products or services, federal or state regulation, and international trade agreements. Economic drivers influence decisions companies make, such as where in the world to construct biomanufacturing capacity.

Technology. Technology drivers are advancements in manufacturing tools, techniques, or processes that influence biomanufacturing capacity. For example, advanced biomanufacturing may include improved yield through existing novel engineering biology approaches to access or develop new feedstocks, or innovation in downstream processing. Advanced biomanufacturing also offers the possibility of producing products or providing services with lower energy input and decreased carbon dioxide emissions, while simultaneously reducing operational costs.

Infrastructure. Infrastructure drivers refer to physical equipment used along the biomanufacturing development and commercialization pipeline, including feedstock pre-processing, fermentation or bioprocessing equipment, and downstream processing and purification infrastructure. A lack of domestic biomanufacturing infrastructure at the pilot-scale is reported to be a key bottleneck for launching new biobased and biotechnology-derived products limiting the testing and evaluation needed to validate commercial launch. Some larger biotechnology companies have in-house facilities for pilot-scale production; however, many turn to commercial development and manufacturing organizations (CDMOs), which were reported through the RFI to have long waiting lists and/or may not be outfitted for all types of biomanufacturing processes. U.S. biomanufacturing capacity has been

reported to be less than Europe and China,[35] implying that a continued reliance on overseas capacity for scale-up and commercial production could persist in the absence of sustained U.S. investment. The high capital investments required for scale-up infrastructure are prohibitive for most startups, and private capital is typically unwilling to invest in building pilot and commercial scale infrastructure without an offtake agreement, creating an impasse that is difficult for new companies to navigate.

Workforce. Workforce drivers include all skillsets workers will need along the biomanufacturing value chain. The biomanufacturing workforce includes both highly specialized bioengineers to design biological systems and the highly skilled process development engineers, automation experts, and maintenance support required for facilities to design, develop, and scale biomanufacturing technologies. Meeting this demand requires workforce expansion not only at biomanufacturing companies themselves, but across all sectors that support biomanufacturing capacity, including agriculture, transportation, data science, and equipment suppliers.

Progress and Current Investments

The Bioeconomy EO directed a number of actions aimed at bolstering biomanufacturing capacity. Progress and current investments are briefly highlighted here. While this list is not exhaustive, it provides examples across all drivers.

Increasing biomanufacturing capacity through innovation and infrastructure. Section 5 of the Bioeconomy EO specifically directs federal investment to expand biomanufacturing capacity, with an emphasis on improving biomanufacturing processes and connecting infrastructure. The following investments align with this policy objective.

- In September 2023, BioMADE, a Department of Defense (DoD) Manufacturing Innovation Institute, announced over $13 million in funding[36] for innovative solutions to expand biomanufacturing capacity for sustainable food sources, efficient downstream processing techniques, and novel biomass utilization. BioMADE also announced the first of a national network of pilot-scale biomanufacturing innovation facilities in Minnesota supported by a federal fiscal year 2023 appropriation of $300 million. In March of 2024, it was announced that California, Georgia, Hawaii, Indiana, Iowa, and North Carolina are currently under consideration as potential sites for the next facility.[37]
- As of November 2024,[38] DoD has announced thirty-four awards, totaling over $60 million, through the Defense Bioindustrial Manufacturing Program (DBIMP). Awardees will deliver a business and technical plan detailing how they intend to build a U.S. bioindustrial manufacturing production facility and catalyze the establishment of a bioindustrial

[35] Blois, M., "The US aims to close its fermentation capacity gap." Chemical & Engineering News, March 12, 2023. **101**(9). https://cen.acs.org/business/biobased-chemicals/US-aims-close-fermentation-capacity/101/i9

[36] BioMADE. "BioMADE Announces Nine Projects, $18.7 Million to Advance Domestic Bioindustrial Manufacturing and DoD Sustainability Goals." September, 2023. https://www.biomade.org/news/new-projects-2023

[37] BioMADE. "BioMADE Names Six States in Review for Expansion of Bioindustrial Manufacturing Infrastructure Network." March, 2024. https://www.biomade.org/news/biomade-names-six-states-in-review-for-expansion-ofnbsp-nbspbioindustrial-manufacturing-infrastructure-networknbsp

[38] DoD. "DoD Releases Final Nine Awards for Distributed Bioindustrial Manufacturing Program." September 2024. https://www.defense.gov/News/Releases/Release/Article/3965368/dod-releases-final-nine-awards-for-distributed-bioindustrial-manufacturing-prog/

manufacturing base. Awardees can receive follow-on awards of up to $100 million for U.S.-based biomanufacturing infrastructure.

- The DoD Office of Strategic Capital announced in September 2024 a Notice of Funding Availability for critical technologies that includes biochemicals, bioenergetics, biomass, and synthetic biology.[39]
- Two of the 12 recently announced Economic Development Administration's (EDA) Tech Hub awardees will focus specifically on biomanufacturing infrastructure; Heartland BioWorks (Indiana) and iFAB Tech Hub (Illinois) were both awarded $51 million.[40] Heartland BioWorks will expand U.S. biomanufacturing for biopharmaceuticals prior to making advancements into animal health and agriculture.[41] The iFAB Tech Hub will enable multi-use scale-up infrastructure for biomanufacturing developers.[42] Both investments are expected to result in investment of additional private capital.
- Department of Energy's (DOE) Office of Science supported $264 million for twenty-nine projects to address the scientific challenges underlying DOE's Energy Earthshots™ Initiative[43] to advance clean energy technologies within the decade and drive broader innovation for a sustainable bioeconomy.
- The DOE's Bioenergy Technology Office (BETO) is supporting $151 million to scale promising technologies that convert biomass to biofuels and bioproducts. DOE's Fossil Energy and Carbon Management Office (FECM) and BETO have also provided $80 million to support research, and field trials for biomass and waste feedstocks including CO_2 gases, micro- and macro algae and energy crops, and over $40 million to support research in the development of industrially relevant biocatalysts/microorganisms.
- DOE's Office of Clean Energy Demonstration (OCED) announced up to $200 million in Federal Cost Share for the Sustainable Ethylene from CO_2 Utilization with Renewable Energy (SECURE) project, with plans to demonstrate an integrated process to utilize captured carbon dioxide from ethylene production, an important building block for many products, by applying a biotech-based process and green hydrogen to create clean ethanol and ethylene.

[39] DoD. "Office of Strategic Capital Announces First Notice of Funding Availability to Secure the U.S. Industrial Base." September 2024. https://www.defense.gov/News/Releases/Release/Article/3921005/office-of-strategic-capital-announces-first-notice-of-funding-availability-to-s/

[40] EDA. "Biden-Harris Administration Announces Next Funding Round of $504 Million for 12 Tech Hubs Across America." July 2024. https://www.eda.gov/news/press-release/2024/07/02/biden-harris-administration-announces-next-funding-round-504-million.

[41] EDA. "Heartland BioWorks." July 2024. https://www.eda.gov/funding/programs/regional-technology-and-innovation-hubs/2023/Heartland-BioWorks.

[42] EDA. "iFAB Tech Hub." July 2024. https://www.eda.gov/funding/programs/regional-technology-and-innovation-hubs/2023/iFAB-Tech-Hub

[43] DOE. "Energy Earthshots Initiative." https://www.energy.gov/policy/energy-earthshots-initiative

- The DOE Loans Program Office (LPO) announced three conditional loan guarantees this year for biomanufacturing projects located in Marshall, Minnesota,[44] Great Falls, Montana,[45] and Lake Preston, South Dakota.[46]
- Since July 2024, the Health and Human Services (HHS) Administration for Strategic Preparedness and Response (ASPR) Center for Industrial Base Management and Supply Chain (IBMSC) announced $30.9 million to three biotechnology companies to fund scale-up[47] biomanufacturing of key starting materials and active pharmaceutical ingredients needed to make essential medicines.

Biomass supply chain. In March 2024, the United States Department of Agriculture (USDA) published a report on Building a Resilient Biomass Supply[48] as directed by Section 5 of the Bioeconomy EO. The report outlines a plan to boost the biomass supply chain for domestic biobased product manufacturing and market opportunities for small and mid-sized producers, providing job opportunities to rural communities and making progress toward U.S. sustainability goals. The report was accompanied by an implementation framework[49] and fact sheet[50] outlining USDA's accomplishments and investment so far. In parallel, DOE released its updated, Billion Ton[51] report cataloging how America can sustainably produce more than one billion tons of biomass per year. This report will guide technology development aimed at broadening the types of biomass used for biomanufacturing.

Biobased products procurement. Federal procurement is one of the most impactful levers the U.S. government has to create demand for emerging industries, as the United States is the single largest purchaser of consumer goods in the world, with $700 billion in annual procurement spending.[52] Programs targeted at increasing federal procurement and consumer purchasing of biobased products can be impactful. For example, an economic impact analysis released in March 2024 by USDA demonstrated an increase in the contribution of biobased products to the U.S. economy of 5.1% from 2020 to 2021.[53]

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[44] DOE. "LPO Announces Conditional Commitment to Solugen's Bioforge Marshall for Sustainable Biomanufacturing." June 2024. https://www.energy.gov/lpo/articles/lpo-announces-conditional-commitment-solugens-bioforge-marshall-sustainable

[45] DOE. "LPO Announces Conditional Commitment to Montana Renewables to Significantly Expand US Sustainable Aviation Fuel Production." October 2024. https://www.energy.gov/lpo/articles/lpo-announces-conditional-commitment-montana-renewables-significantly-expand-us

[46] DOE. "LPO Announces Conditional Commitment to Gevo Net-Zero for Corn Starch-to-Sustainable Aviation Fuel Facility in South Dakota."October 2024. https://www.energy.gov/lpo/articles/lpo-announces-conditional-commitment-gevo-net-zero-corn-starch-sustainable-aviation

[47] ASPR. 2024. "Molecule Regulatory Starting Materials and/or Active Pharmaceutical Ingredients at Commercial Scale." 2024. https://www.biomap-consortium.org/portfolio-items/smallmol_awards/?portfolioCats=141

[48] USDA. "Building a resilient biomass supply: a plan to enable the bioeconomy in America." 2024. https://www.usda.gov/media/press-releases/2024/03/14/usda-outlines-vision-strengthen-american-bioeconomy-through-more

[49] USDA. "USDA implementation framework for a plan to enable the bioeconomy in America: building a resilient biomass supply." 2024. https://www.usda.gov/sites/default/files/documents/usda-implementation-framework.pdf

[50] USDA. "USDA bioeconomy accomplishments." 2024. https://www.usda.gov/sites/default/files/documents/bioeconomy-2023-accomplishments-fact-sheet.pdf

[51] DOE. "2023 Billion-Ton Report: An Assessment of U.S. Renewable Carbon Resources." March 2024. https://www.energy.gov/sites/default/files/2024-03/beto-2023-billion-ton-report_2.pdf

[52] OMB. "Made in America." https://www.madeinamerica.gov/#:~:text=With%20%24700%20billion%20in%20annual,consumer%20goods%20in%20the%20world

[53] USDA. "USDA Celebrates Second National Biobased Products Day." March 2024. https://www.usda.gov/media/press-releases/2024/03/08/usda-celebrates-second-national-biobased-products-day

Section 6 of the Bioeconomy EO makes several directives toward understanding and increasing federal procurement of biobased products. The Office of Management and Budget (OMB) conducted an internal analysis of biobased products procurement across the federal government to serve as a baseline for continued monitoring. [54] To increase federal procurement of biobased products, USDA has recently created a short Biobased Products Purchase Card Holder training video[55] intended to quickly and easily train purchase card holders on biobased purchasing requirements and benefits. This new video is in addition to USDA's existing trainings and resources[56] within their BioPreferred® Program.

Biomanufacturing workforce. The recent White House plan for *Building the Bioworkforce of the Future*,[57] developed in response to the requirements of Section 7 of the Bioeconomy EO, provides detailed recommendations for building and expanding the U.S. biotechnology and biomanufacturing workforce. An expanding bioeconomy and biomanufacturing industry mean increased demand for talent across a range of skills, education, and occupations. The lack of a sufficiently large, trained workforce will hamper the expansion of biomanufacturing capacity across all sectors of the bioeconomy. Some U.S. companies currently offshore a significant portion of their biomanufacturing scale-up to take advantage of expertise abroad. An expanded network of education and workforce development assets with a commitment to equity of opportunity can help build the domestic biomanufacturing workforce and ensure the promise of bioeconomy growth for U.S. economic and national security.

Measuring the U.S. bioeconomy. To more accurately determine the size of the U.S. bioeconomy, Section 10 of the Bioeconomy EO directed the Bureau of Economic Analysis (BEA) to conduct a feasibility assessment[58] on how to formally measure the size of the U.S. bioeconomy through a satellite account. In parallel, the National Institute of Standards and Technology (NIST) created a bioeconomy lexicon[59] to define common terms for the bioeconomy that will enable consistent measurements, and USDA made public a report[60] on recommendations for revising industry and product codes required for economic analyses. Definitions and accurate measurements are important for understanding the impact of increasing biomanufacturing capacity on economic growth.

International engagement. Section 12 of the Bioeconomy EO directs international engagement to grow the bioeconomy, and thus drive biomanufacturing capacity across the globe with like-minded allies and partners. This year the G20 developed high level principles for the bioeconomy.[61] The National Science Foundation (NSF) also recently announced $82 million in six global centers focused on accelerating innovation to advance the bioeconomy.[62] In June 2024, the National Security Council

[54] OMB. "Entity Reporting." https://sam.gov/content/entity-reporting
[55] USDA. "Biobased products purchase card holder training video." October 2024. https://www.youtube.com/watch?v=YP0UBaBnA_Y
[56] USDA. "BioPreferred." https://www.biopreferred.gov/BioPreferred/
[57] The White House. "Building the Bioworkforce of the Future." 2023. https://www.whitehouse.gov/wp-content/uploads/2023/06/Building-the-Bioworkforce-of-the-Future.pdf
[58] BEA. "Developing a National Measure of the Economic Contributions of the Bioeconomy." March 2023. https://www.bea.gov/system/files/papers/bea-bioeconomy-report.pdf
[59] NIST. "NIST Bioeconomy Lexicon." December 2022. https://www.nist.gov/bioscience/nist-bioeconomy-lexicon.
[60] USDA. "Measuring the Bioeconomy: Recommended Revisions to the NAICS and NAPCS." https://www.usda.gov/sites/default/files/documents/OCE-Measuring-the-Bioeconomy.pdf
[61] G20. "G20 reaches consensus and establishes High-Level principles on Bioeconomy." September 2024. https://www.g20.org/en/news/g20-reaches-consensus-and-establishes-high-level-principles-on-bioeconomy
[62] NSF. "NSF and international partners to invest $82M in 6 Global Centers in 2024." October 2024. https://new.nsf.gov/news/nsf-international-partners-invest-82m-six-2024-global

in partnership with the Office of Pandemic Preparedness and Response Policy announced the Biopharma Coalition (Bio-5) to support secure biopharmaceutical supply chains.[63]

Further Expanding U.S. Biomanufacturing Capacity

Progress, actions, and investments reviewed above are contributing to U.S. biomanufacturing capacity, but may be insufficient to fully realize the projected economic potential reported by industry experts. Sustained funding over the next five to ten years to increase U.S. biomanufacturing capacity could have a profound impact on economic and job growth, particularly in nascent biomanufacturing sectors, such as chemicals. An industry assessment[31] concluded that an additional 2.4 billion liters of large-scale production capacity would be required globally to achieve a market potential of $200 billion for biomanufacturing of specialty chemicals (including key ingredients for critical medicines), food, and chemical precursors by 2040. The cost of the infrastructure alone could be in the hundreds of billions of dollars, where pilot and commercial scale facilities will cost hundreds of millions of dollars each. For example, a single commercial scale facility to produce 1,4-BDO[64] is costing $300 million to construct in Eddyville, Iowa, and will produce 65,000 tons per year, the largest market being spandex. As noted above, bioindustrial manufacturing in the United States, which includes chemicals, contributes an estimated $14.9 billion annually in direct value add. To maintain a competitive market share as this sector expands, U.S. biomanufacturing capacity must continue to increase.

EDA's Tech Hubs program project narratives describing scale-up biomanufacturing initiatives in Indiana and Illinois, including infrastructure and workforce development, estimate that the $51 million investments will each generate roughly 1,000-2,000 biomanufacturing jobs and $1-2 billion in direct economic benefit over ten years. Awardees also expect these investments to result in hundreds of millions of dollars in additional private investment. Extrapolating from these estimates, a federal investment of $5-10 billion over the next five years to support similar efforts to increase biomanufacturing capacity could result in at least 100,000-200,000 new jobs and hundreds of billions of dollars a year in direct economic impact, not including indirect benefits, bringing the United States close to anticipated growth. To deploy such funds, programs outlined above or cited in Appendix B could be fully resourced and/or expanded. Such an investment would be subject to the annual President's Budget process and availability of appropriations.

The following eleven actions and sub-considerations are based on feedback received through the RFI and stakeholder engagement. These actions could be considered by federal departments and agencies to drive a strategic direction for a sustained investment in biomanufacturing capacity to grow a sustainable, safe, and secure U.S. bioeconomy.

1. **Further leverage procurement programs and incentives to increase the U.S. market share of biobased and biotechnology-derived products and services, and ensure tools are in place to accurately measure resulting economic growth.**

[63] The White House. "Fact Sheet: Biden-Harris Administration's Actions to Advance American Biotechnology and Biomanufacturing." June 2024. https://www.whitehouse.gov/ostp/news-updates/2024/06/25/fact-sheet-biden-harris-administrations-actions-to-advance-american-biotechnology-and-biomanufacturing

[64] Cargill. "Cargill and HELM partner to build $300M commercial-scale, renewable BDO facility, first in the US, to meet growing customer demand." June 2021. https://www.cargill.com/2021/cargill-and-helm-partner-to-build-$300m-facility

- Utilize existing public outreach programs to increase the visibility of USDA's BioPreferred® program and expand consumer awareness of biobased products.
- Continue to encourage federal procurement of biobased or biotechnology-derived products during scale-up and demonstration to de-risk private sector investment.
- Consider targeted federal incentives for biobased or biotechnology-derived products as solutions when U.S. supply chain vulnerabilities are identified.
- Consider a formal economic assessment of the U.S. bioeconomy as described by BEA in response to Section 10 of the Bioeconomy EO once industry and product codes have been sufficiently revised. Utilize this assessment to monitor market expansion of biobased and biotechnology-derived products.

2. **Create right-sized federal incentives to accommodate the range of sizes of biotechnology and biomanufacturing companies.**

   - Expand public-private partnership opportunities for construction of greenfield biomanufacturing infrastructure to accelerate financing for unproven and first-of-its-kind processes.
   - Incentivize the use of U.S.-based contract manufacturing and development organizations for scale-up and demonstration.
   - Incentivize the use of platform technology companies that reduce cost and time to scale-up for product manufacturers.

3. **Engage in international partnerships to address cross-border challenges that otherwise limit the global footprint of U.S. biomanufacturing, such as intellectual property protection and enforcement, barriers to market entry abroad, and international market competitiveness.**

   - Continue to work with like-minded allies and partners to advance research, development, and innovations in biomanufacturing through initiatives such as the NSF's Global Centers.
   - Align biomanufacturing policy with solutions to global climate goals, such as the Paris Agreement, emphasizing the role of biobased products in achieving sustainability targets.
   - Work with allies and partners to identify opportunities to address global supply chain vulnerabilities by expanding availability of biobased and biotechnology-derived products.
   - Develop mutually agreed technical guidance to enhance or expand biomanufacturing and intellectual property protection and enforcement capabilities in low- and middle-income countries.
   - Minimize risk of intangible technology transfer and theft of intellectual property through export licensing and conduct outreach to the private sector to increase their capacity to protect themselves against these risks.

4. **Enable further technology advances by supporting research and development and initiatives that improve biomanufacturing scale-up efficiency.**

   - Support research and development in modeling and simulation capabilities to predict scale-up requirements across the range of biomanufacturing sectors.
   - Develop biomanufacturing standards through precompetitive knowledge sharing to advance technology.

- Support equipment standardization and development of modular systems that can be reconfigured to enable accelerated scale-up development across a broad range of sectors, including point-of-care and in-hospital manufacturing, to spur innovation.
- Support research and development to better enable product launch and commercialization. This could mean incentivizing technoeconomic and lifecycle analysis and feasibility demonstrations.
- Establish U.S. regional data sets to assist regional planning for biomanufacturing facilities that maximize yield/resource ratio.
- Consider incentives to reduce energy and water demands at biomanufacturing facilities. For example, require that manufacturing processes utilize clean electricity and zero-emission transportation.
- Encourage a robust intellectual property ecosystem to ensure continued innovation.

5. Encourage further development and utilization of a diverse and sustainable biomanufacturing feedstock supply chain as input material for biomanufacturing.

- Consider implementing recommendations from USDA's plan for "Building a Resilient Biomass Supply," which will expand opportunities for rural communities and has the potential to create jobs and lead to economic growth.
- Continue federal support for programs aimed at innovating and expanding the production, pre-processing and demand for a diversity of biomass feedstock (e.g., plant biomass, industrial off gas, and waste streams). Provide additional resources for programs to educate producers about opportunities to develop alternative revenue streams related to biomass feedstock production.

6. Encourage biomanufacturing industry adoption of established corporate manufacturing best practices that minimize environmental impacts and conserve energy to lower operational costs and speed production output timelines.

- Recommend the use of manufacturing processes that minimize negative environmental impacts while conserving energy and natural resources. The National Strategy for Advanced Manufacturing outlines goals for enhancing environmental sustainability and addressing climate change across manufacturing.[65]
- Recommend the use of sustainable material management principles into the development of the commercialization pipeline.
- Encourage co-location of biomanufacturing facilities with biomass feedstock to reduce lifecycle greenhouse gas emissions. Consider how existing infrastructure can be utilized to process and transport feedstock and products.
- Support R&D in the areas of sorting, purification, and deconstruction technologies to enable bioderived chemicals and products. Scale-up sustainable materials design and manufacturing, recycling, and circular methods for multiple materials classes, as well as pilot programs and facilities.

[65] The White House. "National Strategy for Advanced Manufacturing." National Science and Technology Council Subcommittee on Advanced Manufacturing. October 2022 . https://www.whitehouse.gov/wp-content/uploads/2022/10/National-Strategy-for-Advanced-Manufacturing-10072022.pdf.

7. **Continue to expand the availability of U.S. biomanufacturing scale-up infrastructure through a distributed network.**
   - Support R&D aimed at moving low MRL (2-4) innovations to commercial readiness (MRL 5-7) through applied research and demonstration programs across all sectors.
   - Fully enable a national network of pilot-scale infrastructure to facilitate the scale-up of new biobased and biotechnology-derived products.
   - Consider coordinating regional investments through the Manufacturing Innovation Institutes, Tech Hubs program, or the NSF Engines program to maximize impact in rural communities and stimulate job growth.

8. **Further integrate the emerging U.S. bioeconomy with the clean energy economy to enable a sustainable commercial biomanufacturing ecosystem.**
   - Propose guidance to encourage commercial scale facilities to aim for reduced energy and water usage, carbon capture technologies, access to green hydrogen, renewable energy, and zero emission transportation.

9. **Advance U.S. biological risk management for biotechnology and biomanufacturing research and development.**
   - Strengthen the existing foundation of collective biosafety and biosecurity guidance through continued research and risk assessment.
   - Leverage this foundation to make informed investments in developing risk mitigation tools and strategies, such as standard operating procedures, for new technologies. This includes resourcing policymakers and oversight, strengthening the biosafety and biosecurity workforce, and bolstering biorisk management infrastructure.
   - Reinforce and optimize desired outcomes to emphasize a culture of biosafety and biosecurity through whole-of-government coordination and stakeholder outreach.

10. **Continue to modernize biomanufacturing digital infrastructure to meet ecosystem informatics needs**.
    - Implement policy recommendations from the interagency Data for the Bioeconomy report,[66] developed in response to the requirements of Section 4 of the Bioeconomy EO
    - Support programs aimed at developing a comprehensive system that combines data integration across platforms, levels, scales, facilities, and type to gain a more complete perspective on biomanufacturing workflows. Develop policies to encourage nongovernmental institutions and industry to share data at the precompetitive stage.
    - Make the latest computational advances accessible to the workforce and ensure biomanufacturing stays state of the art by incorporating content into bioeconomy workforce development initiatives.
    - Leverage Interagency Working Groups, professional societies, and other mechanisms to maintain coordination across agencies and with stakeholders to support biodata stewardship and promote the use of data standards for rigorous data security, especially for use in computational and artificial intelligence applications.

[66] The White House. "Vision, Needs, and Proposed Actions for Data for the Bioeconomy Initiative." National Science and Technology Council, Interagency Working Group on Data for the Bioeconomy. December 2023. https://www.whitehouse.gov/wp-content/uploads/2023/12/FINAL-Data-for-the-Bioeconomy-Initiative-Report.pdf

- Develop policies for the life cycle security of data, especially for handling sensitive industry or personal data. Develop a data-agnostic infrastructure capable of controlling access for sensitive data and implement of cybersecurity best practices.

11. Further expand and diversify the U.S. talent pool for biotechnology and biomanufacturing jobs and careers to promote innovation and advance equity.

- Strengthen worker-centered sector strategies and other partnerships between employers, labor organizations, community colleges, Land-grant universities, the Cooperative Extensions Systems and other training providers to grow and diversify the bioworkforce.
- Develop, scale, and promote effective approaches to education and training for biotechnology and biomanufacturing jobs and careers.
- Define career pathways and include regional considerations to meet the workforce where they live, such as in rural communities.
- Support easier translation of data and knowledge across sectors and into adjacent workforce, including the financing community and lawyers, to advance equity and support effective workforce development, including the development of industry-recognized credentials and competency models.
- Develop and promote effective approaches to education and training for biotechnology and biomanufacturing jobs and careers in parallel to infrastructure development, including international exchanges.

Conclusion

As other countries ramp up spending on biotechnology and biomanufacturing, the United States must sustain investment in biomanufacturing capacity, including the foundational scientific capabilities, scale-up and commercial production infrastructure and incentives, and workforce to not only maintain, but grow the global market share of biobased and biotechnology-derived products. If not, the United States risks concentrating scale-up and commercialization capacity with strategic adversaries and losing out on good-paying jobs and other economic development opportunities.

Realizing the full economic potential of the bioeconomy could be achieved through investment in biomanufacturing capacity based on the drivers identified above, including scale-up infrastructure and incentives to bring new, advanced products to market. Infrastructure expansion could leverage opportunities to incorporate sustainability and energy efficiency to achieve cost-competitive biobased and biotechnology-derived products, enable a well-trained workforce, consider all aspects of biosafety and biosecurity, and include continued engagement with international partners and allies. In doing so, data infrastructure requirements and streamlining and clarifying biotechnology regulations[67] must also be considered, both of which are discussed in detail in other U.S. government reports.

This report presents the current landscape and investments in U.S. biomanufacturing capacity, as well as recommended actions for federal departments and agencies to consider as the basis for a comprehensive effort across government to increase infrastructure and drive demand for biobased and biotechnology-derived products. These actions provide a strategic direction for coordinating and

[67] USDA, EPA, and Food and Drug Administration (FDA). "The Coordinated Framework for the Regulation of Biotechnology: Plan for Regulatory Reform under the Coordinated Framework for the Regulation of Biotechnology ." May 2024. https://usbiotechnologyregulation.mrp.usda.gov/eo14081-section8c-plan-reg-reform.pdf.

aligning current investments within federal agencies, such as through the National Bioeconomy Board, to establish priorities, identify funding gaps, and create a government wide roadmap to grow biomanufacturing capacity.

Appendix A. Biomanufacturing Development and Commercialization Pipeline

In the 1970s, National Aeronautics and Space Administration (NASA) developed Technology Readiness Levels (TRLs) to describe the maturity level of a new technology. More than 30 years later, DoD established MRLs[68] to assess the manufacturing readiness of a given technology or product. TRLs and MRLs have recently been adapted to describe biobased and biotechnology-derived products in both the biopharmaceutical sector using Biomanufacturing Readiness Levels (BRLs),[69] and across non-health sectors using Bioindustrial Manufacturing Readiness Levels (BioMRLs).[70]

The biomanufacturing development and commercialization pipeline includes the processes and decision points for biobased and biotechnology-derived products from ideation through product launch and commercialization (Figure A-1). The pipeline can generally be broken into three phases that align with specific BRLs or BioMRLs using typical scale/production volumes for commodity chemical biomanufacturing, and noting these parameters will vary for other sectors such as biopharmaceuticals or certain high value specialty chemicals:

1. **Proof of concept (MRL 1-3)**: At this phase, researchers in industry and academia develop a biological system to synthesize a molecule (e.g., commodity chemical or biological product) of interest. They work to optimize this system at a small, lab scale to demonstrate that a given product is feasible. This laboratory-based work often leverages the tools of molecular biology, engineering biology, automation, bioinformatics, and machine learning to iterate on a "design-build-test-learn" cycle before making meaningful quantities of a potential product. For technologies that use fermentation as the method of production, this phase typically does not exceed 100 liters. As a result of increasing public and private investment in modern biotechnology, companies can make small quantities of an increasingly vast array of materials in a predictable and reliable manner.
2. **Pilot-scale development and product testing (MRL 4-7)**: Biomanufacturing must undergo process development, and then the process must scale up to make sufficient quantities of a proposed product for testing and validation. This quantity of product may be much larger than that which can be made at a laboratory scale, typically ranging from 1 kilogram to 1 ton. For biomanufacturing technologies that use fermentation, pilot-scale demonstration (typically 5,000 to 70,000 liters) and downstream processing (separations & purification) infrastructure is required for companies to generate sufficient material for testing and to develop and optimize their manufacturing processes. For each order of magnitude change in fermentation volume up to 20,000 liters, the dynamics of the fermentation process can significantly affect the final titer. In some cases, computational models may allow more rapid scaling, but customer validation still requires producing some initial material.

[68] DoD. "Manufacturing Readiness Levels." https://www.dodmrl.com/

[69] Kedia, S.B., et al. "Biomanufacturing readiness levels [BRL]—A shared vocabulary for biopharmaceutical technology development and commercialization." *Biotechnology and Bioengineering.* 2022. **119**(12): p. 3526-3536. https://doi.org/10.1002/bit.28227.

[70] Smanski, M.J., et al. "Bioindustrial manufacturing readiness levels (BioMRLs) as a shared framework for measuring and communicating the maturity of bioproduct manufacturing processes." *Journal of Industrial Microbiology and Biotechnology*, 2022. **49**(5). https://doi.org/10.1093/jimb/kuac022.

3. **Commercialization and production-scale manufacturing (MRL 8-9)**: Once proven at a pilot-scale, biomanufacturing can transition to commercial production scale. For many products in the chemicals industry, the global markets are measured in the millions of tons and, for products made through fermentation, often require infrastructure greater than 200,000 liters in production capacity. Several American businesses have established significant infrastructure at this scale throughout the country to deliver products and yield profitable companies.

While most products made by biomanufacturing will proceed through the three phases described above, the specific infrastructure needs at those phases—including size, regulatory, and processing requirements—can vary dramatically by product sector. For example, biomanufacturing of commodity chemicals will require millions of liters of production volume to achieve a meaningful commercial quantity, whereas biologics require biomanufacturing volumes in the hundreds to thousands of liters with additional Good Manufacturing Practices in place to meet Food and Drug Administration (FDA) guidelines.

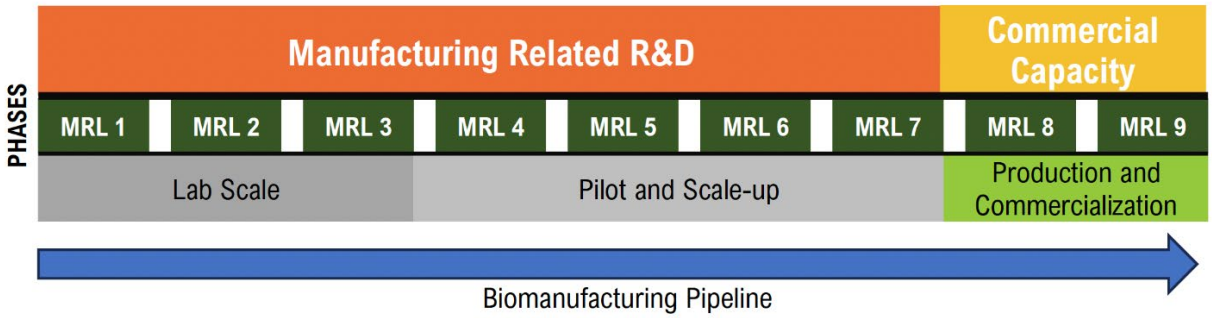

Figure A-1. Manufacturing readiness levels (MRLs) for biobased and biotechnology-derived products. Biomanufacturing process and product development is a systematic, life cycle approach that tracks the MRL of a technology or product as it matures through R&D proof of concept (MRL 1–3), pilot-scale and scale-up (MRL 4–7), and the realization of commercial production (MRL 8+).

Appendix B. Current Government-supported Biomanufacturing Capacity

The trajectory of the U.S. bioeconomy, including retention of talent, intellectual property, and supply chain commodities that may otherwise be lost to other countries, is dependent on near-term and sustained investments. The U.S. government has therefore been investing in a broad array of biotechnology and biomanufacturing applications and infrastructure to harness their power to further societal goals.

Biomanufacturing process and product development is a systematic, life cycle approach that progresses through R&D, pre-commercial, and commercial phases, and as such, investments should be made and tracked as a function of this cycle. MRLs are a commercial maturation classification system for describing the maturity of new technologies from the concept phase to commercialization. BRLs or BioMRLs are adapted from DoD's manufacturing readiness levels to include bioeconomy sector-specific considerations associated with biopharmaceutical and industrial biomanufacturing, respectively. BRLs or BioMRLs also serve as a mechanism to categorize U.S. investments in the bioeconomy through R&D proof of concept (MRL 1–3), pilot-scale and scale-up (MRL 4–7; i.e., translational science), and the realization of commercial production (MRL 8+).

Table B-1 highlights several examples of U.S. government-funded infrastructure and capabilities, each of which is categorized by MRL life cycle stage. They are available to support expanded partnerships and serve as examples upon which to build as the U.S. bioeconomy continues to grow.

Table B-1. Selected Program Examples

MRL	Agency	Relevant Programs	Description
1–3	NSF	Bioeconomy MetaProgram	Coordinates the efforts of core programs and a number of focused funding opportunities, including: • Designing Synthetic Cells Beyond the Bounds of Evolution • Reproducible Cells and Organoids via Directed-Differentiation Encoding • Understanding the Rules of Life: Microbiome Interactions and Mechanisms • Designing Materials to Revolutionize and Engineer our Future • Molecular Foundations for Biotechnology
		BioFoundries to Enable Access to Infrastructure and Resources for Advancing Modern Biology and Biotechnology	Supports infrastructure that is designed to accelerate advances in the biological sciences, chemical biology, biotechnology, and bioengineering via access to modern infrastructure, technology, and capacity.
	DOE	Office of Science National Scientific User Facilities Specifically: • High performance computing resources for basic research • Synchrotron light and neutron sources for structural biology • Joint Genome Institute • Environmental Molecular Sciences Laboratory • X-Ray Light Sources, Neutron Scattering Facilities, and Nanoscale Science Research Centers	The DOE Office of Science national scientific user facilities provide researchers with the most advanced tools of modern science for studying the nano world, the environment, and the atmosphere. User facilities that directly support research relevant to biomanufacturing include the high-performance computing centers, synchrotron light and neutron sources and electron microscopy capabilities for structural biology, genome sequencing for microbial communities and plants at the Joint Genome Institute, and environmental interactions that underpin bioenergy and environmental research at the Environmental Molecular Sciences Laboratory.
		Bioenergy Research Centers, Genomic Science Program	Research addresses key basic science challenges in converting plant biomass to fuels and products.

MRL	Agency	Relevant Programs	Description
1-9	NIST	NIST Living Measurement System Foundry	Enables the engineering of cells for reliable and safe use in dynamic and unpredictable environments for applications such as living therapeutics, environmental sensing, and structured materials fabrication.
		NIST-hosted Consortia: Genome Editing Consortium NIST Flow Cytometry Standards Consortium NIST Rapid Microbial Testing Consortium	Addresses the measurements and standards needed to accelerate research, development, manufacturing, and commercialization of products.
		NISTCHO Reference Material	Provides a publicly available, industry-like CHO cell line for fostering open data sharing and development of new biomanufacturing technologies.
3–4	DOE	Agile BioFoundry	Consortium of seven national laboratories focused on developing biomanufacturing tools, processes, and partnerships that enable sustainable industrial production of renewable fuels and chemicals.
		Advanced Biofuels and Bioproducts Process Development Unit	Industry-scale test beds to bridge the gap between promising research and large-scale production of biofuels/bioproducts.
4–5	DOE	Biomass Feedstock National User Facility	Technology and expertise to help the U.S. bioenergy industry overcome biomass challenges during scale-up and integration of biomass preprocessing facilities.
		Integrated Biorefinery Research Facility	Technology and expertise to develop, test, evaluate, and demonstrate processes and technologies to produce biobased products and fuels at pilot-scale.
4–7	DoD	BioMADE	Bioindustrial manufacturing innovation, education, and collaboration.
		BioFabUSA	A highly diverse, competitive, capable, and innovative domestic cell, tissue, and organ manufacturing ecosystem.
	Department of Commerce (DOC), NIST	The National Institute for Innovation in Manufacturing Biopharmaceuticals	A public-private partnership whose mission is to accelerate biopharmaceutical innovation, support the development of standards that enable more efficient and rapid manufacturing capabilities, and educate and train a world-leading biopharmaceutical manufacturing workforce, fundamentally advancing U.S. competitiveness in this industry.

MRL	Agency	Relevant Programs	Description
1-7	USDA	Agricultural Research Service (ARS) Culture Collection (NRRL)	The ARS Culture Collection is one of the largest public collections of microorganisms in the world, and the only collection in the federal government containing approximately 98,000 isolates of bacteria and fungi important to biomanufacturing.
1-7		Agricultural Research Service Germplasm Resources Information Network (GRIN)	The Germplasm Resources Information Network (GRIN) provides information about USDA national collections of animal, microbial, and plant genetic resources (germplasm) important for food and agricultural production and biomanufacturing.
1-7		Agricultural Research Service Regional Biomass Research Centers	USDA Regional Biomass Research Centers provide a coordinated, region-based research focus designed with relatively short-term deliverables to help accelerate the biomanufacturing of biomass and other biofuel feedstocks: the Southeast Regional Biomass Research Center : USDA ARS (Tifton, GA); Central-East Biomass Research Center (Lincoln, NE); Northwestern Biomass Research Center (Sidney, MT); Western Biomass Research Center (Maricopa, AZ). Research at these centers focuses on feedstock development, production, and conversion.

MRL	Agency	Relevant Programs	Description
1-7	USDA	Agricultural Research Service (ARS) Utilization Centers	ARS utilization centers spur development of novel food sources, including new crops and protein sources to augment our current food system, increasing food quality and nutrition, utilizing waste streams for value-added opportunities, providing viable and cleaner biobased alternatives to fossil fuels, enabling biobased health products and healthful alternative foods through bioprocesses, protecting against plant and animal pests and diseases, and cultivating novel food sources to improve food and nutrition security.
		The Western Regional Research Center	The Western Regional Research Center develops technologies that enable growth and profitability in biomanufacturing the wide range of California crops (>400 commodity crops) and byproducts via their pilot plant incubator space.
		Eastern Regional Research Center	The Eastern Regional Research Center develops technologies that enable growth and profitability in biomanufacturing packaging films and biobased products, biofuels and coproducts, advanced food processing technologies, bioactive ingredients, and functional foods via pilot plant incubator space.
		Southern Regional Research Center Commodity Utilization Research Unit	The Commodity Utilization Research Unit Southern Regional Research Center develops technologies that enable growth and profitability in biomanufacturing southern crops (e.g., sugarcane, sweet sorghum, energy beets, cottonseed, rice, peanuts, and cotton) via their pilot plant incubator space.
		National Center for Agricultural Utilization Research	The National Center for Agricultural Utilization develops technologies that enable growth and profitability in biomanufacturing plant-based materials (e.g., soybeans, pulses, sorghum, millet, hemp, alfalfa, oilseeds, and lignocellulosics) via their pilot plant incubator space.

MRL	Agency	Relevant Programs	Description
1-7	USDA	Agricultural Research Service Scientific Computing Initiative (SCINet)	Biomanufacturing processes are a complex biosystem where new opportunities will be created by leveraging SCINet's machine learning in predicting new optimization pathways. SCINet is an effort by ARS to grow USDA's research capacity by providing scientists with access to high-performance computing clusters, high-speed networking for data transfer, and training in scientific computing.
2-4		National Institute of Food and Agriculture Agriculture and Food Research Initiative Foundational and Applied Sciences (AFRI FAS)	The AFRI FAS program funds a variety of bioeconomy- and biomanufacturing-related research and development projects. For example, the Sustainable Bioeconomy through Biobased Products (A1414) and Biorefining and Biomanufacturing (A1531) program area priorities support projects to advance biobased products, biomass systems, or biomass-generated power to enable the bioeconomy in a manner which reduces adverse impacts to the environment.
2-6		National Institute of Food and Agriculture The Agriculture and Food Research Initiative Sustainable Agricultural Systems (SAS)	The AFRI SAS program funds large, transdisciplinary projects across several priority areas, including Strengthening the Bioeconomy, which seeks to fund biobased energy and products from feedstock improvement through the supply chain to final products, including positive environmental, social, and economic outcomes.
2-4		National Institute of Food and Agriculture The Bioproduct Pilot Program	The Bioproduct Pilot Program was authorized and funded by the Infrastructure Investment and Jobs Act to support the scale-up of sustainable value-added products from agricultural commodities.
2-4		National Institute of Food and Agriculture Small Business Innovation Research and Technology Transfer (SBIR/STTR)	The SBIR/STTR program supports research and development across a wide range of topic areas including many aspects of biomanufacturing from feedstock improvement, conversion systems, supply chain improvements, and biobased product development.
2-4		National Institute of Food and Agriculture Foundational Knowledge of Plant Products	Foundational Knowledge of Plant Products funds research into determining and using the metabolic pathways that produce biochemicals and phytochemicals. This knowledge is then translated into synthetic biology for commercial scale.
8+		Rural Development Biorefinery, Renewable Chemical, and Biobased Product Manufacturing Assistance Program	Provides guarantees on loans up to $250 million to assist in the development, construction, and retrofitting of biorefineries, including new and emerging technologies, to process biomass and intermediates into advanced biofuels, renewable chemicals, and biobased products.

MRL	Agency	Relevant Programs	Description
8+		Rural Development Higher Blends Infrastructure Incentive Program	Provides grants to increase the sales and use of higher blends of ethanol and biodiesel by expanding the infrastructure for renewable fuels derived from U.S. agricultural products.
8+		Rural Development Business & Industry Guaranteed Loan Program	Provides guarantees on loans up to $25 million to assist rural businesses including biomanufacturing facilities, biobased product manufacturing facilities and other rural businesses.
8+		Rural Development Rural Energy for America Program (REAP)	REAP provides guarantees on loans up to $25 million and grant funding up to $1 million to agricultural producers and rural small businesses for renewable energy systems including the production of biofuel and advanced biofuel.
8+		Rural Development BioPreferred® Program	The USDA BioPreferred® Program requires federal agencies and contractors to give purchasing preference to biobased products. This program also includes a voluntary certification and labeling initiative for biobased products.
5–8	NASA	International Space Station National Lab	This cost-shared partnership includes a focus on risk reduction efforts and research to explore new processes and materials for in-space manufacturing, largely by leveraging the capabilities of the International Space Station National Lab. In-space biomanufacturing has shown tremendous potential by leveraging the unique environment of microgravity to produce novel materials, goods, and products with characteristics that are unable to be achieved on Earth. Microgravity, and in some cases vacuum environments, have been shown to enable promising improvements over the Earth's environment for the ability to produce crystals with increased quality and uniformity, which are applicable to things such as protein crystals for pharmaceuticals, precision control of thin films for artificial retinas, and the growth of tissues in three dimensions without strain on the fragile biological structures.