

Addressing Gaps in US Biomanufacturing Capacity

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In December 2022, the President’s Council of Advisors on Science and Technology (PCAST) submitted a report to Joe Biden about biomanufacturing in the United States. In a letter prefacing the report, the council cochairs noted that the bioeconomy is “poised for enormous growth over the coming decades” (1). On 22 March 2023, the White House Office of Science and Technology Policy responded with a set of five initiatives to help realize the potential of the nation’s bioeconomy. The broad goal is for 30% of chemicals and 90% of plastics in the United States to be produced through sustainable replacements derived from synthetic biology (2).

“With this revolution comes great opportunity: desirable new jobs for skilled workers, a reduced carbon footprint, and new products that will expand US manufacturing and accelerate our economy, all with the potential to enhance access to these benefits in under-served regions of the country,” the cochairs wrote in their letter (1). “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 [President Biden’s] goal that biotechnologies invented in America lead to products that are made in America.”

However, the report identified key gaps that are slowing the country’s progress and threatening to undermine its success if not adequately addressed. Concerns include regulatory uncertainty, an outdated national strategy, and a lack of biomanufacturing capacity. “Too often companies encounter a bottleneck when searching for available biomanufacturing facilities and trained workforce needed to expand production to market scale,” the cochairs stated (1). “This bottleneck leads some companies to move to Europe or Asia, where manufacturing facilities and trained workforce are more readily available.”

AN UNPARALLELED OPPORTUNITY

We live in a time of unprecedented scientific innovation that could revolutionize how we manufacture goods. The United States is poised to



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help lead the move away from energy-intensive and polluting chemical processes toward sustainable biotechnologies. A landmark May 2020 report from McKinsey Global Institute reported that, in 10–20 years, a pipeline of emerging applications could create US\$2–4 trillion of direct economic impact (3). Such innovations include all manner of products, from biotherapies to leather made from mushroom roots and plastics derived from yeast rather than petrochemicals.

Schmidt Futures found that, in the next two decades, biomanufacturing could account for 25% of liquid transportation fuels, 50 billion pounds of biobased chemicals, and 1.1 million jobs in the United States (4). Among many proposals, the organization notes that the federal government could expand bioproduction capacity by incentivizing the repurposing of existing scale-up infrastructure housed within established companies.

The Bioprocess to Product Network (BioP2P), a national initiative established by the public–private nonprofit California Biomanufacturing Center in 2022, is working to identify capacity and help biomanufacturers accelerate their expansion from pilot- to commercial-scale capabilities. Backed with support from Schmidt Futures, BioP2P has assembled a group of leaders from industry, academia, and research institutions who have a deep understanding of the challenges that biomanufacturers face, from finding production capacity to building a workforce. These leaders are working to address barriers that threaten to slow the growth of the new bioeconomy.

As a first step, BioP2P is creating a database of organizations with scale-up fermentation capacity in the United States. Organizations with scale-up capacity can go to the BioP2P Network website and add their information to an online directory at no cost (5). The intent of this project is not only to understand the nation's existing infrastructure and associated gaps, but also to accelerate participants' movement from the laboratory bench to the market. My team has learned about numerous companies being unable to find adequate capacity, causing significant delays to operations and compelling additional investments — e.g., in constructing a facility or outsourcing overseas. Curated resources such as the BioP2P directory are needed to enable companies to remain focused on the complexities of scaling their processes rather than hunting for capacity to bring products to market.

A RESOURCE FOR A NEW AGE

The bioeconomy is not a new concept, but it is entering a new phase. The expansive attention being paid to biomanufacturing scale-up often fails to recognize the foundations laid by first-generation biotechnology products and processors. Industry titans such as DuPont and Genencor (a producer of industrial enzymes and bulk protein born out of a 1982 joint venture by Genentech and Corning Incorporated) invented entirely new categories of bioproducts but went largely unheralded for such work in the 1980s and 1990s. If that period served as a first generation, then the biofuels era of the mid-2000s was essentially the second. The current cohort of advanced materials, foods, and synthetic-biology companies could be considered a third generation of industrial biotechnology.

When James E. Flinn published his 11th (and final) edition of the *Directory of Toll Fermentation and Cell Culture Facilities* in 2015, the microbial industry didn't fully appreciate what he had done (6). He effectively launched a series of reports under the banner of his own company, Bio-Endeavors International. The publications predated the “sound and fury” of biofuels during the mid-2000s and coincided with the expansion of the industrial bioeconomy. In some ways, Flinn cataloged industrial biotechnology's coming of age.

Industry insiders used Flinn's manually curated print editions to keep up to speed with new capacity trends and available infrastructure for processing and refining. Flinn made a point to report updates about fermentation capacity at providers such as the BioCentury Farm at Iowa State University, the University of Georgia, Rutgers University, and dozens of others.

Unfortunately, perhaps because of timing and limited connectivity, the Flinn directories reached only a niche audience in the industrial biotechnology space.

Although Flinn ceased updating the directory, one of his missions — to match client companies desiring manufacturing support with entities that offer such services — has gained traction through the years. Two generations of biomanufacturing have come and gone, yet they did so without investing in infrastructure that might have achieved his goal of providing durable, transparent, and freely available capacity information. The pharmaceutical industry has long tracked global biotherapeutic-production capacity through BioPlan Associates and other specialized analysts. However, the larger biomanufacturing industry has felt the absence of such an informational nexus. More important, insufficient attention has been given — for decades — to the total scale-up capacity of bioindustry in the United States and abroad. The BioP2P Network and other such initiatives are addressing those gaps and are poised to provide the open-access resources needed to support an innovative and growing biomanufacturing community.

FILLING THE GAPS

By some estimates, the biomanufacturing industry will require tens of billions of dollars in new capacity investments over the next two decades to satisfy demand among the latest cohort of client companies. Design and engineering firm CRB surveyed hundreds of industry leaders for its 2022 *Horizons: Alternative Proteins* report (7). Among its key findings, CRB recommends that the biomanufacturing industry take a lesson from the past three decades of biotherapy production: Manufacturing to scale is possible.

Before moving to commercial production scales, most companies will optimize their processes at pilot scale, which typically ranges between 50 L and 50,000 L in volume. CRB found that 54% of respondents to the *Alternative Proteins* survey worked at laboratory or pilot scale. Those same respondents reported that unavailability of equipment to produce at scale was a significant obstacle to their companies' success. That issue ranked second only to cost of goods (CoG).

Such concerns have become common themes in the venture-backed biotechnology universe. The PCAST report paints a dire picture about American biocapacity. Although the report notes that earlier recommendations led to the creation of biomanufacturing centers that have made significant advances, such efforts are insufficient to support product development at the point of transition from

prototype- to pilot-scale manufacturing. Such shortfalls, the report states, will create “a major impediment to growing the biomanufacturing capacity needed to develop and scale bioproducts” (1).

A HIGH-STAKES RACE

Capacity gaps have grown enough to capture the attention of the White House, where they are recognized as an issue not only for economic competitiveness, but also for national security. Among several recommendations, the PCAST called for creation of a network of biomanufacturing hubs throughout the United States. Too often, companies encounter a bottleneck when searching for available biomanufacturing facilities and the trained personnel needed to expand production to market scale.

Warning signs have been clear for many years. In 2013, Verenum (now part of BASF) included in its annual report that its industrial-enzyme manufacturing needs led it to partner with a contract manufacturer in Mexico (8). Europe is also attracting international companies in need of manufacturing capacity. In 2022, Israeli start-up Remilk selected Denmark as the location for a large-scale precision fermentation facility, and in February 2023, the company announced that it will offer additional contract manufacturing capacity in Western Europe (9, 10). The same trend can be observed across Asia with the adoption of government policies and new investments in the manufacturing sector (11).

Until now, federal agencies in the United States had yet to establish a focused initiative to advance scale-up domestically. The PCAST report states, “Much like [when] 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” (1).

Too often, companies encounter a bottleneck when searching for available biomanufacturing facilities and the trained personnel needed to expand production to market scale. Among several recommendations, the PCAST called for creation of a domestic network of biomanufacturing hubs that would serve as scalable, shared facilities made available to American product developers. Imagined as public-private partnerships, the hubs would be established in different US regions and seeded with \$50 million each. That strategy, the report stated, would spur growth, create well-paying jobs, and provide needed medicines, consumer goods, and materials across the country.

Looking to the future, the question isn't whether biotechnology will reshape American manufacturing;

it is whether the United States will maintain a leadership role in biomanufacturing, capturing the benefits of the third-generation bioeconomy, or fall behind Asia and Europe.

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