Public Meeting of the

President's Council of Advisors on Science and Technology (PCAST)

November 29, 2021

Meeting Minutes

Meeting Participants

PCAST Members

1. Frances Arnold, Co-Chair
2. Eric Lander, Co-Chair
3. Maria T. Zuber, Co-Chair
4. Marvin Adams
5. Dan E. Arvizu
6. John Banovetz
7. Ash Carter
8. Frances Colón
9. Lisa A. Cooper
10. John O. Dabiri
11. William Dally
12. Sue Desmond-Hellmann
13. Inez Fung
14. Andrea Goldsmith
15. Laura H. Greene
16. Paula Hammond
17. Eric Horvitz
18. Joe Kiani
19. Jon Levin
20. Steve Pacala
21. Saul Perlmutter
22. William Press
23. Penny Pritzker
24. Jennifer Richeson
25. Vicki Sato
26. Lisa Su
27. Kathryn Sullivan
28. Terence Tao
29. Phil Venables
30. Catherine Woteki

PCAST Staff

1. Anne-Marie Mazza, Executive Director
2. Ambika Bumb, Deputy Executive Director
3. Sarah Domnitz, Deputy Executive Director and PCAST Designated Federal Officer

Invited Speakers (in order of presentation)

1. Michael Chui, McKinsey Global Institute
2. Michelle McMurry-Heath, BIO

3. Gintaras Reklaitis, Purdue University and chair of 2021 National Academies of Sciences, Engineering, and Medicine (NASEM) report, *Innovations in Pharmaceutical Manufacturing on the Horizon*
4. Richard Murray, California Institute of Technology and chair of 2017 NASEM report, *Preparing for Future Products of Biotechnology*
5. Reshma Shetty, Gingko Bioworks
6. Jay Keasling, University of California, Berkley and Lawrence Berkeley National Laboratory
7. Doug Friedman, BioMADE
8. Candice Wright, Government Accountability Office
9. Bruce Rodan, Environmental Protection Agency
10. Marie Bernard, National Institutes of Health
11. Lisa Friedersdorf, National Nanotechnology Coordination Office

START DATE AND TIME: MONDAY, November 29, 2021, 12:15 p.m. Eastern Time

LOCATION: Virtual Meeting via Zoom.gov

WELCOME

PCAST Co-chairs: Frances Arnold, Eric Lander, Maria Zuber

The PCAST co-chairs—Frances Arnold, Eric Lander, and Maria Zuber—called the meeting to order.

Arnold opened the session noting that the United States is a global leader in biotechnology research and in developing innovations in engineered biology, also referred to as synthetic biology. Many industries are impacted by this field, such as healthcare, chemicals, fuels, personal care products, agriculture, nutrition, and others. The United States has some roadblocks to industrialization of these innovations, however. Without changes, investment capital may go outside the United States for commercialization and manufacturing at scale.

SESSION 1: ADVANCING U.S. BIOMANUFACTURING

The Global Market

Michael Chui, McKinsey Global Institute

Michael Chui commented that there has been a convergence of biological innovations and information technologies such that some biological technologies are advancing faster than would be predicted by Moore's Law, and this has the potential to revolutionize economies. An example is the development of mRNA vaccines for protection against COVID-19. Chui identified five potentially transformative capabilities that have resulted from these innovations and could change economies: 1) biology-based production, which can improve the performance and sustainability of many physical inputs to and

outputs from an economy; 2) more control and precision to target actions based on biology; 3) increased ability to reengineer and reprogram organisms; 4) research and development (R&D) productivity enabled by automation and artificial intelligence (AI); and 5) perhaps a more distant goal, the ability to use biology as a substrate for computing.

Chui discussed the potential of this field, suggesting that at least 45 percent of the world's disease burden could be alleviated with biological interventions, 60 percent of physical inputs to the global economy could be produced through biological means, 30 percent of current R&D in the private sector could be impacted by biology, and nearly 10 percent of annual greenhouse gas emissions could be mitigated with biological interventions by 2040 or 2050. Chui said that McKinsey Global Institute reviewed a variety of industry sectors with the potential for using biological technology to improve performance, including assessment of about 400 potential use cases, and found that the overall economic impact could be substantial. All told, McKinsey Global Institute estimated the economic benefit could be $2-$4 trillion and would fall into four categories: 1) human health and performance; 2) materials, chemicals, and energy; 3) consumer products and services; and 4) agriculture, aquaculture, and food.

Finally, Chui addressed scaling, which requires scientific research, design of a commercialization process, and ultimately diffusion of results throughout the population and economy. The transition from lab-sized models to industrial scale production will require serious engineering work to be done. And risks will have to be managed—some of which will be unique to biotechnology—and dialog across all market participants and regulators will be required.

Michelle McMurry-Heath, BIO

Michelle McMurry-Heath commented that companies represented by BIO—a trade association representing biotechnology companies, academic institutions, and related organizations in the United States and more than 30 other countries—have launched more than a thousand vaccine and therapeutic research programs for combatting COVID-19, more than half of which were conducted in the United States. Companies represented by BIO are on track to produce over 12 billion doses of COVID-19 vaccine by the end of 2021.

McMurry-Heath said that lessons can be learned from the American semiconductor industry, which has lost 70 percent of its manufacturing capacity over the last three decades. In contrast, government policies such as the Bayh-Dole Act contributed to the United States' strong biotechnology innovation ecosystem and intellectual property regime. McMurry-Heath said that if the United States does not attend to the bioeconomy, it risks repeating the mistakes it made in the semiconductor industry.

McMurry-Heath said advanced biomanufacturing uses cross-cutting manufacturing technologies like continuous manufacturing and 3-D printing to accelerate the production of drugs, shorten supply chains, and improve manufacturing resilience. Looking beyond the medical field, advanced biomanufacturing has the ability to create new classes of materials for use in packaging and apparel, to streamline manufacturing processes to reduce carbon emissions in the supply chain, and to improve access to nutritious foods in underserved communities.

McMurry-Heath said there is tension between supporting efforts to enhance onshoring of U.S. manufacturing capacity and ensuring continued function and resilience of global supply chains. McMurry-Heath said U.S. policy should focus on both of these areas—onshoring manufacturing and strengthening global supply chains—not solely one or the other. Within the United States, challenges have included unclear regulatory frameworks to support biomanufacturing, large upfront costs paired with uncertain commercial viability of some ventures, and insufficient financial incentives. U.S. federal agencies, like the Food and Drug Administration (FDA), could clarify the regulatory framework so investors can understand the risks and benefits of adopting new technologies. And regulatory submission requirements should be harmonized globally to support global acceptance of biomanufacturing technologies. BIO supports tax credits for investment in advanced manufacturing equipment and reduced tax rates on income for domestic manufacture of specific medical products.

McMurry-Heath stated that BIO's recent bioeconomy report showed that the bioscience sector employs almost 2 million individuals in the United States—more than twice the number in the U.S. automotive industry—and the jobs pay well, averaging more than $107,000 per year. The sector also has strong growth, increasing by 7.2 percent since 2016, which is more than twice the rate of the overall private sector. Continued growth depends on scaling up education initiatives. There are already good models of collaboration between industry, academia, and individual states. One such example of success is North Carolina's biotech ecosystem.

In conclusion, McMurry-Heath emphasized two points. First, if the United States is to maintain a competitive edge, it must be mindful of similar biomanufacturing efforts in Europe, China, and other regions of the world. Second, just as it has taken small and large companies working together to fight COVID-19, it will take similar collaborations between small and large companies to drive the bio revolution forward and advance biomanufacturing.

Arnold moderated the Q&A and discussion between PCAST Members and Chui and McMurry-Heath.

Key Technologies, Platforms, and Regulatory Framework

Gintaras Reklaitis, Purdue University

Gintaras Reklaitis stated that in 2019 the National Academies of Sciences, Engineering, and Medicine (NASEM) was asked by FDA to undertake a study to identify emerging technologies in pharmaceutical manufacturing, describe the technical and regulatory challenges associated with those innovations, and provide recommendations for overcoming them. Some of the manufacturing innovations on the horizon that were identified in the study included: 1) new routes to synthesize drug substances; 2) additive manufacturing technologies that can tailor and customize characteristics of a drug product; 3) process intensification to create more efficient, higher-yielding processes and enable smaller manufacturing footprints; and 4) the creation of modular systems to allow integrated, flexible, and distributed manufacturing networks.

Reklaitis said the study committee identified five areas of concern in the regulatory process: 1) the process by which products and technologies are reviewed by FDA; 2) the incentives—or lack thereof—for manufacturing innovation; 3) the lack of global regulatory harmonization; 4) the regulatory

requirements that must be met if the manufacturing process changes after a product has been approved by FDA, which impede innovation in the generic manufacturing domain, among others; and 5) the limitations of the FDA workforce.

Reklaitis said that the FDA only reviews new manufacturing technology in the context of new product applications. As a result, when a new technology is useful for a range of products, the first product takes on the uncertainty associated with the new technology and becomes the focus of the review. The NASEM committee recommended that there be a way to review innovative technologies separately from the products those technologies will be used to produce.

Reklaitis said the FDA has made some progress through its Emerging Technology Program, which provides a mechanism for companies to obtain informal feedback on new ideas for both products and processes. Reklaitis said that the feedback from industry representatives was generally positive, although the program functioned more like a pilot program—not sufficiently funded or staffed—and the categories of new technologies that the program could review was too narrow. Therefore, the NASEM committee recommended expanding the scope and capacity of the Emerging Technology Program.

The NASEM report also recommended an expanded role for the FDA in efforts to achieve global regulatory harmonization and that the FDA pay more attention to hiring, retaining, training, continually educating, and investing in its workforce. This includes supporting the FDA workforce so they can gain hands-on experience with technology, attend conferences, and actively participate in professional organizations.

In closing, Reklaitis said that at the end of October 2021—several months after the NASEM committee had released its report—the FDA asked the committee to convene a workshop during which the FDA shared its responses to the NASEM report. The FDA said it would expand the Emerging Technologies Program and made a commitment to re-envisioning the regulatory process and to identifying and addressing gaps.

Richard Murray, California Institute of Technology

Richard Murray chaired the 2017 NASEM study that looked at modernizing the biotechnology regulatory system. The charge to the committee called for an analysis of likely future products of biotechnology and consideration of the attendant regulatory system needed to ensure protection of human health and the environment. The charge included several areas of inquiry but explicitly excluded review of human drugs and medical devices.

Murray said that looking ahead 5 to 10 years, the committee evaluated three classes of products: 1) contained-use products (for example, things sitting inside a fermenter); 2) products that are open-release to the environment (for example, agriculture, biomining); and 3) platforms (that is, biotechnology products used to create other biotechnology products). The committee found that the scale, scope, complexity, and pace of biotechnology products are likely to increase in the next 5 to 10 years. Many new biotechnology products will be similar to existing biotechnology products, but they will be created using new processes, while others may be entirely unlike existing products. To evaluate the regulatory challenges, the committee grouped emerging biotechnologies into four categories of

increasing novelty and complexity: 1) Products that have multiple comparators and few genetic changes, such as crops that have been engineered to integrate insecticides. 2) More complex products involving new genome engineering techniques and multiple gene pathways being altered, with few or no comparators. 3) Products that involve many candidate organisms being modified or affected, with genetic changes being driven through a whole population, such as gene drive in mosquitoes. 4) Genetically engineered communities of microbes or multicellular plants and animals.

Murray said the second issue the committee considered was whether existing risk analysis systems could be applied to new products of biotechnology. The committee found that although the Coordinated Framework for the Regulation of Biotechnology was flexible and could be applied to many new products, there were some gaps that might generate jurisdictional issues among federal agencies. For example, cosmetics could be classified as a drug or a medical device, and a do-it-yourself consumer product meant to be used by the consumer to create a new product could require regulation for both the kit and the resulting product. The committee also thought that the complexity and fragmentation of the regulatory process had the potential to slow innovation and decrease public confidence.

Murray said the committee had several other findings. The committee considered whether future biotechnology products could pose different risk assessment endpoints, that is, damage to human health or the environment. The committee found that while the *endpoints* might not be new, the *pathways* to those endpoints might be new. The committee also determined that the existing levels of staffing, expertise, and resources at federal agencies may not be sufficient to support oversight of the expected scope and scale of the biotechnology products on the horizon. And the committee found that it would be helpful to have a single point of entry into the federal regulatory process.

Reshma Shetty, Gingko Bioworks

Reshma Shetty began her comments by reiterating what earlier speakers had said that biomanufacturing represents a huge economic opportunity. It also offers a more sustainable manufacturing alternative to current industrial practices. Unfortunately, the United States lacks the biomanufacturing infrastructure to take full advantage of that opportunity because of limitations in physical domestic biomanufacturing capacity and the supply of qualified workforce. Shetty stated that her company, Ginko Bioworks, for example, has eight products in commercial production, six of which are produced outside of the United States.

Concerning the lack of physical capacity, even though agricultural regions such as the American Midwest and South are obvious locations for biomanufacturing capacity because of their easy access to feedstocks, most of the existing fermentation facilities are built for one large volume commodity product—often corn-derived ethanol. Shetty stated that the United States needs more facilities designed to be both "multi-product and multi-organism," with fermentation facilities co-located with multiple downstream processing options to improve flexibility for shifting to produce different products at a single facility based on product demand. China and the European Union have invested in this approach. Many U.S. companies now go to the European Union for their biomanufacturing needs, and Shetty said she thinks it is only a matter of time before U.S. companies also go to China for

biomanufacturing. Shetty recommended that the U.S. federal government retrofit and upgrade existing fermentation sites or invest in new facilities that can support biomanufacturing multiple products.

Concerning the lack of workforce capacity, Shetty said that the United States does a good job of educating students to prepare them for biotechnology research, but it does not offer enough educational programs in bioprocess engineering, which is the knowledge needed to support biomanufacturing. Many of those jobs do not require a graduate degree—an associate's degree, bachelor's degree, or certificate would be sufficient. There is an opportunity to provide federal support for community college programs and the development of high school curricula to train people in bioprocess operations.

Jay Keasling, University of California, Berkeley and Lawrence Berkeley National Laboratory

Jay Keasling stated that almost all fuels, commodity chemicals, specialty chemicals, and precursors to pharmaceuticals originate in petroleum. There has been an effort for many years to produce these products from renewable sources, like biomass, that could be converted in biorefineries. Several years ago, the Department of Energy (DOE) and the U.S. Department of Agriculture assessed the total amount of biomass that could be produced to be a billion dry tons, which would be enough for one-quarter to one-third of American fuels. Without a mandate or carbon tax, however, it is unlikely that biomanufacturing will replace petroleum manufacturing for fuels or for making the products in which petroleum is already used because petroleum-based manufacturing is so inexpensive.

Keasling said that companies will need many very large, dedicated facilities for producing fuels and commodity products. The process of scaling up from the laboratory to full-scale production can be very expensive for large companies and prohibitively expensive for small companies, even to get just to the pre-pilot scale. Companies will need three types of facilities:

1) Many highly flexible, small-scale pre-pilot and pilot facilities. Example: The Advanced Biofuels and Bioproducts Process Demonstration Unit at Lawrence Berkeley National Laboratory, which offers flexible biomass pretreatment, fermentation, and downstream processing.

2) Several less flexible but larger demonstration facilities. Example: The bioprocessing pilot plant at the National Renewable Energy Laboratory, which offers larger scale fermentation and downstream processing.

3) A few toll manufacturing facilities (that is, third-party manufacturing facilities), which could be public-private partnerships or privately owned and operated.

Keasling also suggested that technoeconomic analysis (TEA) models and lifecycle analyses need to be standardized and incorporated widely into biomanufacturing. TEA models can help evaluate what is economically viable, while lifecycle analyses can help assess the carbon and energy inputs and outputs of a production process.

Keasling said there must be effective research, training, and workforce development in biomanufacturing. Biomanufacturing companies need engineers trained in bioprocess engineering, but few American universities offer this training because of a lack of funding for faculty to conduct research

in this field, unlike in Europe and Asia, where students can obtain this training. Keasling recommended that the federal government, particularly the National Science Foundation and DOE, fund research in bioprocess engineering, which will encourage students to seek graduate education in this field. Similarly, more undergraduate, master's level, and community college programs should be offered in this field.

Doug Friedman, BioMADE

Doug Friedman said BioMADE is a large non-profit, public-private partnership sponsored by the Department of Defense and launched in 2021 as part of the ManufacturingUSA ecosystem focused on bioindustrial manufacturing and bioindustrial products. In the United States there has been an incredible investment early on in synthetic biology, metabolic engineering, and a wide range of biological technologies. A number of centers have been created to support this field in the United States and abroad.

Friedman agreed with earlier speakers that supporting a large number of jobs across the entire spectrum of educational backgrounds is essential, including the community college system, which is a severely untapped resource. In addition to considering the technical and workforce elements of biomanufacturing, Friedman said it is equally important for the community of biomanufacturing practitioners—industry, academia, and government—to include safety, security, sustainability, and social responsibility as biotechnology advances. Over time, Friedman speculated, markets may not care about the science underlying biomanufactured products, and eventually biomanufacturing may become so commonplace that the bioeconomy and the traditional economy become synonymous.

Arnold moderated the Q&A and discussion between PCAST Members and Reklaitis, Murray, Shetty Keasling, and Friedman.

SESSION 2: ENSURING A VIBRANT FEDERAL S&T WORKFORCE

Candice Wright, Government Accountability Office

Candice Wright stated that in 2001, the General Accountability Office added strategic human capital management for science and technology to its "high-risk list" because many federal agencies face significant challenges in identifying, strengthening, and sustaining a highly trained science and technology workforce. There are important things to consider with this sector of the federal workforce, the first of which is ensuring that there is a strategic workforce planning process in place. A current inventory of skills should be taken, including identifying current and projected gaps. Agencies should focus on competitive pay scales, building a diverse and inclusive workplace culture, and developing strategies to source and recruit talent and maintain a continuous recruitment program.

Wright said agencies typically rely on universities as the pipeline for recruitment, but they sometimes delay the on-campus recruiting process until they have budget authorization, which can put them behind the competition that begins talking to prospects early in the school year. It is important to

develop a program of incentives and a compensation philosophy that can compete with the private sector. Prospective employees must be engaged throughout the process and sensitive topics, such as disparities and diversity, must be factored into the process.

Wright said that less obvious—but still important—considerations include eliminating limitations and obstacles to participating in conferences and presenting research, and instilling confidence in a culture of scientific integrity that protects intellectual product from distortion or misrepresentation. Impressions that agency work may be overly bureaucratic, lack innovation, and be less prestigious than private sector work must be overcome, while the importance of working in the federal government as a benefit to society, the economy, and the security of the nation should be emphasized.

Marie Bernard, National Institutes of Health

Marie Bernard stated that a September 2021 report from the National Science and Technology Council's Interagency Working Group on Inclusion in STEM stated that approximately 16 percent (more than 280,000 individuals) of the 2.1 million individuals in the federal workforce were in STEM positions. Only 29 percent of this STEM workforce are women and only 10 percent are from underrepresented racial and ethnic groups, however. Bernard said the report provided several recommendations to increase diverse participation.

Bernard explained that the National Institutes of Health (NIH) conducted a survey between January and March 2019 which found that 20 percent of respondents had experienced sexual harassment, 50 percent experienced instability in their working environment, 10 percent reported bullying, and 6 percent reported experiencing intimidation on the job. (Nearly 16,000 people in the NIH workforce completed the survey. The response rate was 44 percent for NIH overall and 56 percent for NIH federal employees.) The survey results led to the establishment of the Anti-Harassment Steering Committee, which meets on a monthly basis to assess employment conditions.

In February 2021, the NIH UNITE Initiative was launched to reinforce efforts to ensure an inclusive workforce at NIH. NIH director Francis Collins acknowledged the reality that in the United States there is disproportionate morbidity and mortality related to race and ethnicity, and he promised to institute new efforts to support diversity, equity and inclusion. He also announced that an Anti-Racism Steering Committee would be established to work in parallel with the Anti-Harassment Steering Committee. NIH leadership also would rely on feedback from staff to assess data about inequities, use those data to develop specific interventions, and measure their effectiveness.

Finally, Bernard noted that NIH's successful Distinguished Scholars Program will be expanded to include senior investigators. The program brings in groups of investigators to be hired at NIH rather than hiring individual investigators. It is designed to reduce barriers to recruitment and increase the success of principal investigators from underrepresented groups.

Bruce Rodan, Environmental Protection Agency

Bruce Rodan explained that the Environmental Protection Agency (EPA) is somewhat unusual among federal agencies because it is involved in regulation, research, and program implementation. Half of EPA's workforce is in science and technology job categories—more than 7,000 people across EPA's national and regional offices.

EPA's budget must cover facilities, salaries, laboratory expenses, contracts, and grants. Within EPA, the Office of Research and Development's (ORD's) annual budget has steadily declined over the last decade (both in absolute terms and when adjusted for inflation), while the cost-of-living adjustment that EPA must factor into its salaries has increased. As a result, ORD must cut costs in other areas of its budget. The number of full-time equivalent (FTE) positions (that is, full-time employees) in ORD have followed a decline that is similar to the overall budget. Rodan noted that the White House Office of Management and Budget sets FTE number caps for federal agencies. The current Biden administration budget calls for increased funding for ORD.

Rodan commented that the Biden administration's emphasis on increasing workforce diversity will help EPA do a better job of engaging with the most environmentally impacted communities, including disadvantaged and disenfranchised communities, and supporting environmental justice. The annual staff attrition rate is 5 to 6 percent, which has remained consistent over several years. Twenty-six percent of ORD's current staff are eligible for retirement, which could lead to a big loss of expertise and knowledge in the near future. The new talent recruitment pathways include the Presidential Management Fellows program and the Schedule R Post-Doctoral program. Maintaining the EPA's science and technology workforce remains challenging in the face of several limitations—salary competitiveness with industry, bureaucratic impediments, and lack of flexibility to rapidly compete for talent.

Zuber moderated the Q&A and discussion between PCAST Members and Wright, Bernard, and Rodan.

SESSION 3: OVERVIEW OF THE NATIONAL NANOTECHNOLOGY INITIATIVE

Lisa Friedersdorf, National Nanotechnology Coordination Office

Lisa Friedersdorf said the National Nanotechnology Initiative (NNI) was announced by President Clinton in 2000 and signed into law by President Bush in 2003 under the 21st Century National Nanotechnology Research and Development Act. More than 30 federal agencies are engaged in the nanotechnology R&D ecosystem. The agencies participate based on their own roles and responsibilities, and they work together to advance the vision and goals of the NNI. There is no central funding that supports the program—the NNI is a roll up of all of the agencies' investments. The 2021 NNI budget request was $1.7 billion, and the investment over the life of the program totals more than $30 billion.

Friedersdorf said the NNI is set up through the National Science and Technology Council's Subcommittee for Nanoscale Science, Engineering, and Technology and is one of the few federal programs that has a national coordination office—the National Nanotechnology Coordination Office (NNCO), which Friedersdorf directs. The NNCO's role is to facilitate collaboration among the participating federal agencies; provide technical and administrative support; promote commercialization; provide outreach,

education, and engagement; and serve as the public face of the NNI. NASEM and PCAST each review the program every four years on an alternating schedule such that a NASEM or PCAST review is released approximately every two years.

Friedersdorf said the NNI released its latest strategic plan in October 2021. The plan discussed five goals: 1) ensure the United States remains a world leader in nanotechnology R&D; 2) promote commercialization of nanotechnology R&D; 3) provide the infrastructure to sustainably support nanotechnology R&D and deployment; 4) engage the public and expand the nanotechnology workforce; and 5) ensure the responsible development of nanotechnology.

Friedersdorf said the NASEM review of NNI released in 2020 included recommendations to work closely with other federal initiatives, which NNI does, but the program is now trying to be clearer and more deliberate about those collaborations. The NNI is also looking at how to support and connect the entire nanotechnology innovation ecosystem and seamlessly connect resources from early-stage research tools at user facilities all the way through the resources available at manufacturing institutes. The NNI also launched National Nanotechnology Challenges to address critical issues in nanotechnology, inspired in part by the role the nanotechnology community played in responding to the COVID-19 pandemic. For example, 20 percent of COVID-19 tests are enabled by nanotechnology. Other topics under consideration for National Nanotechnology Challenges are climate change, food security, and water treatment, access, and purification.

Lander moderated the Q&A and discussion between PCAST Members and Friedersdorf.

MEETING ADJOURNED: 4:30 p.m. Eastern Time

I hereby certify that, to the best of my knowledge, the foregoing minutes are accurate and complete.

Frances Arnold, Ph.D.
Co-Chair
President's Council of Advisors on Science and Technology

Eric Lander, Ph.D.
Co-Chair
President's Council of Advisors on Science and Technology

Maria Zuber, Ph.D.
Co-Chair
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