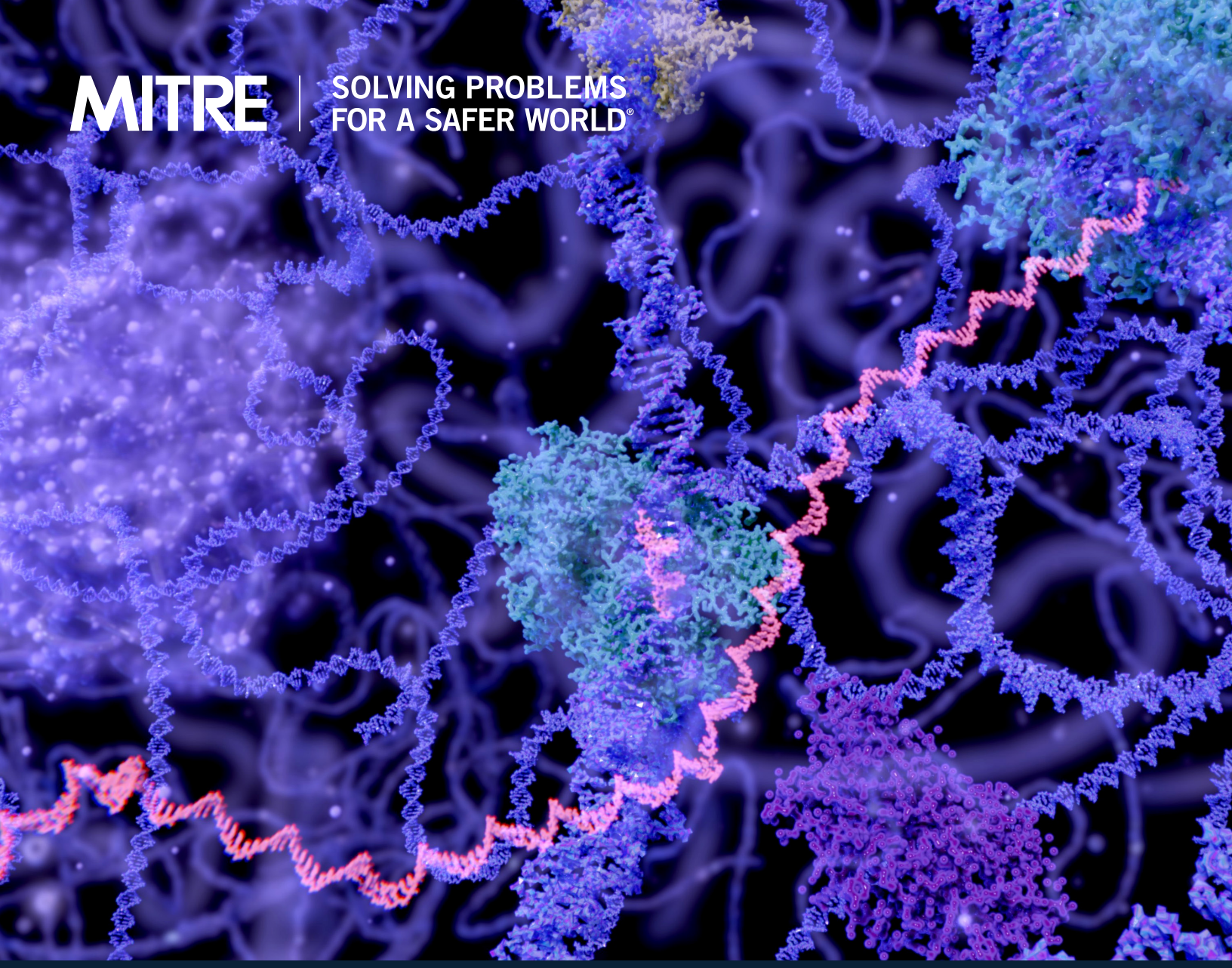

BUILDING A SUSTAINABLE BIOPREPAREDNESS INDUSTRIAL BASE

The MITRE Corporation

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Executive Summary

The ability of the US Government (USG) to develop, procure, and secure access to critical medical technologies, products, and supplies is integral to national, health, and economic security for three reasons. First, the United States requires sufficient access to these goods to protect the homeland and US partners abroad against biological threats (intentional, accidental, or naturally occurring) that pose grave risks to global safety, stability, and security. Second, the US health care system depends on continual access to critical medical supplies and medicines during crisis and between crises. Finally, the bioeconomy[1] will dominate 21st Century national security and economic interests as a rapidly growing segment of the global economy.

The USG relies heavily upon the private sector for research and development (R&D) in the area of biopharmaceuticals, including development of medical countermeasures. The biopharmaceutical sector demonstrated its value during the Coronavirus 2019 (COVID-19) pandemic, when the industry used mRNA [messenger ribonucleic acid] technology to rapidly develop and then scale and deliver two highly effective vaccines. Based on this success, the industry is poised for tremendous growth globally. However, The MITRE Corporation considered the USG unprepared to meet the threats to the biopharmaceutical industrial base. In particular, the team found that the biopharmaceutical industry, though one of the most advanced in the world, faces both internal and strategic competition from foreign competitors, principally China.

This report first provides background on the global state of the biopharma industry, and then summarizes the objectives that the USG should pursue. Next, it presents MITRE's findings regarding the shortfalls in the USG's current ability to

SUSTAINING THE BIOPHARMA INDUSTRIAL BASE REQUIRES AN INTEGRATED SYSTEM OF ACTIONS ACROSS THE WHOLE OF GOVERNMENT. MITRE RECOMMENDS FOUR INTERRELATED COURSES OF ACTION (COAS) AS A SYSTEM OF EFFORT THAT THE USG MUST UNDERTAKE SIMULTANEOUSLY TO BE EFFECTIVE.

sustain a robust mRNA industrial base, centered on three primary areas: USG capabilities, the mRNA industry, and the mRNA supply chain and ecosystem. To counter strategic competition in this industry, the United States needs a focused approach to drive action and accountability on sustaining needed capacity and capabilities. However, a history of inconsistent priorities and funding constitutes a significant barrier to creating a strong partnership between government and industry in this sector.

Sustaining the biopharma industrial base requires an integrated system of actions across the whole of government. MITRE recommends four interrelated courses of action (COAs) as a system of effort that the USG must undertake simultaneously to be effective. The first COA is defining and implementing an industrial base strategy, which should be tied to the appropriate policy, authorities, and accountabilities to execute against it. Second, the USG needs to identify the financing infrastructure to enable sustained investment in industrial base capability and capacity, to include an adequate and trained workforce. Third, the USG needs the situational awareness to act on

risks and threats to market access and capacity of the industrial base. Fourth, the USG needs to reframe the government and industry relationship from a transactional one to one of mutual long-term benefit.

To initiate these COAs, the USG should develop a strategy and implementation plan for sustaining and expanding the biopharma industrial base. The strategy should center on protecting the US population from future biological threats (naturally occurring, accidental and intentional), as aligned with core global health security principles. Developing supply chain resilience will help secure needed supplies to respond to these threats. Finally, the strategy should support maintenance of the US leadership of the bioeconomy to meet domestic needs as well as global export requirements during both crises and peacetime. The USG should support the strategy with policy, programs, funding, and clear accountability. This strategy should be supplemented with a strategic implementation plan with clear roles across industry and government and incorporating implementation into the FY23 budget request.

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Background and Context

International competition is no longer necessarily interlinked with a nation's ability to win wars; today nonmilitary areas of power largely define geopolitical competition. Bolstering areas of technological advantage, such as biopharmaceutical innovation, has risen to the forefront of USG levers of global influence.[2] Retaining this advantage serves national security interests and ensures US resilience against transnational threats such as pandemics. In other words, the biopharma industrial base has become an area that advances national, health, and economic security.

However, strategic competitors in this sector, particularly China, present a growing challenge to the strength and technology growth potential of the sector. China has demonstrated a historical pattern, or playbook, to gain global leadership in the biopharma sector. To pursue the goal of "Made in China in 2025," China has taken a number of "innovative mercantilism" measures, whereby it seeks to distort the market at the expense of the United States and other free market economies, in effort to dominate the global industry at all phases of the drug development lifecycle.[3] "In other words, China is seeking to challenge the United States in one of the most high-value-added, innovation-intensive industries in the world….".[4] At the same time as China emerged as a strategic competitor in the global market, the US biopharmaceutical value-added output has experienced a drop of almost one-third.[5] Unchecked mercantilist practices in the bioeconomy create risk of waning US preeminence in this sector, affecting the country's long-term national, health, and economic security.

THE BIOPHARMA INDUSTRIAL BASE IS THE INDUSTRIAL COMPLEX THAT ENABLES RESEARCH AND DEVELOPMENT AS WELL AS DESIGN, PRODUCTION, DELIVERY, AND MAINTENANCE OF BIOPHARMACEUTICAL PRODUCTS AND BIOTECHNOLOGY, AND RELATED SYSTEMS/SOFTWARE SYSTEMS, SUBSYSTEMS AND COMPONENTS OR PARTS, AS WELL AS PURCHASED SERVICES TO MEET U.S. HEALTH REQUIREMENTS.[1]

This risk became evident when competitor nations recognized mRNA platform technology as a critical emerging biopharma technology. Prior to COVID-19, no licensed mRNA or DNA vaccines existed. However, the potential of the mRNA platform to revolutionize pandemic response was anticipated years before,[6] driven by a very successful Defense Advanced Research Projects Agency (DARPA) program.[7] As anticipated, and in line with China's motives and "playbook," Chinese companies, with support of the state, have ramped up mRNA vaccine development efforts and investments over the course of the COVID-19 pandemic. The USG shows no evidence of a parallel biopharma industrial policy and strategy to sustain this important sector.

As reinforced by a recently published Office of the Director of National Intelligence (ODNI) report concerning critical and emerging technologies, the status quo puts access to biotechnologies such as mRNA at risk and illustrates larger, persistent challenges in global industrial competition.[8] Increasing strategic competition between the United States and China in its current state can harm US security interests by (1) decreasing leadership and preeminence in the bioeconomy, which undermines US economic competitiveness, and (2) increasing dependency on foreign supply chains due to lack of industrial base capability and capacity, which undermines US health system operations and resilience to transnational threats such as pandemics.

Objectives and Outcomes

MITRE used a rigorous mixed-methods analyses to (1) establish a data-driven approach for identifying national capacity for the biopharma industry (including emerging biotechnology, such as the mRNA platform) and risks to that capacity and (2) inform USG decision making to secure and sustain a robust biopharma industrial base and retain preeminence in biopharmaceutical R&D. MITRE met these objectives by using two pilot use cases that represent distinct parts of the product lifecycle: mRNA platform technology and heparin. This paper focuses on the mRNA use case as demonstrative of the challenges and opportunities to building a national biopharma industrial base.

The analytical approach involved four major steps: (1) gaining strategic understanding of the problem space through secondary research, expert consultation, and company financial analyses; (2) scoping the effort through three lanes of effort, including strategy and policy, economy and finance, and supply chain; (3) performing the analysis through Porter's five forces model,[9] supply chain, and institutional landscape assessments, and finally (4) informing impact by mapping COAs to inform decision making across the whole of government in building this industrial base to protect national, economic, and health security interests. Figure 1 illustrates the study approach.

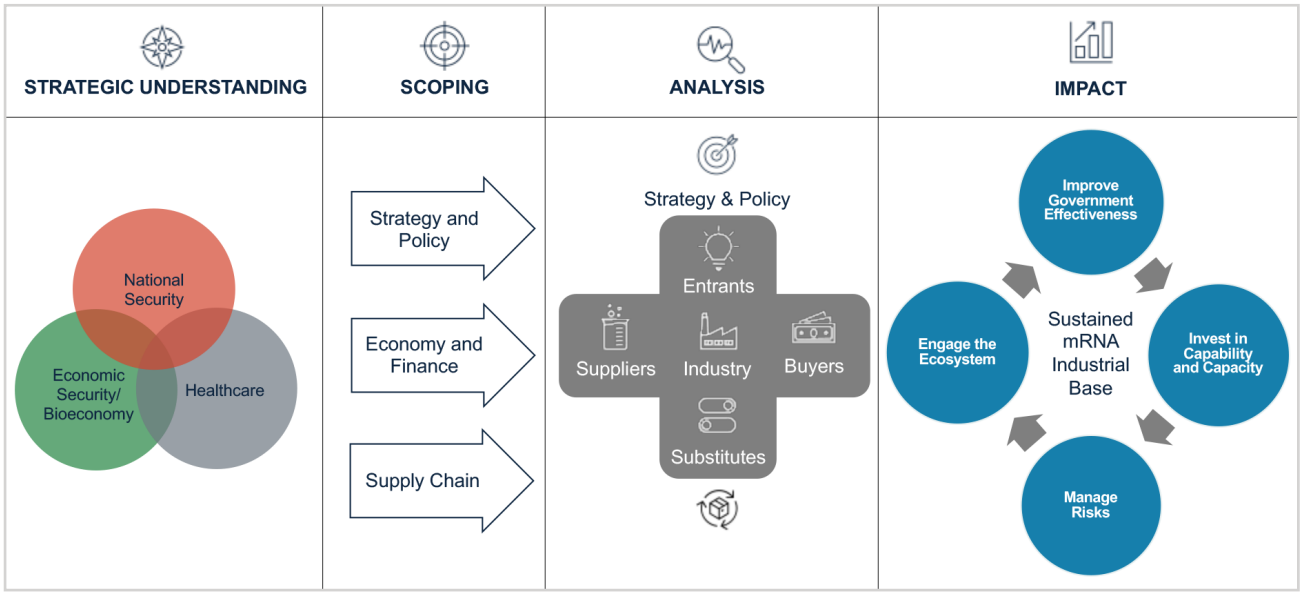

FIGURE 1: GPC BIOPHARMA STUDY APPROACH

Key Findings

The MITRE team reviewed the mRNA landscape and industry operations in detail, along with the USG capabilities, policies, and actions to engage with the industry. Through this analysis, several findings became apparent. This section addresses these findings in three categories: (1) USG capabilities, (2) mRNA industry, and (3) mRNA supply chains.

USG Capabilities

Finding 1: The USG lacks a biopharma industrial base policy and strategy.

The USG has multiple touch points with the biopharma industry, including the Food and Drug Administration (FDA), Assistant Secretary for Preparedness and Response (ASPR), National Institutes of Health (NIH), and Centers for Disease Control (CDC) within the Department of Health and Human Services (HHS) as well as DARPA, the Defense Health Agency DHA, and Defense Logistics Agency (DLA) within the Department of Defense (DoD) and, during the COVID-19 response, the Federal Emergency Management Agency (FEMA), Operation Warp Speed (OWS), and others. Each of these organizations has its own priorities and objectives in interfacing with the industry. In addition, the USG relationship with industry and funding for biopreparedness and new technologies has been inconsistent.

Of particular note, the USG does not have a biopharma industrial base development and sustainment capability for emerging biotechnologies, such as mRNA. DARPA developed mRNA and identified it as a vaccine platform critical for national health security long before the COVID-19 pandemic; however, the government support for the platform was inconsistent and short-lived because it had no overarching objectives or mechanisms to support the platform capabilities.

Lack of an industrial base strategy for this sector has consequences that became evident in the inward-looking foreign policy during the COVID-19 response. During the response, the USG support, including financing, regulations, and supply chain for vaccine development, production, and distribution focused on developing the doses needed to vaccinate the US population. Other countries, including China, Russia, and the participants in the COVAX Facility, focused efforts on global vaccination. The global distribution activity of China and Russia appeared to take the form of "vaccine diplomacy," where the provision of vaccine to certain nations is part of a broader plan to advance geopolitical interests.[10] The United States was conspicuously absent from these efforts, leading to charges of "vaccine nationalism" and neglect of low-to-middle income country (LMIC) population needs. As China filled a role the United States traditionally plays in health diplomacy, the status of the United States as a major power and global public health leader suffered.

Finding 2: The USG lacks cohesion among the policy, processes, authorities, which should support an industrial base.

The National Defense Authorization Act (NDAA) FY 2017 directed the Secretary of Defense, the Secretary of HHS, the Secretary of the Department of Homeland Security (DHS), and the Secretary of Agriculture to develop a National Biodefense Strategy (NBS) and Implementation Plan. This plan was to describe the roles and responsibilities of the Executive Agencies in biodefense and set the strategic direction for the United States to combat biological threats, "whether naturally occurring, deliberate, or accidental."[11] The current version of the strategy includes a Biodefense Steering Committee (BSC) comprising the heads of seven federal agencies and chaired by the Secretary

of HHS. The BSC is assisted by the Biodefense Coordination Team (BCT) in overseeing and coordinating implementation of the Strategy" and "currently led by . . . ASPR"[12]

Despite the NDAA's explicit direction to the Executive Branch with regard to development of the NBS and associated implementation plan, the COVID pandemic has exposed the nation's biodefense enterprise as lacking clear lines of authority and responsibility and being "extremely fragmented" so that "a herculean level of coordination at the higher levels of the federal government" is required "to guarantee coherent efforts and avoid duplication."[13] As of 2018, statutes or White House guidance and the NBS imposed 400 duties and responsibilities on 22 federal departments and agencies in the realm of biodefense.[14]

A 2019 Government Accountability Office (GAO) report addressing implementation of the NBS notes that the governing bodies overseeing the NBS's implementation—the BSC and BCT—did not clearly document key components of the assessment process and roles and responsibilities for joint decision making. The GAO further reported that the "Biodefense Steering Committee [established pursuant to the Implementation Plan] does not have the authority to decide how individual agencies in the broader biodefense enterprise should allocate resources or prioritize programs" and identified "limitations in [the] authority [of the BSC and BCT] to direct action and the difficulty of achieving consensus across so many actors."[15] GAO then reinforced this finding in its January 2022 report, with the designation of HHS leadership and coordination of public health emergencies as a 'high-risk' area.[16]

Several other stakeholders in the biopharma industrial base ecosystem have observed similar challenges and provided recommendations to reform the leadership and governance of the mission space. During the COVID-19 pandemic, senior ASPR officials, for instance, have noted that ASPR has been unable to live up to its full potential in connection with the COVID crisis and suggested a need for additional specific authority.[17] Similarly, the Center for Strategic and International Studies (CSIS) Commission on Strengthening America's Health Security has asserted that US programs on global health security are "fragmented, scattered across diverse executive agencies, and not clearly prioritized" and that "weakness of White House leadership has left unanswered the persistent question of how to streamline programs, eliminate redundancies, and achieve higher efficiencies in the use of scarce resources."[18] This challenge of leadership undermines national industrial base management and resilience and puts the nation at risk in the face of strategic competition and, more gravely, existential transnational threats such as biological incidents.

Finding 3: The USG requires a data analytics and monitoring capability to manage industrial base risks and capacity.

While mRNA is a highly dynamic industry, the USG lacks the situational awareness tools and measures and metrics needed to understand the state of industry, economic trends impacting industry decisions, and the readiness of industry to meet public health and global health emergency needs. OWS developed several dashboards that allowed tracking of the industry during the COVID-19 response; however, these tools focused on immediate vaccine deployment issues and were not suited for more strategic monitoring of the industrial base. Without such measures in place, the USG lacks the data needed to develop effective sustainment decisions and actions that are coordinated across agencies.

mRNA Industry

In large part USG DARPA investments drove mRNA technology early on and mRNA platform is now a leading technology for rapid response to novel biological threats (e.g., vaccines, therapeutics). In the USG response to COVID-19, mRNA was a priority platform for USG/OWS investments in biopharmaceutical manufacturers. This directly led to the development of mRNA-based vaccines-to-patients within a 1-year timeframe. As SARS-COV-2 evolves (via variants), the biopharmaceutical industry will leverage the mRNA platform to rapidly generate new "booster" vaccines. Several platform characteristics make it a disruptive and attractive biotechnology for global investment, which could eventually decrease access to domestic capacity as competing capacity is built overseas.

Finding 4: mRNA is poised for and focused on growth, which presents risks and opportunities to the domestic industrial base.

The mRNA technology industry has significant growth potential that will attract foreign investment and ownership, creating competition among companies in the United States and other major powers. Increased investment seeking profit and the reduced technology risk from mRNA is likely to fuel growth in the mRNA market. At the same time, first mover advantages are likely to reduce competition and entry into multiple indications (i.e., health concerns that mRNA products are developed to treat), resulting in significant advantages for those already experienced with products in the market.

In the pipeline, many other profitable indications will compete internally for influence on decision-makers and portfolio support and funding. This may well result in high internal competition between infectious disease and national security aims, extending commercial opportunities at the expense of lower profit national security needs. Lack of profit potential could potentially reduce firms' willingness to produce strategic and necessary biodefense products for the USG.

The vast increase in mRNA industry intellectual property content and value presages therapeutic advancements in a new technology class. Therefore, as the market grows companies will compete heavily for resources in short supply, such as production capacity and workforce. From a market standpoint, large, established, global companies see COVID-19 contracts as fueling expansion. Growth in the sector may reduce competition for post-COVID growth.

MITRE's analysis of mergers and acquisitions showed that continued consolidation could drive price increases and reduce competition. This is a trend to watch in the post-COVID space, especially if consolidation in China or Russia appears in the supplier space. From an intellectual property perspective, tacit knowledge built through in-process manufacturing partnerships could create barriers to entry for new suppliers separate from any growth in the number of patents.

Finding 5: The mRNA supply chain is global, growing, and integrated with many entrants.

The mRNA industry was a niche biopharma platform prior to the COVID-19 pandemic. The industry had some success in developing vaccines for other coronavirus diseases, but none of those completed clinical trials. The industry primarily looked to cancer treatments as a path to profitability. However, COVID-19 presented an opportunity for mRNA companies to demonstrate the value and ability of the platform to quickly develop novel vaccines and deliver them at scale.

INDUSTRY *mRNA Developers*		ENTRANTS *New RNA Approaches*		SUPPLIERS *Materials and Manufacturing*		SUBSTITUTES *DNA, Vector, Inactivated*	
	Moderna **Pfizer** Translate Bio	***US*:**	Arcturus, Gilead, Greenlight Biosciences, Chimeron/GMU, IDRI/Amyris, Replicate Biosciences, RNAImmune, Vaxess	***US*:**	AMRI, Avanti Lipids, Catalent, CIADMs, **Corden, Lonza**, Recipharma, Rentschler, ROVI	***US*:**	Altimmune, City of Hope / NIH, Epivax, Heat Biologics, Immunity Bio, Inovio, J&J, Medigen / Dynavax / NIH, Merck, Novavax, Providence Cancer Institute, Vaxart
		***Canada*:**	Precision NanoSystems	***Canada*:**	Precision NanoSystems		
	BioNTech **CureVac**	***EU*:**	AstraZeneca, GSK, Max Plank Institute, Novartis, Roche, Sanofi, VaxEquity	***EU*:**	CureVac, Fareva, Maravai	***EU*:**	AstraZeneca, Sanofi / GSK, Imperial College, Max Plank Institute
NA		***Japan*:**	Takeda	***China*:**	RNACure	***Russia*:**	Gamaleya, Federal Budgetary Research Institution, St. Petersburg Scientific Research Institute
		***Russia*:**	BIOCAD Federal Budgetary Research Instit.				
		***China*:**	CanSino, **PLA Academy of Military Sciences,** RNACure, Providence Therapeutics, Shanghai Jiaotong University, **Suzhou Abogen Biosciences, Walvax**			***China*:**	Cansino, Shenzhen Genomics, Univ of Hong Kong / Xiamen Univ, West China Hospital / Sichuan Univ

BUYERS

Current:
Governments
Multi-Lateral Organizations

Future:
Commercial Insurance
Distributors
Self-Funded Employers

Note: **Bold** font denotes companies selected for a deeper dive.

Source: MITRE research.

FIGURE 2: GLOBAL ENTRANTS TO THE MRNA INDUSTRY

Building on this success, many companies and countries are now entering the mRNA industry, as shown in Figure 2. This includes most established biopharma companies as well as new entrants and several Chinese firms. Significant interest from investors in the technology willing to fund new mRNA ventures bolsters this flurry of new entrants. The Chinese entrants present the greatest challenge to the US-based mRNA capability, since China has a history of building economies of scale that undercut established industry players on pricing.

Finding 6: mRNA entrants from China are poised for success; at least seven organizations are already active in the field, including the People's Liberation Army (PLA).

Currently, it appears that entrants from China are poised for success: at least seven companies are already operational (including some funded by the PLA)The ability of these companies to raise capital on public and private markets is likely to fuel significant growth. Although patent data is not available for the specific companies of interest, joint ventures with Western mRNA companies fuel technology transfer, including trade secrets and process information not included in patents. Chinese partnerships with Western companies outside the United States should help expand nascent pipelines as Western partners "teach" capability and PLA-connected facilities build capacity for production.

Overall, innovation occurring overseas could undermine US industry and USG access to new technology. Chinese entrants are flush with cash through public and private markets, as well as support from the Peoples' Republic of China (PRC) and foreign subsidiaries. Both strategic investment (e.g., by the PRC) and investors seeking profit will fuel growth. Key foreign subsidiaries will allow Chinese companies to tap other markets (e.g., India).

Finding 7: Current mRNA buyers are governments seeking to counter COVID-19; future buyers will be more diverse.

Currently, most mRNA buyers are governments already participating in the COVID-19 mRNA market, which constitutes 38.6% of the COVID-19 vaccine market. The USG represents only 17% of the current mRNA market, with early purchase agreements currently meeting or exceeding local demand. Most mRNA buyers are predominantly high-income countries. Currently, China has only announced purchase commitments that will be filled later, possibly with local production.

mRNA Supply Chain and Ecosystem

The mRNA industrial base is a complex network of companies and organizations working together to develop, produce, and distribute vaccines at a global scale. Pfizer has stated that roughly 280 components from 19 countries are needed to produce its mRNA vaccine.[19] This complexity makes it difficult to predict the long-term impact of government decisions; however, the USG must remain aware of the potential impacts of decisions when looking to sustain the biopharma industrial base.

Finding 8: USG supply chain interventions often do not account for second-order consequences to industry.

As an example, the USG used the Defense Production Act (DPA) Title 1 to increase mRNA vaccine production capacity by compelling companies to prioritize USG contracts and to accept new contracts. While this effectively increased mRNA production capacity, it also significantly disrupted the production of other biopharma products in those facilities and constrained the global availability of some raw materials.[20]

Likewise, the USG's support for waiving the World Trade Organization Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) for mRNA vaccines was controversial.[21] While some proponents suggested that TRIPS waivers would increase vaccine availability, in reality shortages of raw materials and specialized mRNA production expertise remained barriers. Furthermore, industry objected to the government's willingness to waive their IP rights, and, thus, jeopardize their ability to recoup investments in vaccine development. Thus, the USG's waiver support may have increased industry mistrust of government while producing little to no benefit in terms of global vaccine availability.[22]

Finding 9: The mRNA industry relies on a complex, global, and heavily outsourced supply chain ecosystem.

The mRNA industry base is global, as is demand for the platform technology. In addition, the production of mRNA vaccines relies heavily on contracts with suppliers and manufacturers to achieve the global scale needed. For example, Moderna has a network of 9 companies involved in vaccine production (not including raw materials or distribution) in the United States and Europe, and Pfizer/BioNtech, which has greater internal capabilities, has a network of 12 companies. Many of these mRNA production partners also manufacture other biopharma products for other companies. It is nearly impossible to separate mRNA production capacity from overall needs for biopharma production capacity.

The current US biopharma workforce is insufficient to support mRNA growth; meanwhile other nations invest heavily in building this workforce. In addition, the mRNA manufacturing and supply chain lacks mature capacity and the partnerships with key entities across the value chain needed to compete for raw materials, supplies, and capacity. Overall,

suppliers may represent the key sector to support to ensure domestic access amidst possibly negative trends. With respect to investment, longer-term distributed manufacturing possibilities could erode the attractiveness of established companies or encourage geographic-centric investment.

Biopharma companies anticipated the complex and global nature of the industry and therefore pursue global markets through global supply chains. Contracted manufacturing partners are a regular component of most biopharma operations. As the USG engages with industry, it must understand the structure of biopharma supply chains as a guide for how best to engage and with whom. In the case of mRNA, simply engaging with the mRNA companies (Pfizer, Moderna, etc.) would likely not ensure the availability of capacity during an emergency.

Recommended Courses of Action

Sustaining the biopharma industrial base requires an integrated system of actions across the whole of government. MITRE recommends four interrelated COAs, as shown in Figure 3. These COAs represent a system of effort that the USG must undertake simultaneously to be effective. Not engaging in any one COA will prevent the USG from effectively sustaining mRNA technology as a component of the biopharma industrial base.

Improve Government Effectiveness

Under the first COA, the USG should start by improving government capability and effectiveness in managing the biopharma industrial base. This starts with creating an industrial base strategy and implementation plan that drives systematic government action and accountability. The strategy should be built around three primary objectives:

1. Protect the US population from future biological threats (naturally occurring, accidental and intentional), as aligned with core global health security principles
2. Provide supply chain resilience that absorbs supply and demand shocks and scales to meet national needs
3. Maintain US leadership of the bioeconomy to meet domestic needs as well as global export requirements during both crises and peacetime.

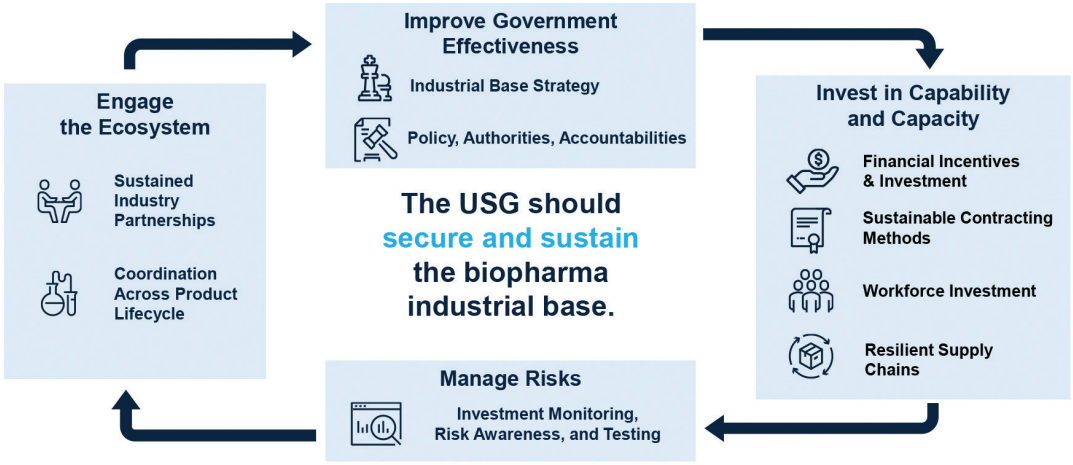

FIGURE 3. BIOPHARMA COURSES OF ACTION

With these three objectives, the strategy depends on appropriate policy to support the planned actions, accountabilities for achieving the strategy, budgets to fund the strategy, and programmatic plans for implementing and executing the strategy. Since the strategy will require action from across government, the Executive Office of the President should lead it, with active participation from industry and executive agencies, including HHS, DoD, Commerce, Treasury, State, the US Agency for International Development (USAID), the Department of Agriculture (USDA), and DHS, all of which have a role in engaging and sustaining the biopharma industrial base. The creation of the industrial base expansion office (IBx) within HHS ASPR presents an opportunity to inform focus and interagency colloboration surrounding the mission of building a sustainable biopharma industrial base.[23]

Invest in Capability and Capacity

The USG should invest in the capability and capacity of the biopharma industrial base needed to achieve the strategic objectives of becoming a sustainable industry, including a robust workforce and resilient supply chains. This COA includes four key elements for building and sustaining capability and capacity.

The first element consists of investment mechanisms and incentives (e.g., tax credits) to protect and enhance domestic capacity and capability. Since the USG should seek to sustain the entire industrial base, the USG should consider all components of the supply chain when deciding where to invest. This requires an industrial base approach to build the capabilities not only to develop products, but also to produce and deliver the products at the scale and speed needed. The investments should target sustainability, which includes identifying dual use opportunities where everyday commercial demand can help sustain critical capabilities.

The second element consists of employing contracting mechanisms aimed at sustaining industry capabilities, which leverage best practices. Here, the government should leverage the DoD contracting and acquisition practices that have succeeded in engaging and sustaining industry capabilities while achieving fiscal value for the government.

The third element involves investing in growing the biopharma R&D and manufacturing workforce to compete with other major powers in this sector. In building the workforce, the USG must note that the industry needs a variety of skill sets to sustain the needed capacity. This includes building a workforce of production technicians (typically persons with two-year degrees) who can manage and operate biopharma production processes. This represents an excellent opportunity to train people as a skilled workforce and encourage capacity investment in economically depressed areas of the country.

The fourth element consists of investing in resilient supply chain capacity and capabilities that support domestic production, agility, and coordinated surge capability. While this can include sustaining additional production capacity, the nature of biopharma supply chains means that the USG can likely accomplish this by investing in contract manufacturing capacity that can serve multiple biopharma technology platforms. With this approach, the investment can increase access to capacity across multiple platforms. This investment can also support the growth of the domestic biopharma industry by providing ready capacity to produce and scale niche products developed by smaller companies.

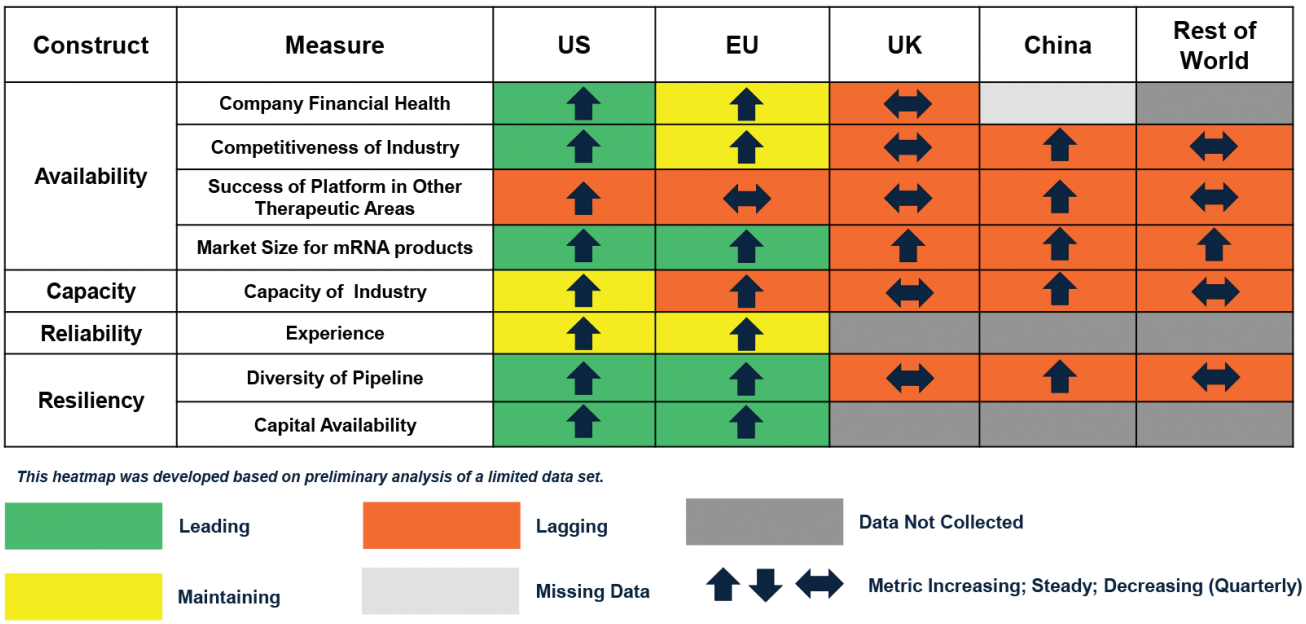

FIGURE 4. NOTIONAL MRNA INDUSTRY COMPETITIVENESS HEATMAP

Manage Risks

The government should manage risks to the biopharma industrial base. This includes establishing the measures and mechanisms to track investment and supply chain risks and create a test and evaluation (T&E) capability with industry. As an example, the USG can use the capabilities under the Committee on Foreign Investment in the United States (CFIUS) to monitor sources of capital, joint ventures, and mergers and acquisitions in the mRNA supply chain. The government should develop a repeatable approach for assessing the state of market dynamics and competitiveness for critical biopharma industrial base assets. Figure 4 presents a notional example of a heatmap measuring the competitiveness of the mRNA industry. This heatmap is a prototype and represents data only from BioNTech, Moderna, Pfizer, and CureVac for the United States and the European Union. It is meant to be used as a snapshot of the industry and must be updated regularly.

The government should also manage risks by investing in T&E capabilities with industry to track the ability to rapidly scale in response to biological threats. With an established T&E capability, the government can work with and compensate industry to run live tests of industry capabilities and capacity. The USG also compensates industry for the resources needed for the tests, and the tests should be geared toward producing items needed for stockpiles or commercial use. Building a T&E capability will require developing the funding and contracting mechanisms to support a test and engaging with industry to define shared objectives for T&E.

Engage the Ecosystem

The USG should engage industry across product lifecycles through sustained partnership models. The USG already has various mechanisms to engage with industry, but they are dispersed throughout the government and often suffer from tactical or transactional approaches. Executive Order

14017, "America's Supply Chains," establishes a government-industry consortium, led by HHS, to engage on industrial base capacity issues.[24] The USG can leverage this consortium, or a similar structure, to create a sustained forum for engaging with the biopharma industrial base. The government also needs to improve coordination of industry engagement across agencies and departments, especially by adding continuity to industry engagement as products transition from R&D to clinical trial to production phases of the lifecycle.

Conclusion

MITRE's proposed COAs provide a roadmap aligned with USG policy priorities. The COVID-19 pandemic has exposed many of the gaps in US management of the biopharma industrial base, and the Biden Administration and Congress have shown interest in closing those gaps to better prepare the country for the next health emergency. The USG should capitalize on this momentum and establish the foundation for industrial base sustainment building on aligned policy and legislation. Four initial actions can launch the process of building a sustained biopharma industrial base, including:

1. Clarifying government roles and accountabilities related to the biopharma industrial base
2. Building a whole-of-government biopharma industrial base strategy with objectives and accountability for success
3. Establishing a strategic implementation plan with clear roles across industry and government
4. Incorporating implementation into the FY23 budget request.

References

1. National Bioeconomy Blueprint (bioeconomy defined as the "economic activity that is fueled by research and innovation in the biological sciences"), https://obamawhitehouse.archives.gov/sites/default/files/microsites/ostp/national_bioeconomy_blueprint_april_2012.pdf
2. "Understanding the Emerging Era of International Competition," https://www.rand.org/pubs/research_reports/RR2726.html
3. "China's Biopharmaceutical Strategy: Challenge or Complement to U.S. Industry Competitiveness?," https://itif.org/publications/2019/08/12/chinas-biopharmaceutical-strategy-challenge-or-complement-usindustry
4. Ibid.
5. "Ensuring U.S. Biopharmaceutical Competitiveness," https://itif.org/publications/2020/07/16/ensuring-us-biopharmaceutical-competitiveness
6. "Vaccines 'on demand': science fiction or a future reality," https://pubmed.ncbi.nlm.nih.gov/25582273/
7. "How a secretive Pentagon agency seeded the ground for a rapid coronavirus cure," https://www.washingtonpost.com/national-security/how-a-secretive-pentagon-agency-seeded-the-ground-for-a-rapid-coronavirus-cure/2020/07/30/ad1853c4-c778-11ea-a9d3-74640f25b953_story.html
8. "PROTECTING CRITICAL AND EMERGING U.S. TECHNOLOGIES FROM FOREIGN THREATS," https://www.dni.gov/index.php/ncsc-newsroom/item/2254-ncsc-fact-sheet-protecting-critical-and-emerging-u-s-technologies-from-foreign-threats
9. Porter, M (1980). Competitive Strategy. The Free Press.
10. "America Can—and Should—Vaccinate the World," https://www.foreignaffairs.com/articles/united-states/2021-03-19/america-can-and-should-vaccinate-world
11. 2019 National Biodefense Public Report, https://www.phe.gov/Preparedness/biodefensestrategy/2019-report/Documents/2019-Biodefense-Public-Report-508.pdf. NOTE: National Security Presidential Memorandum 20-14 directs federal agencies, through a series of required annual activities, to implement the Strategy.
12. Ibid.
13. "Clear Lines of Responsibility Would Facilitate Implementation of the National Biodefense Strategy," https://www.heritage.org/defense/report/clear-lines-responsibility-would-facilitate-implementation-the-national-biodefense
14. Pacific Northwest National Laboratories, Biodefense Policy Landscape Analysis Tool v2.0, https://bplat.pnnl.gov/
15. "National Biodefense Strategy: Additional Efforts Would Enhance Likelihood of Effective Implementation," https://www.gao.gov/products/gao-20-273
16. "Significant Improvements Are Needed for Overseeing Relief Funds and Leading Responses to Public Health Emergencies," https://www.gao.gov/products/gao-22-105291
17. "COVID shows US needs stronger legislation for effective public health agencies," https://thehill.com/opinion/healthcare/538273-the-next-pandemic-will-require-strong-legislation-for-effective-public?rl=1
18. "Ending the Cycle of Crisis and Complacency in U.S. Global Health Security: A Report of the CSIS

Commission on Strengthening America's Health Security," https://www.csis.org/analysis/ending-cycle-crisis-and-complacency-us-global-health-securitya

19. "Pfizer requires 280 components to produce Covid-19 vaccine," https://www.opportimes.com/pfizer-requires-280-components-to-produce-covid-19-vaccine/
20. "Towards Vaccinating The World Landscape of Current COVID-19 Supply Chain and Manufacturing Capacity, Potential Challenges, Initial Responses, and Possible "Solution Space" - a Discussion Document," https://www.ifpma.org/wp-content/uploads/2021/03/Summit_Landscape_Discussion_Document.pdf
21. "Statement from Ambassador Katherine Tai on the Covid-19 Trips Waiver," https://ustr.gov/about-us/policy-offices/press-office/press-releases/2021/may/statement-ambassadorkatherine-tai-covid-19-trips-waiver
22. "The Debate Over a Patent Waiver for COVID-19 Vaccines: What to Know," https://www.cfr.org/in-brief/debate-over-patent-waiver-covid-19-vaccines-what-know
23. "Expanding the domestic public health supply chain is a matter of national security," https://www.statnews.com/2021/08/26/expanding-domestic-public-health-supply-chain-matter-of-national-security/
24. "Executive Order on America's Supply Chains," https://www.whitehouse.gov/briefing-room/presidential-actions/2021/02/24/executive-order-onamericas-supply-chains/

Appendix A: Acronyms

ASPR	Assistant Secretary for Preparedness and Response
BCT	Biodefense Coordination Team
BSC	Biodefense Steering Committee
CDC	Centers for Disease Control
CFIUS	Committee on Foreign Investment in the United States
COA	Course of Action
COVID-19	Coronavirus 2019
CSIS	Center for Strategic and International Studies
DARPA	Defense Advanced Research Projects Agency
DHA	Defense Health Agency
DHS	Department of Homeland Security
DLA	Defense Logistics Agency
DoD	Department of Defense
DPA	Defense Production Act
FDA	Food and Drug Administration
FEMA	Federal Emergency Management Agency
GAO	Government Accountability Office
HHS	Department of Health and Human Services
LMIC	low-to-middle income country
mRNA	Messenger ribonucleic acid
NBS	National Biodefense Strategy
NDAA	National Defense Authorization Act
NIH	National Institutes of Health
ODNI	Office of the Director of National Intelligence
OWS	Operation Warp Speed
PLA	People's Liberation Army
PRC	Peoples' Republic of China
R&D	Research and Development
T&E	Test and Evaluate
TRIPS	Trade-Related Aspects of Intellectual Property Rights
US	Unites States
USAID	US Agency for International Development
USDA	US Department of Agriculture
USG	United States Government

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