

BRIEFER

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Key U.S. Initiatives for Addressing Biological Threats Part 5: The Future Industrial Base for Rapid Medical Countermeasure Development

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INTRODUCTION

As the global community continues to struggle with the COVID-19 pandemic, it must also prepare for subsequent infectious disease outbreaks - outbreaks that experts predict will occur more frequently. Further, biological threats do not just emerge from nature; greater distribution of equipment, materials, and knowledge are lowering barriers for developing biological weapons, and advances in the specificity of biotechnology are potentially opening new avenues for novel biological threats.²

Fortunately, COVID-19 also accelerated significant advances in how we stop biological threats from creating mass harm. One of the most significant advances has been in the rapid development, manufacturing, and deployment of medical countermeasures.

In the United States, this work was driven by Operation Warp Speed (OWS), an effort predominantly between the Departments of Health and Human Services (HHS) and Defense (DoD).³ OWS leveraged

¹ The authors and the Council on Strategic Risks would like to thank the subject matter experts who were consulted to help us define and explore these recommendations on a non-attribution basis.

² Michael Moodie, "Chapter 14. Options and New Dynamics: Chemical and Biological Weapons Proliferation in 2020," in James W. Wirth and Peter R. Lavoy, *Over the Horizon Proliferation Threats* (Redwood City: Stanford University Press), 2020. pp. 266 - 290.

³ U.S. Department of Defense, "[Coronavirus: Timeline](#)," August 2, 2021.

interagency and public-private cooperation with judicious strategies to accelerate vaccine development, mitigate safety risks, and jump-start commercial-scale manufacturing.⁴ Despite ongoing issues with distribution and communications, the accomplishments of this initiative are clear: the game-changing development and deployment of vaccines against COVID-19 in just 11 months after the genetic sequence for the SARS-CoV-2 virus that causes it was in the hands of researchers.⁵

It is critical to capitalize on the successes of OWS and apply lessons from the experience to improve the industrial base for producing medical countermeasures. OWS should serve as the new minimum baseline, building on it for increased speed, scaling, and resilience.

To this end, the U.S. government is setting strong goals, including the targets of having the “capability to design, test and approve safe and effective vaccines within 100 days of detecting a pandemic threat” and “manufacture enough doses to supply the world within 200 days.”⁶ These goals are achievable through a framework which we present in this briefer, which focuses on fostering a medical countermeasure ecosystem with core capacities and greater surge capacity---one that promotes diversity in the U.S. bioeconomy and resilience. Such an approach would simultaneously strengthen the U.S.’s ability to address all manner of biological threats, strengthen supply chains to minimize disruptions to valuable life sciences work, and even shrink target timelines towards life-saving medical countermeasures in adverse events.⁷

This briefer provides background on OWS and factors that contributed to its success. It then provides recommendations for improving capacity for rapid medical countermeasure development, production, and delivery for addressing the full range of biological threats.

OPERATION WARP SPEED

There is no definitive timeline on the emergence of SARS-CoV-2. It was first reported in humans in December 2019 but may have been in circulation in the human population as early as October 2019.⁸ Its spread and severe symptoms led the World Health Organization (WHO) to declare COVID-19 a

⁴ U.S. Government Accountability Agency, [Operation Warp Speed: Accelerated COVID-19 Vaccine Development Status and Efforts to Address Manufacturing Challenges](#), February 11, 2021.

⁵ Helen Branswell, [“12 Lessons COVID-19 Taught Us About Developing Vaccines During a Pandemic,”](#) *PBS News Hour*, July 2, 2021.

⁶ Eric Lander, [“As bad as COVID-19 has been, a future pandemic could be even worse — unless we act now.”](#) *The Washington Post*, August 4, 2021.

⁷ For examples, see Gerald L. Epstein, [Testimony before the Bioterrorism and Public Health Preparedness Subcommittee, Committee on Health, Education, Labor, and Pensions - Biodefense: Building a Medical Countermeasure Capability](#), February 8, 2005; [“HHS Takes Immediate Action to Secure Pharmaceutical Supply Chain,”](#) *HHS-ASPR*, June 8, 2021; and Marcy E. Gallo, [Congressional Research Service - The Bioeconomy: A Primer](#), August 19, 2021.

⁸ See Lauren M. Sauer, [“What is Coronavirus?”](#) *Johns Hopkins School of Medicine* and Scott LaFee, [“Novel Coronavirus Circulated Undetected Months before First COVID-19 Cases in Wuhan, China,”](#) *University of California San Diego Health*, March 18, 2021.

pandemic on March 11, 2020, with the U.S. declaring it a national emergency shortly afterwards.⁹

The U.S. government announced OWS in April 2020. Its aim was to bring the COVID-19 pandemic under control by accelerating the research, development, manufacturing, scaling, and distribution of vaccines, therapeutics, and diagnostics. Further, OWS was designed to put promising candidates through difficult hurdles while simultaneously walking their manufacturers through the FDA approval process. The end goal was to deliver tens of millions of effective and safe SARS-CoV-2 vaccines by the end of 2020, and as many as 300 million doses by mid-2021.¹⁰

This initiative was bold given the history of vaccine research and development. Vaccines historically take 10-15 years to develop. However, today gene sequencing and synthesis technologies have become faster and cheaper and disciplines like bioinformatics have enhanced researchers' ability to understand emerging infectious diseases.¹¹ Challenges lie more in coordination and regulatory processes which, done poorly, can stifle innovation and slow progress towards the completion of complex scientific tasks like vaccine development.¹²

OWS succeeded in the rapid development, safety and efficacy testing, and manufacture of five vaccine candidates. In terms of development, OWS sought to minimize risk and maximize success by selecting vaccine candidates that stimulate immunological responses against COVID-19 through different mechanisms. In terms of safety and efficacy, OWS took steps to accelerate the clinical trial and review process by relying on data from other vaccines that used the same platforms and conducting animal studies alongside clinical trials (rather than the normal process of these steps being sequential). In terms of manufacturing, vaccine candidate companies began large-scale manufacturing during clinical trials---supported by government purchase orders---to ensure that the capacity was there as soon as their products received emergency use authorization (EUA) from the Food and Drug Administration (FDA).¹³ The U.S. government also used advanced purchase contracts to ensure manufacturers had a clear market incentive to do vaccine research.¹⁴ By January 2021, OWS officials reported that vaccine companies had produced and released 63.7 million doses of vaccine.¹⁵

⁹ [“WHO Director-General’s Opening Remarks at the Media Briefing on COVID-19 - 11 March 2020,”](#) *World Health Organization*, March 11, 2020 and [“Proclamation 9994 of March 13, 2020: Declaring a National Emergency Concerning the Novel Coronavirus Disease \(COVID-19\) Outbreak,”](#) *Federal Register*, March 18, 2020.

¹⁰ Moncef Slaoui and Matthew Hepburn, [“Perspective: Developing Safe and Effective Covid Vaccines - Operation Warp Speed’s Strategy and Approach,”](#) *New England Journal of Medicine*, October 29, 2020.

¹¹ National Research Council, [The Genomic Revolution: Implications for Treatment and Control of Infectious Disease: Working Group Summaries](#), November 10 - 13, 2005.

¹² See Heidi Legg, [“Interview with Kendall Hoyt,”](#) and Mark Toshner, [“Less Than a Year to Develop a COVID Vaccine - Here’s Why You Shouldn’t Be Alarmed,”](#) *The Conversation*, November 25, 2020.

¹³ U. S. Government Accountability Office, [Report to Congressional Addressees: Operation Warp Speed - Accelerated COVID-19 Vaccine Development Status and Efforts to Address Manufacturing Challenges](#), February, 2021.

¹⁴ Simi V. Siddalingaiah, [Congressional Research Service - Operation Warp Speed Contracts for COVID-19 Vaccines and Ancillary Vaccination Materials](#), March 1, 2021. Note: Pfizer produced an additional vaccine candidate now in use without using all available government financial incentives.

¹⁵ U. S. Government Accountability Office, [Report to Congressional Addressees: Operation Warp Speed - Accelerated COVID-19 Vaccine Development](#), February, 2021.

Three primary factors facilitated the U.S. government and private partners in achieving this unprecedented outcome. First, the severity and scope of COVID-19 raised it to the top of the priority list for many countries, including the United States, and created the collective political will needed to surge resources. This allowed for fast policymaking and helped the federal government meet the challenges of inadequate supply chains while researching, developing, testing, and producing diagnostics, therapeutics, and vaccines for COVID-19.

Of particular note were the Coronavirus Preparedness and Response Supplemental Appropriations Act of 2020 and the Defense Production Act. These policies simultaneously appropriated funding for HHS activities related to COVID-19 and allowed the U.S. government to pivot and address shortages in COVID response-related materials ranging from personal protective equipment to essential reagents for diagnostics and therapeutics.¹⁶

Second, OWS was built on past successes and experiences with other infectious disease events, including the 2014-2017 Zika epidemics. These experiences helped galvanize an integrated structure for COVID-19 countermeasure research that included capabilities and expertise from private industry, as well as government assets across HHS, DoD, the National Institutes of Health, and other agencies.¹⁷

Third, OWS leveraged decades of research and development that led to platform technologies for the development of vaccines and other countermeasures. One platform type that showed significant potential was based on the much-studied and well-understood biological component known as messenger ribonucleic acid (mRNA). Scientists have studied mRNA since the 1970s, resulting in the robust characterization of this mechanism that bridges the gap between protein-encoding DNA and the actual production of cellular proteins.¹⁸ Additionally, mRNA vaccines have been tested and used in animal populations with promising results against maladies ranging from cancers to infectious diseases.¹⁹ Platforms based on mRNA and other mechanisms can now be used to produce the key ingredients of vaccines with speed and great consistency.

THE FUTURE MEDICAL COUNTERMEASURE ECOSYSTEM

Both the technologies and expert experiences that made OWS transformative built on decades of efforts and investments. Now, the OWS approach must become the new minimum baseline from which the United States and other nations reshape their bioeconomic industrial bases in order to prevent future pandemics and deter the use of biological weapons.

¹⁶ For examples, see Anshu Siripurapu, “[What is the Defense Production Act?](#)” Council on Foreign Relations, January 26, 2021; U.S. Government Accountability Office, [Defense Production Act - Opportunities Exist to Increase Transparency and Identify Future Actions to Mitigate Medical Supply Chain Issues](#), November 2020; and White House, [National Strategy for the COVID-19 Response and Pandemic Preparedness](#), January, 2021.

¹⁷ Slaoui and Hepburn, “[Perspective: Developing Safe and Effective Covid Vaccines](#).”

¹⁸ Norbert Pardi, Michael J. Hogan, Frederick W. Porter, and Drew Weissman, “mRNA Vaccines - A New Era in Vaccinology,” *Nature Reviews Drug Discovery*, Vol. 17, 2018; pp. 261 - 279.

¹⁹ Pardi, et al., “mRNA Vaccines,” *Nature Reviews Drug Discovery*, Vol. 17, 2018.

In this context, the United States should take an ecosystem approach to encouraging a strong industrial base for rapid countermeasure development, manufacturing, and deployment. To this end, public and private sectors must map and update the landscape of available capacities, supply chains, and expertise on a regular basis.

This ecosystem will look different than it has in the past. Greater roles will go to mRNA and other platform technologies, and cell-free manufacturing approaches that proved to be reliable and time-saving in COVID-19 countermeasure development. Supply chain bottlenecks have proven that capacity and redundancies to quickly produce consumables will be critical to rapid and effective responses to pandemic-potential pathogens. COVID-19 responses also showcased the growing role of machine learning and artificial intelligence, and helped inspire and expand start-up companies focused on designing systems to quickly identify existing therapeutics and vaccines that could help address newly-concerning disease threats, including drugs that may already be tested and approved for other purposes.

As such, **the broad U.S. bioeconomy should be considered a strategic asset capable of surge capacity to quickly and effectively respond to novel infectious disease threats.** This requires constant support of the infrastructure and supply chains that expanded in response to COVID-19.

Sustained support for DoD and HHS Advanced Development and Manufacturing (ADM) facilities is a key aspect of this recommendation. ADM facilities have faced many challenges in the past, including financial sustainability issues. During the COVID-19 pandemic, they were forced to troubleshoot through the ambitious, first-ever scale and speed of production that OWS required. Lessons from that fast ramp-up must inform plans on maintaining the longevity of these facilities. This should include creative and revenue-generating approaches, including annual exercises and steady-state processes recommended below, as well as diversifying the portfolio of ADM facilities to include biomanufacturing and other projects that contribute to the U.S. bioeconomy.

In addition to fixed assets like ADMs, significant COVID-19 response capacity came from academic labs, the U.S. National Labs, nonprofits, and private companies pivoting their existing assets to aid in testing, data collection and sharing, production of consumables, and other functions.²⁰ These assets need to be maintained and incentivized to pivot toward rapid and robust outbreak responses in the future. Multipurpose biofoundries located in geographically dispersed cities should also be part of this bioeconomy surge capacity.²¹ This will naturally entail some updates to the authorities and resources of key U.S. departments and agencies.

²⁰ For examples, see Anup Singh, Christine Parthemore, and Andrew Weber, [Making Bioweapons Obsolete: A Summary of Workshop Discussions](#), The Council on Strategic Risks, August 27, 2019; and Christine Parthemore, Anup Singh, and Andrew Weber, [Critical Steps in Preventing Future Pandemics](#), The Council on Strategic Risks and Sandia National Laboratories, February 22, 2021.

²¹ For examples, see Nathan Hillson, Mark Caddick, Yizhi Cai, Jose A. Carrasco et al., “Building a Global Alliance of Biofoundries,” *Nature Communications*, Vol. 10, Article 2040, 2019; “[The NIST Biofoundry: Taking Engineering Biology from Artisanal to Automated](#),” *U.S. Department of Commerce - National Institute of Standards and Technology*, March 13, 2020; and Melody M. Bomgardner, “[Ginkgo Opens Facilities to Help COVID-19 Coronavirus Response](#),” *Chemical and Engineering News*, March 20, 2020.

COVID-19 also showcased how fragile, interconnected and international supply chains are, especially for large-scale vaccine production. Fostering a healthy supply base within the United States, in particular for some critical materials like reagents and enzymes, is a required first step to address this. The U.S. also needs to take a global leadership perspective to fix the supply chain issues that hampered COVID-19 responses. Diplomacy and expanded trade relationships must be part of the solution, just as DoD supports a multinational industrial base with international partners and allies contributing to logistics, co-manufacturing, and readiness for wide-ranging crises.

A strong core of domestic development and manufacturing assets, a healthy bioeconomy ready to surge to help quash infectious disease outbreaks, and strong international partnerships can provide sufficient assets to allow the United States to experiment with and refine approaches to biological threat prevention and preparedness such as virtual stockpiling, best uses of the Defense Production Act, and rapid response funding and business models.

New, small, and innovative companies will become increasingly central features of the U.S. rapid medical countermeasures ecosystem. Though the medical countermeasure landscape is still characterized by large-scale IT, consulting, and pharmaceutical companies, that landscape was already evolving in advance of the COVID-19 pandemic.²² OWS experiences highlighted that the complexity of navigating federal contracts makes it difficult for any but the largest and well-resourced private companies to contribute.²³ Moving forward, the U.S. government must **improve its ability to work with younger, innovative companies and small businesses.**

Some hurdles are financial. Newer companies at times rely on Small Business Innovation Research (SBIR) funds for early-stage research. Yet SBIR grants are incredibly small and often do not cover the costs of conducting the research the U.S. government seeks to foster. Further, for start-up companies that do seek SBIRs, these funds may not become available until the long process of review and approval is complete; there are even circumstances where successful start-ups may no longer even require the SBIR they applied for. These issues lead many small and new businesses to rely on nongovernmental financing, which can exacerbate the issues of companies doing well but not producing what the U.S. government needs for purposes like strong biological event responses, and U.S. officials at times not having access to cutting-edge technology developments and trends.

Other hurdles stem from lack of public-private interactions. Promising entrepreneurs and technologists may not know how to collaborate with U.S. departments and agencies unless their network includes people with knowledge of how the U.S. government works. Establishing and maintaining better networks across public and private sectors in advance of a biological event is crucial---a capacity we are developing

²² Chad P. Bown and Thomas J. Bollyky, "[How COVID-19 vaccine supply chains emerged in the midst of a pandemic.](#)" Peterson Institute of International Economics, August 2021.

²³ The listings of top OWS contracts for COVID-19 vaccines and ancillary vaccination materials contain highly-established companies, as opposed to small-scale or start-up biotech companies. The U.S. Committee on Small Business and Entrepreneurship realizes this is an issue. Some attribute this inequity to the bandwidth constraints that small businesses face when applying for federal government grants. For examples, see "[Issues.](#)" *U.S. Senate Committee on Small Business & Entrepreneurship* and Geoff Orazem, Greg Mallory, Matthew Schlueter, and Danny Werfel, "[Why Startups Don't Bid on Government Contracts.](#)" *Boston Consulting Group*, August 22, 2017.

at the Council on Strategic Risks through the Alliance to End Biological Threats and other projects.²⁴ Other initiatives, such as a Biosecurity Reserve Corps where nongovernmental experts serve weekends at the National Labs or within DoD and HHS for networking, collaboration, and surge preparedness purposes, also hold great promise.²⁵

Increasing the size of SBIR grants, as well as streamlining the timeline it takes to review and approve such grants, would help. Breaking government projects into smaller scopes of work that are better integrated by government personnel and expanding requirements for small-business consortiums and sub-contracts by larger companies are also commonly-used techniques that can be applied to the bio industrial base. However, it is critical that such measures are used to foster and de-risk innovative countermeasure developers rather than perpetuate outdated tools and methods. Eliminating funding requirements that are overly-biased toward the largest companies (e.g., recent BARDA requests that require existing, large-scale countermeasure manufacturing capacity) will also be important and increasingly feasible as manufacturing methods change and as a more diverse and interconnected ecosystem fosters broader partnership options.

Additionally, **the U.S. government must set guidance for early warning signals triggering medical countermeasure and diagnostics development responses.** This guidance must accompany the ongoing U.S. and international development of pathogen early warning and disease forecasting systems, and indicate the conditions when senior leaders should approve the ramp-up of identification and development of therapeutics, vaccines, and diagnostics.

While some nations such as South Korea developed diagnostic tests within weeks of their COVID-19 outbreaks starting, this took the United States several months. A core mechanism for improving this is to ensure U.S. leaders have the authorities and resources needed to trigger the start of countermeasure and diagnostics development early after a pathogen of high concern is identified, or when an outbreak originating in another country is clearly starting.

Triggering development and production processes earlier in responding to infectious disease threats will naturally take dedicated funding, just as the nation continually resources response infrastructure such as fire departments. Similar to how many nations maintain preparedness for natural disasters, the United States should **launch an annual exercise program to practice and improve countermeasure development and production.** This can help keep the medical countermeasure ecosystem prepared for emergencies and be used to identify gaps and methods for improvement in advance of the next biological event. A strong goal would be to use this exercise program to halve the time that OWS took to produce COVID-19 vaccines.

²⁴ The Alliance to End Biological Threats, The Janne E. Nolan Center on Strategic Weapons, an institute of the Council on Strategic Risks, <https://councilonstrategicrisks.org/bioalliance/>

²⁵ Chris Fall, Yong-Bee Lim, and Christine Parthemore, [*Key U.S. Initiatives for Addressing Biological Threats Part 2: The U.S. Department of Energy National Laboratories*](#), The Council on Strategic Risks, June 22, 2021; and Trent Northen, Nancy Hagel, Daniel Sinars, Johnny Green, Dawn Wellman, and Daniel T. Schwartz, [*Attracting and Retaining Top Scientists and Engineers at U.S. National Laboratories and Universities: Listening to the Next Generation*](#) (2018), 1-6.

Additionally, the nation can **use expanded production capacities catalyzed by COVID-19 to help bring existing, promising medical countermeasure candidates across the line of FDA approval.** HHS and DoD have invested in early-stage research and development of several candidate therapeutics and vaccines for diseases of concern to U.S. public and military forces. When the current drive to produce COVID-19 vaccines subsides, the nation can use these assets to produce sufficient doses for any clinical trials needed for these candidates to be approved.

The nation used an analogous process to authorize Ebola vaccines and treatments. When the West Africa Ebola crisis hit in 2014-16, DoD used its prior research and development of Ebola countermeasures to bring strong candidates closer to FDA approval. When the epidemic subsided, pharmaceutical companies lost interest. Creative military and civilian personnel in DoD and HHS helped ensure these Ebola countermeasure investments did not languish. The result was approved vaccines and therapies in use today to help quash regular Ebola outbreaks before they cause mass devastation. Notably, offices and individuals involved in this effort leveraged learnings from the process in creating OWS. Making this a standing, annual process (e.g., with a target of at least one new FDA-approved vaccine or therapeutic) will create good jobs, ensure the nation can capitalize on past early-stage research and development investments, and showcase a world-leading U.S. ability to quickly bring countermeasures to infectious disease threats to fruition.

As U.S. capacities expand and evolve as outlined here, **it will change the landscape of threats to that infrastructure, and responses must outpace these threats.** With OWS, federal law enforcement and the intelligence agencies flagged that nation-states were targeting COVID-19 research organizations. In May 2020, the U.S. government issued a statement warning that organizations working on COVID-related research were being targeted by cyber actors and collectors associated with the People's Republic of China.²⁶ A few months later, additional intelligence revealed that Russian Intelligence Services were targeting American, British, and Canadian COVID-19 research and vaccine development sites.²⁷ Mitigating these attacks requires thoughtful, layered action on the part of the United States and its private sector collaborators.

Increasing countermeasure development and production speed is critical for preventing future pandemics and deterring bioweapon production and use by nefarious actors. Due to innovations like those highlighted in this briefer, the regulatory process is now one of the longest and most daunting aspects. **OWS should be further mined for lessons on producing safe and effective countermeasures faster.** Having registries for clinical trials that capture the population diversity needed and more regular dialogue regarding standards and needs among the FDA, HHS, DoD, and others will help.

Finally, the rapid medical countermeasures industrial base the United States fosters should be **designed to be flexible and agile.** Changes in development and production methods will continue to occur. Some will be game-changing, such as the movement toward skin patches and oral doses of vaccines and medications. This would significantly change the demand for many supplies (such as sterile glass vials)

²⁶ FBI and CISA, "[Public Service Announcement: People's Republic of China \(PRC\) Targeting of COVID-19 Research Organizations](#)," May 13, 2020.

²⁷ National Security Agency Central Security Service, "[NSA Teams with NCSC, CSE, DHS-CISA to Expose Russian Intelligence Services Targeting COVID-19 Researchers](#)," July 16, 2020.

and the still-long and technically-precise fill-and-finish process of getting vaccines into safe vials and ready for distribution. OWS demonstrated that steering this kind of change into significantly enhanced national preparedness for infectious disease threats will pay dividends in lives saved and jobs created.

CONCLUSION

OWS overcame significant challenges to ultimately succeed in the rapid development, production, and scaling of vaccines. These challenges included initial limitations in manufacturing capacity, disruptions to manufacturing supply chains due to the global pandemic, and gaps in the hiring and training of personnel with the specialized skills and knowledge required for successful facility management and COVID-19 vaccine production.²⁸ Building on the success of OWS, it is imperative that the U.S. government, along with nongovernmental organizations and partners, develop a rapid medical countermeasure ecosystem on the foundation of an agile, diverse, and resilient bioeconomy.

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²⁸ U.S. Government Accountability Office, [*Report to Congressional Addressees: Operation Warp Speed - Accelerated COVID-19 Vaccine Development Status and Efforts to Address Manufacturing Challenges*](#), February, 2021.