Policy Brief

A Shot of Resilience

A Critical Analysis of Manufacturing Vulnerabilities in Vaccine Production

Authors
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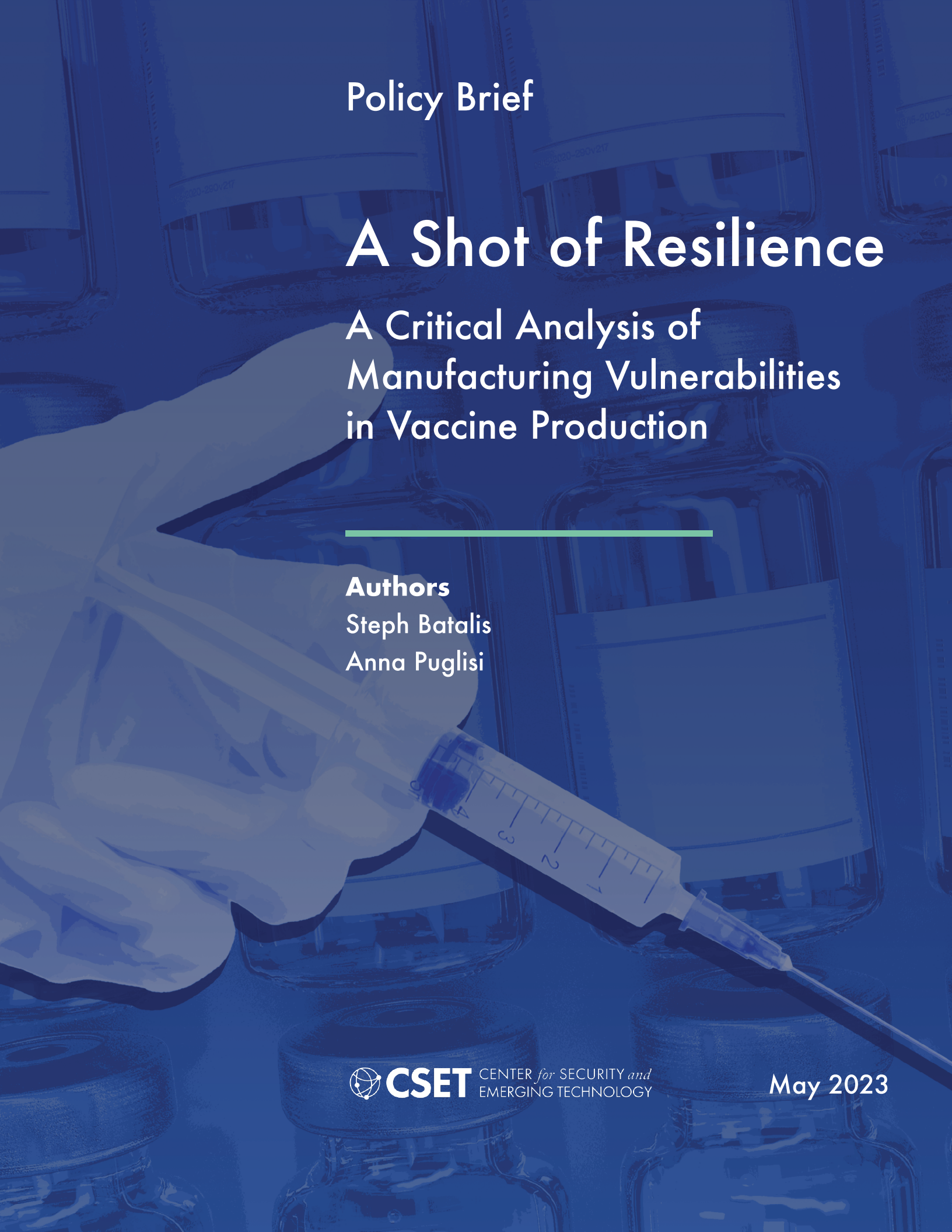

CSET CENTER for SECURITY and EMERGING TECHNOLOGY

May 2023

Executive Summary

Vaccines are a key aspect of national security and underpin U.S. strategies for public health, biosecurity, and pandemic preparedness. Routine vaccinations keep the American public healthy, decrease healthcare spending, and increase workforce productivity.[1] In a public health emergency, vaccines are an important line of defense against new and emerging threats.

Despite the importance of a secure vaccine supply, our analysis finds two major vulnerabilities in the biomanufacturing landscape for U.S. vaccines: a reliance on foreign manufacturers and a lack of manufacturing redundancy. Together, these two factors limit the country's ability to respond to emerging health threats.

Key findings include:

- The United States relies on foreign vaccine manufacturers for the majority of its vaccines—fewer than one third of the vaccines in this analysis are manufactured domestically. Vaccines that are not made in the United States are produced in Canada, Israel, and across Europe. The United States will face long supply chains that limit timely distribution in a public health emergency if it cannot control the production of its own vaccines, even if they are produced in allied countries.

- The majority of the vaccines in this analysis do not have redundant manufacturing supply chains and instead are entirely produced at a single manufacturing site. Twenty-nine of the 73 vaccines in this analysis are made at one of just four facilities. Redundancy in the manufacturing process would allow continual vaccine production even if one facility shuts down during a crisis.

- Vaccines on the U.S. Food and Drug Administration's list of Essential Medicines––which identifies the most critical medicines to have available for acute care in emergencies—are vulnerable to manufacturing disruptions. Of the 33 vaccines on the list, 19 have no domestic manufacturing capability and 22 have no manufacturing redundancy.[2]

- The U.S. government spent nearly as much on foreign-made vaccines as American-made vaccines in 2020—approximately $930 million and $1 billion respectively—through Medicare and Medicaid. Onshoring vaccine manufacturing would allow these taxpayer dollars to support American manufacturing jobs at U.S. facilities.

The vulnerabilities to the U.S. vaccine supply outlined in this report highlight where market forces and national security goals diverge. Biomanufacturers make decisions aimed at recouping large initial investments while maximizing return. The U.S. government, on the other hand, must consider vaccine supply as a matter of national security. Long-term strategies will need to take into account the private sector's economic interests, the economic challenges presented by developmental timelines and large initial investments, and U.S. public health and biosecurity needs.

Government action in the following three areas would help to address these challenges and have the most significant impact:

1. **Protect the existing vaccine supply**. Current vaccine manufacturing should be protected now, before long-term strategies have time to take effect. Recommendations include designating manufacturing facilities as critical infrastructure, including routine and seasonal vaccines in the Strategic National Stockpile, and developing a quality management maturity rating system for biologics to reward manufacturers who implement robust quality systems.

2. Identify and monitor vaccine manufacturing vulnerabilities. U.S. policymakers, regulators, and consumers need visibility into the vaccine manufacturing landscape to identify vulnerabilities and develop risk-mitigation strategies. The United States could require manufacturers to disclose manufacturing locations on vaccine labels, or create a public-facing dashboard of manufacturing resiliency that does not disclose specific facility information.

3. **Increase vaccine manufacturing resiliency.** Efforts to make the U.S. vaccine supply more resilient need to include both increased domestic manufacturing and manufacturing redundancy. Specific recommendations include implementing talent development programs to expand the biomanufacturing workforce, using public procurement funds to encourage new manufacturers to enter the market, using export financing to secure a market for American-made vaccines, and investing in innovative biomanufacturing technologies.

Table of Contents

Introduction

From existing diseases to new and emerging threats, a secure vaccine supply protects a broad range of U.S. interests including public health, economic stability, and biosecurity. Routine vaccinations—from measles and influenza to polio and shingles—keep the American public healthy while increasing life expectancy and decreasing hospitalizations for preventable diseases.[3] Healthy workers contribute to a stable economy by working more productively for longer,[4] and American-made vaccines further advance economic interests by contributing to the growing U.S. bioeconomy.[5] Vaccines are also key to biosecurity, ensuring that our military personnel and communities are protected in the event of a biological attack.

Despite the necessity of a resilient vaccine supply, this report identifies two vulnerabilities that threaten the American public's access to vaccines: limited domestic manufacturing and a lack of manufacturing redundancy. A reliance on foreign biomanufacturing means that the United States cannot control vaccine production levels during a public health emergency. Nonredundant manufacturing further increases the risk of vaccine shortages if a vaccine's sole manufacturing facility is disrupted.

While the United States can take steps to secure its vaccine supply, potential solutions may not align with traditional market forces. Pharmaceutical companies invest heavily in vaccine development, and can increase efficiency while maximizing returns by operating as few manufacturing facilities as possible across the globe.* As the private sector deals with market pressures that maximize profit, the U.S. government should consider vaccine supply as a matter of national security. This report explores the inherent risks in the current vaccine manufacturing landscape and highlights the need for continued government support, coherent and coordinated prioritization, and long-term investment in biomanufacturing.

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* When accounting for the number of failed vaccine candidates per approved candidate, the cost to develop a new vaccine from preclinical through Phase II clinical trials alone is in the billions of dollars. The societal benefits that these vaccines provide are highly distributed and may not be returned to the manufacturer as profit. See Gouglas et al., *Estimating the Cost of Vaccine Development against Epidemic Infectious Diseases: A Cost Minimisation Study.*

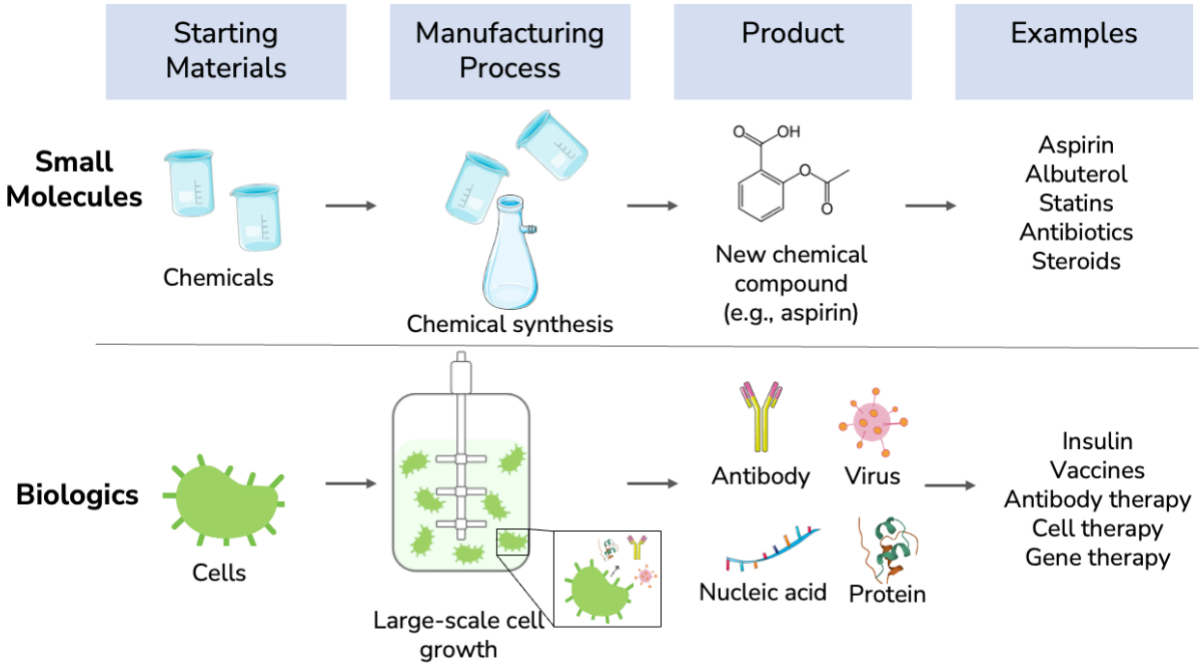
Biomanufacturing—A specialized process

Vaccines are large molecule "biologics" that are made with a different manufacturing process than traditional small-molecule "medicine cabinet" drugs like aspirin or blood thinners (Figure 1). Vaccines are made using the production power of living cells—human, animal, or bacterial—in a process called biomanufacturing. Biomanufacturing programs these cells to make the vaccine's active ingredients, usually a peptide, nucleic acid, or whole virus. This process requires a trained workforce, specialized equipment, and purpose-built facilities to manipulate, grow, and monitor thousands of liters of living cells. This biomanufacturing infrastructure is very different than the infrastructure needed to make small-molecule drugs, and the countries that lead in traditional drug manufacturing may not lead in vaccine or biologic manufacturing.[*]

Vaccine biomanufacturers cannot quickly add or change manufacturing sites in an emergency due to the specialized manufacturing process. Each facility that produces a vaccine is inspected individually because site-specific features like air flow, air quality measurements, equipment specifications, and nearby product lines can influence vaccine quality and play a role in the potential for contamination. Manufacturing a vaccine at a new facility requires an additional submission, inspection, and approval by the U.S. Food and Drug Administration (FDA) even if that site is owned by the original manufacturer and approved to manufacture other vaccines.

[*] China and India produce a significant portion of the small-molecule finished drug products and active pharmaceutical ingredients (APIs) that are sold in the United States; See: Department of Commerce, Department of Energy, Department of Defense, and Department of Health and Human Services. "Building Resilient Supply Chains, Revitalizing American Manufacturing, and Fostering Broad-Based Growth.," June 2021. (https://www.whitehouse.gov/wp-content/uploads/2021/06/100-day-supply-chain-review-report.pdf).

Figure 1. Small Molecule Manufacturing versus Biomanufacturing



Source: CSET.

Scope Note

This analysis specifically focuses on sites that produce vaccine drug products—the final form of the vaccine that has been combined with inactive ingredients, stabilizers, and adjuvants and packaged into a vial or syringe. In contrast, drug substance manufacturing involves production of the active vaccine components including live or killed pathogens, antigens, nucleic acids, or conjugates. These activities may or may not take place at the same facility; for example, a vaccine product may be made in the United States using ingredients that were produced elsewhere. Although drug substance manufacturing is a critical aspect of the vaccine supply chain, it is beyond the scope of this report.

Additionally, this paper highlights vulnerabilities in the U.S. vaccine supply while recognizing that solutions may not align with traditional market forces. A localized and nonredundant manufacturing supply chain can help biomanufacturers to streamline their manufacturing processes while decreasing costs and increasing returns. However, supply chain failures have the potential to threaten U.S. public health, biosecurity, and economic stability. Long-term strategies will need to harmonize the private sector's economic interests with state and federal public health and biosecurity interests.

Methodology

The vaccines included in this analysis came from the FDA's list of Vaccines Licensed for Use in the United States.[6] Of the 78 vaccines included on the list as of November 2022, 73 were included in this analysis (Appendix Table A1). We excluded discontinued vaccines (Gardasil, Cervarix*, Poliovax†, Menomune-A/C/Y/W-135‡, and Zostavax§).

To identify manufacturing locations, we downloaded the FDA submission documents and approval letters from the "Product Information" and "Supporting Documents" sections of the FDA's Vaccines Licensed for Use in the United States for each individual vaccine, as available in November 2022.[7] Where available, we inspected each vaccine's package insert, approval letter(s), and Summary Basis for Regulatory Action(s), each of which may contain information about manufacturing locations. This analysis was limited by the fact that the FDA website did not contain all of these documents for some vaccines, the documents were often heavily redacted, and some of the information was out of date or conflicting. For example, the most recent package insert on the FDA website for the typhoid fever vaccine, Vivotif, was from 2013.[8] A more recent package insert on the vaccine's website reveals that the information in the 2013 document became outdated when the vaccine was acquired by another company.[9]

Information on Medicare and Medicaid spending came from the following Centers for Medicare and Medicaid Services datasets: Medicare Part B Spending by Drug, Medicare Part D Spending by Drug, and Medicaid Spending by Drug.[10] The amount spent on each vaccine was classified as "domestic," "not domestic," or "undetermined" based on our previous analysis.

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* Gardasil and Cervarix prevent certain cancer-causing human papillomaviruses (HPVs) and were discontinued in favor of the updated Gardasil 9.

† Poliovax is a single-antigen polio vaccine, which was replaced with IPOL.

‡ Menomune-A/C/Y/W-135 was discontinued in favor of quadrivalent meningococcal conjugate vaccines.

§ Zostavax is a shingles vaccine that was discontinued in favor of Shingrix.

Vaccine Manufacturing Landscape

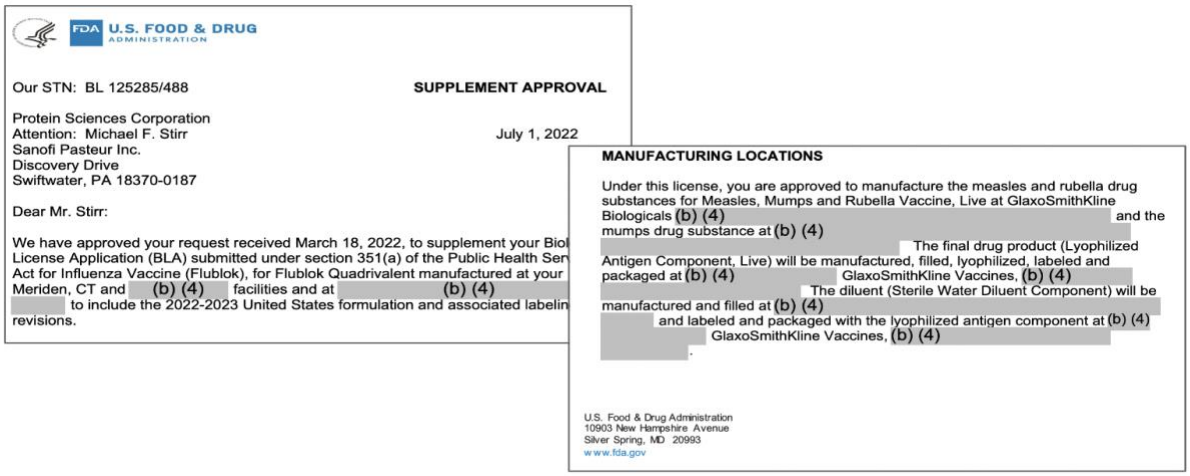
Based on publicly available FDA documentation, the current vaccine manufacturing landscape—and critical production shortfalls—are characterized here in terms of limited visibility, domestic manufacturing capacity, and manufacturing redundancy.

Limited Visibility into the Vaccine Manufacturing Supply Chain

U.S. policymakers, regulators, and consumers need visibility into the vaccine manufacturing landscape in order to identify vulnerabilities and develop mitigation measures. However, we found that openly available information regarding vaccine manufacturing locations was not sufficient to fully assess U.S. vaccine resilience.

The FDA documents we analyzed were heavily redacted (representative example, Figure 2), contradictory,* or otherwise unavailable. Therefore, we were only able to confidently assign manufacturing locations to approximately 70 percent of the vaccines available for use in the United State. The remaining 30 percent of vaccines represent a blind spot in the ability to assess the vaccine manufacturing supply chain.

Figure 2. Representative Examples of Redacted Manufacturing Information



U.S. FOOD & DRUG ADMINISTRATION

Our STN: BL 125285/488

SUPPLEMENT APPROVAL

Protein Sciences Corporation
Attention: Michael F. Stirr
Sanofi Pasteur Inc.
Discovery Drive
Swiftwater, PA 18370-0187

July 1, 2022

Dear Mr. Stirr:

We have approved your request received March 18, 2022, to supplement your Biol License Application (BLA) submitted under section 351(a) of the Public Health Ser Act for Influenza Vaccine (Flublok), for Flublok Quadrivalent manufactured at your Meriden, CT and (b) (4) facilities and at (b) (4) to include the 2022-2023 United States formulation and associated labelin revisions.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture the measles and rubella drug substances for Measles, Mumps and Rubella Vaccine, Live at GlaxoSmithKline Biologicals (b) (4) and the mumps drug substance at (b) (4) The final drug product (Lyophilized Antigen Component, Live) will be manufactured, filled, lyophilized, labeled and packaged at (b) (4) GlaxoSmithKline Vaccines, (b) (4) The diluent (Sterile Water Diluent Component) will be manufactured and filled at (b) (4) and labeled and packaged with the lyophilized antigen component at (b) (4) GlaxoSmithKline Vaccines, (b) (4) .

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
www.fda.gov

Note: FDA Approval Letters for Flublok Quadrivalent (left) and Priorix (right).

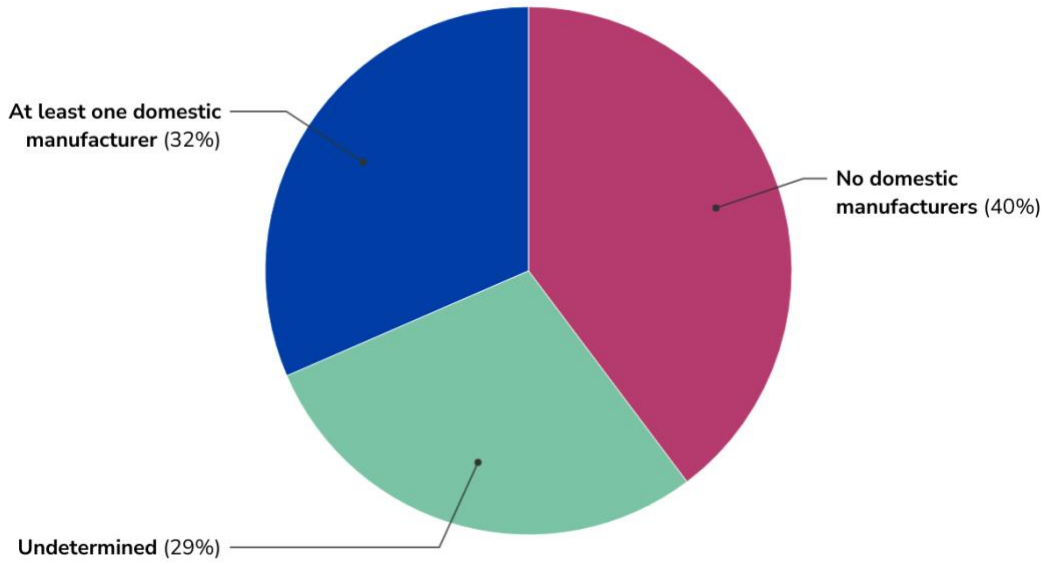
Source: FDA.

* For example, the most recent package insert on the FDA website is from 2013 and contradicts a more recent package insert on the vaccine's website from 2020.

Reliance on Foreign Vaccine Manufacturers

The majority of the vaccines with available manufacturing information are not manufactured in the United States (Figure 3). Fewer than one third (32 percent) of the vaccines in this analysis have at least one domestic manufacturer, while 40 percent are manufactured solely abroad. We could not verify whether 21 of the vaccines in this analysis were manufactured domestically (29 percent). Nineteen of the vaccines with no domestic manufacturers are included in the FDA's Essential Medicines list of the most critical medicines to have available in an emergency (Appendix Table A1).[11]

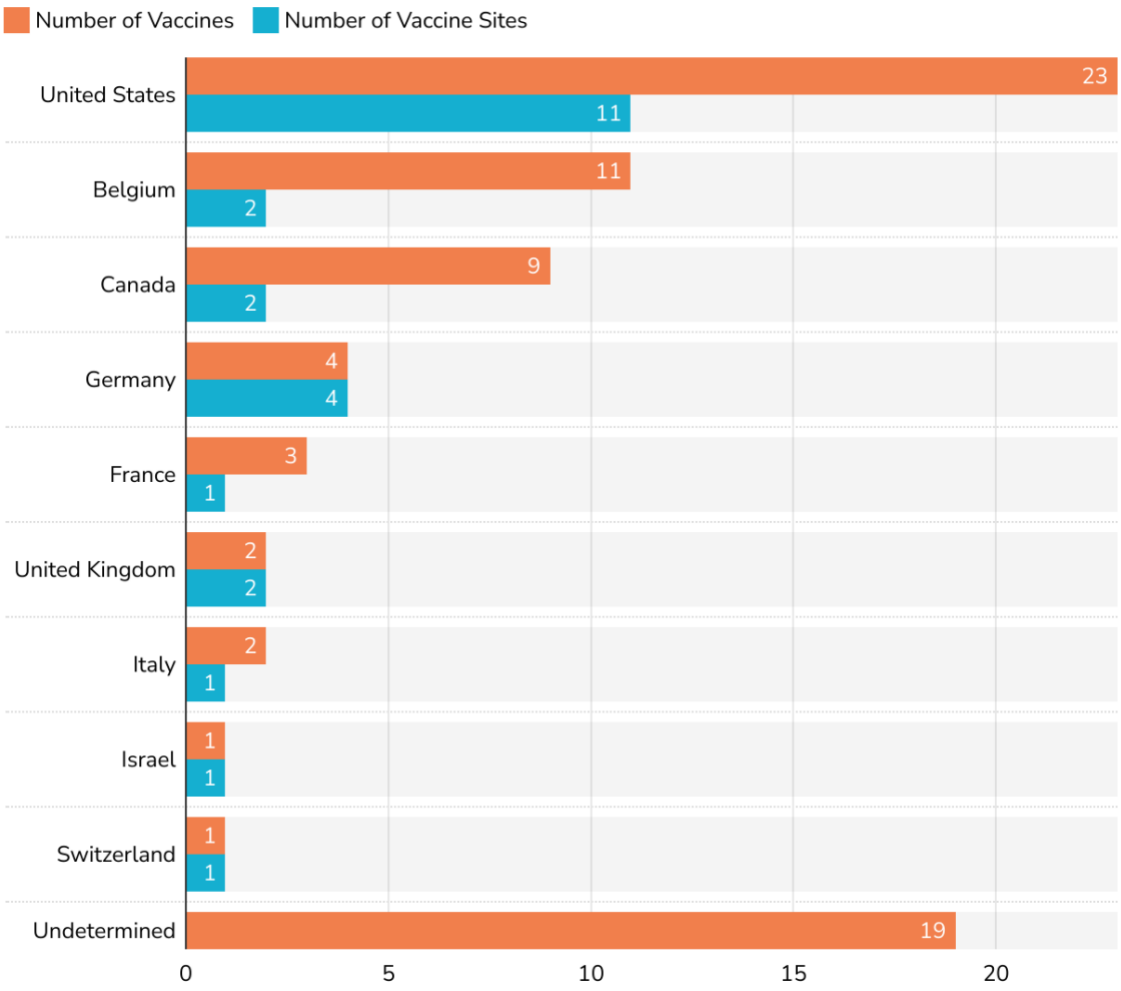
Figure 3. Proportion of Vaccines with at Least One Domestic Manufacturer



Source: CSET analysis of FDA documentation.

Fewer than half (11 out of 25) of the manufacturing sites that we identified are located in the United States (Figure 4). The remaining sites are located in Canada, Israel, and across Europe.

Figure 4. Geographic Distribution of Vaccine Supply



Source: CSET analysis of FDA documentation.

Although no other country has more than four manufacturing sites, some of these countries are still major suppliers because these sites produce more than one vaccine. For example, both Belgium and Canada contain two identified manufacturing sites but produce 11 and nine different vaccines, respectively (Figure 4).

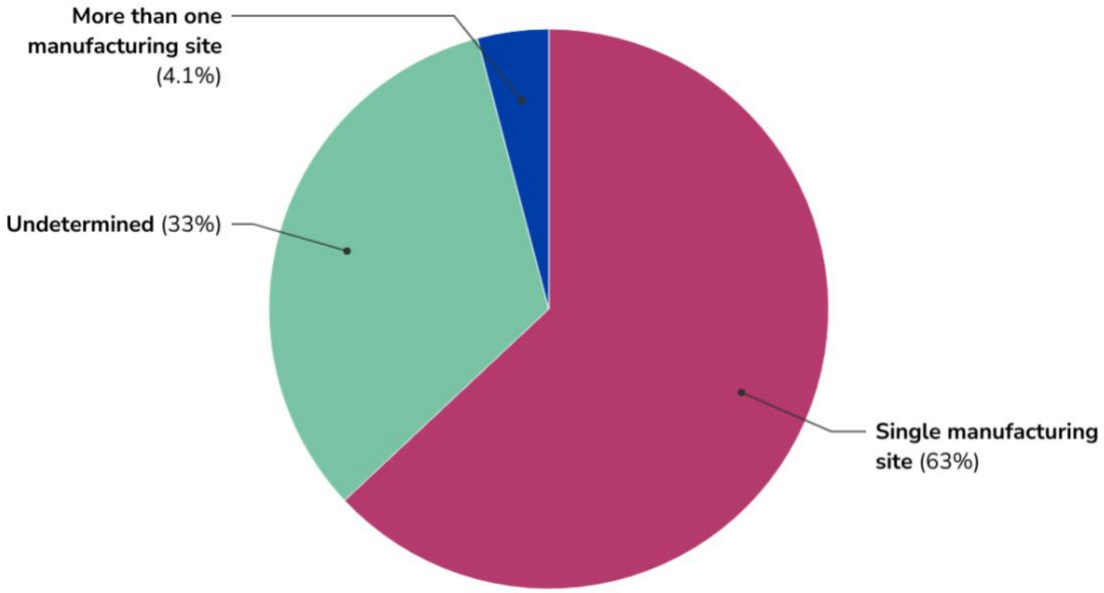
Nineteen vaccines did not contain adequate information to determine a manufacturing location (Figure 4). We do not know how many additional sites these vaccines correspond to because they may be manufactured at the same sites as other vaccines. We would need standardized manufacturing information for each vaccine to fully assess vaccine manufacturing resilience.

Insufficient Manufacturing Facility Redundancy

Domestic manufacturing capacity is not the only factor that contributes to a secure vaccine supply; having multiple manufacturing sites for each vaccine product is also critical. Redundancy in the manufacturing process allows vaccines to continue to be manufactured even if one facility is shut down following a cyberattack, natural disaster, contamination issue, or another circumstance.

The majority (63 percent) of the vaccines available for use in the United States are only licensed to be manufactured at a single facility (Figure 5) and therefore do not have redundant manufacturing capability. Only three of the vaccines in our analysis specifically state that the vaccine product is authorized to be manufactured at more than one site. Of the 46 vaccines without redundant manufacturing, 22 are on the FDA's list of Essential Medicines (Appendix Table A1).[12]

Figure 5. Proportion of Vaccines with More than One Manufacturing Site



Source: CSET analysis of FDA documentation.

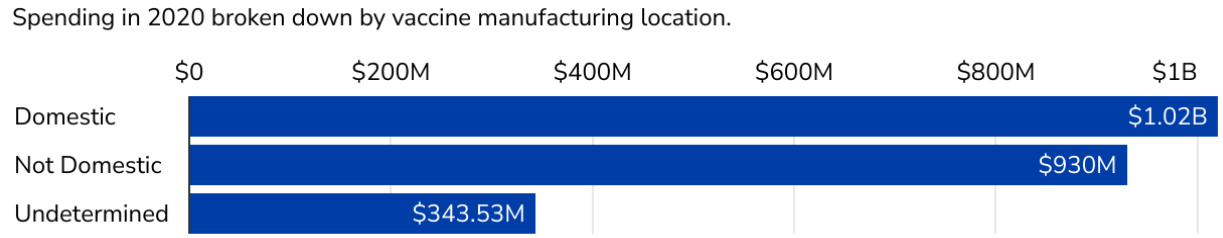
Our analysis reveals that 29 vaccine products are manufactured in one of just four facilities. Failure at any one of these four sites would have a disproportionate impact on the United States' access to critical vaccines.

Impact: Government Healthcare Spending

U.S. tax dollars are used to purchase foreign-made vaccines for government healthcare programs if no domestic versions are available. Onshoring vaccine manufacturing would allow these funds to support American manufacturing jobs at U.S. companies.

In 2020, the U.S. government purchased $930 million of foreign-made vaccines and $1 billion of vaccines made domestically for Medicare and Medicaid programs (Figure 6).* Vaccines for which we could not confidently determine a manufacturing location accounted for another $344 million.

Figure 6. Medicare and Medicaid Spending by Vaccine Manufacturing Location, 2020[13]



Source: CSET analysis of Centers for Medicare and Medicaid Services (CMS) dashboards Medicaid Spending by Drug, Medicare Part B Spending by Drug, and Medicare Part D Spending by Drug.

* 43 vaccines had associated spending data on the CMS spending dashboards, the remaining 30 vaccines were not included in this analysis.

Conclusions

A Vulnerable Vaccine Supply Chain

Two key vulnerabilities threaten the United States' access to already approved, critical public health vaccines: a lack of manufacturing redundancy and limited domestic manufacturing. The combination of these two factors will also limit the country's ability to increase manufacturing capacity in response to emerging health threats and could mean long supply chains that limit timely distribution during a public health emergency.

These vulnerabilities are not future concerns; the lack of redundancy in particular is already impacting the American public's access to vaccines. Of the seven vaccines that are or have been in shortage since 2016, three are manufactured at a single, nonredundant facility and four did not include enough information to determine manufacturing redundancy.[14] Shortages can occur for a variety of reasons, from product contamination and labor shortages to natural disasters or cyberattacks. In 2017 the pharmaceutical giant Merck had to borrow $240 million worth of its own Gardasil 9 vaccine from the national stockpile after being infected with NotPetya malware.[15] When manufacturers choose operational efficiency over emergency preparedness, the American public is left vulnerable to vaccine shortages.

While the vaccine manufacturing sites that we could identify are located in the United States or allied countries, this "friend-shoring" is still subject to long supply chains that limit timely distribution in a public health emergency. The COVID-19 pandemic highlighted how global emergencies can disrupt international shipping and distribution routes—the first half of 2020 was marked by shipping container shortages, cancelled shipping voyages, and decreased global air freight volume.[16] Domestic manufacturing would get U.S. vaccines to members of the public with less reliance on the complex global interdependencies of international shipping.

The friend-shored vaccine manufacturing landscape may also be threatened in the near future due to China's increasing focus on the biomanufacturing market. China's Fourteenth Five-Year Plan highlights biomanufacturing expansion plans, including the prioritization of biotech and bioengineering as an "industrial pillar" that will build the

size and strength of its bioeconomy.[17] While the United States is not currently reliant on China for its vaccines, this could become the case without timely action.*

The road to vulnerability . . . How did we get here?

The vaccine supply vulnerabilities outlined in this report highlight the divergence between market forces and national security goals. As participants in a market-based economy, biomanufacturers make decisions aimed at recouping large initial investments while maximizing return. The cost of vaccine development alone is estimated to be in the billions of dollars,[18] and building and maintaining manufacturing facilities can add hundreds of millions of dollars or more.

Faced with this high price tag, biomanufacturers reduce costs in ways that weaken supply chain security. For example, building a single facility to manufacture multiple vaccines or centralizing production in a single country decreases the expense of vaccine manufacturing at the cost of redundancy. If a supply chain disruption does occur, the industry cannot quickly compensate by adding new manufacturers because the timeline to design and construct a new facility, test and validate equipment, and recruit and train new workers can take anywhere from two to five years or more.[19] Taken together, these lengthy time considerations and high costs have driven biomanufacturers to design production lines that maximize efficiency and profit, but that are vulnerable to disruption.

Recommendations

The United States should take action to protect against vaccine supply chain failures, which have the potential to threaten U.S. public health, biosecurity, and economic stability. Long-term strategies will need to harmonize the private sector's economic interests with state and federal public health and biosecurity interests.

We have identified three stages of the vaccine supply chain in which focused policy efforts would have the most impact: protecting the existing vaccine supply, monitoring vaccine manufacturing vulnerabilities, and increasing vaccine manufacturing resiliency.

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* While none of the vaccine product manufacturers that we identified were located in China, manufacturers may rely on China for key inputs. These inputs—including raw starting materials, active and inactive ingredients, reagents, sterilization equipment and supplies, consumables, packaging materials, and personal protective equipment (PPE)—have opaque and unpredictable supply chains.

1. Protect the existing vaccine supply

Steps should be taken to protect the existing vaccine supply while long-term efforts to increase manufacturing resilience are underway. Even with government action and targeted investments, onshoring and diversifying vaccine manufacturing will take several years. In the meantime, the United States should enact policies that will minimize the risk of manufacturing disruptions and prevent vaccine shortages, including:

- **Designate vaccine manufacturing facilities as critical infrastructure**. Nonredundant vaccine manufacturing facilities should receive additional protection from the U.S. government because a cyberattack, natural disaster, or physical attack would lead to widespread vaccine shortages.

- **Include routine and seasonal vaccines in the Strategic National Stockpile with special focus on vaccines that are manufactured abroad or at a single site**. The FDA's Essential Medicines List is being used as a blueprint for SNS prioritization efforts, but it does not include routine or seasonal vaccines with substantial public health impacts like measles or seasonal influenza vaccines.[20] Rather, the list's selection criteria only focused on medicines that could be used in urgent, critical-care scenarios. We recommend that the SNS include a broader range of vaccines against the infectious diseases that could destabilize public health if vaccine access was disrupted.

- **Develop a quality management maturity (QMM) rating system for biologics to reward manufacturers who implement robust quality systems**. Manufacturers should be incentivized to continuously improve their quality management systems to prevent quality failures like contamination that can shut down an entire manufacturing line and cause a vaccine shortage. A QMM rating system would evaluate each facility's quality management systems and give higher ratings to those that go above and beyond FDA-mandated minimum requirements. Improved quality management systems would increase supply resilience while giving a competitive advantage to companies that invest in in robust quality management systems and receive high ratings. The voluntary QMM rating system that is being developed by the FDA's Center for Drug Evaluation and Research should be extended to the Center for Biologics Evaluation and Research in order to apply to vaccine manufacturers.

2. Identify and monitor vaccine manufacturing vulnerabilities

U.S. policymakers, regulators, and consumers need standardized information regarding the manufacturing locations of starting materials, intermediates, and finished vaccine products in order to identify risks and develop strategic policies that mitigate those risks.* We recognize that public disclosure of vaccine manufacturing locations may not be possible due to national security concerns or manufacturers' trade interests. In light of this constraint, we offer the two following policy options:

- **Option 1: Require manufacturers to disclose manufacturing location(s) on vaccine labels.** We agree with recommendations from both the White House and the National Academies to require drug labels to include the city and country of manufacture and FDA Firm Establishment Identifier for all drug product(s) and drug substance(s).[21] This would allow third parties, including supply chain experts and policy analysts, to conduct robust risk analyses and would give consumers insight into who is making their medications.

- **Option 2: Use FDA data to create a public-facing dashboard of vaccine manufacturing resiliency that does not share specific facility information.** If detailed labeling requirements are not feasible, the FDA should create a dashboard with aggregated information that shows manufacturing by country and manufacturing redundancy for vaccine drug products, intermediates, and critical inputs. This would highlight the most vulnerable areas of the supply chain without revealing specific facility information.

3. Increase vaccine manufacturing resiliency

If the United States wants to build a more resilient vaccine manufacturing ecosystem, it will need to adjust market incentives to stimulate both domestic and redundant manufacturing. Without government investment, targeted incentives for industry, and strategic planning, biomanufacturers will continue to maximize efficiency and profits by

* The FDA requires submissions to include the manufacturing locations of drug substances, intermediates, and drug products and the supplier information for raw materials and packaging systems. However, a recent Majority Report by the United States Committee on Homeland Security and Governmental Affairs found that the FDA cannot use this information to conduct supply chain mapping or predictive modeling because it is not compiled in a usable database. See: United States Committee on Homeland Security and Governmental Affairs. "Short Supply: The Health and National Security Risks of Drug Shortages." HSGAC Majority Staff Report, March 2023. (https://www.hsgac.senate.gov/wp-content/uploads/Drug-Shortages-HSGAC-Majority-Staff-Report-2023-03-22.pdf).

operating as few manufacturing facilities as possible, at the expense of national security. The path to vaccine resilience will be challenging, and will require federal commitment and significant investments over many years. Yet, maintaining the status quo leaves the United States vulnerable to vaccine shortages and unable to respond to public health emergencies.

The United States has used the following strategies in the past, and should consider these options in future plans to create a resilient vaccine supply:[22]

- **Expand the biomanufacturing workforce through talent development programs**. Human capital needs to be a priority, as new vaccine manufacturing facilities will not succeed without a technically proficient workforce to power them. The U.S. government should create, standardize, and subsidize training programs as well as develop outreach strategies to access new candidate pools.

- **Use public procurement dollars to encourage new manufacturers to enter the market.** Small and mid-sized manufacturers will be an invaluable asset for vaccine resilience, and federal procurement dollars can help them to overcome the significant initial startup costs.

- **Use export financing to secure a market for American-made vaccines**. Building additional facilities to achieve redundancy will decrease manufacturers' profits if they are left with unused product, and will be especially damaging to small or mid-sized manufacturers. The United States can help to guarantee a market for this additional capacity by providing strategic financial support to foreign firms to purchase American-made vaccines.

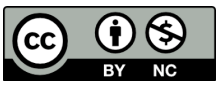
- **Increase federal research and development (R&D) spending on biomanufacturing innovation to decrease vaccine production costs**. Next-generation technologies—including process control, process optimization, platform technologies, and advanced manufacturing—can offset the cost of building and maintaining redundant facilities by making biomanufacturing cheaper and more efficient.[23] The United States can promote innovations in biomanufacturing processes by investing in early-stage R&D and pre-competitive technologies.

Authors

Steph Batalis is a biotechnology research fellow at CSET, where Anna Puglisi is a senior fellow and leads CSET's biotechnology programs.

Acknowledgments

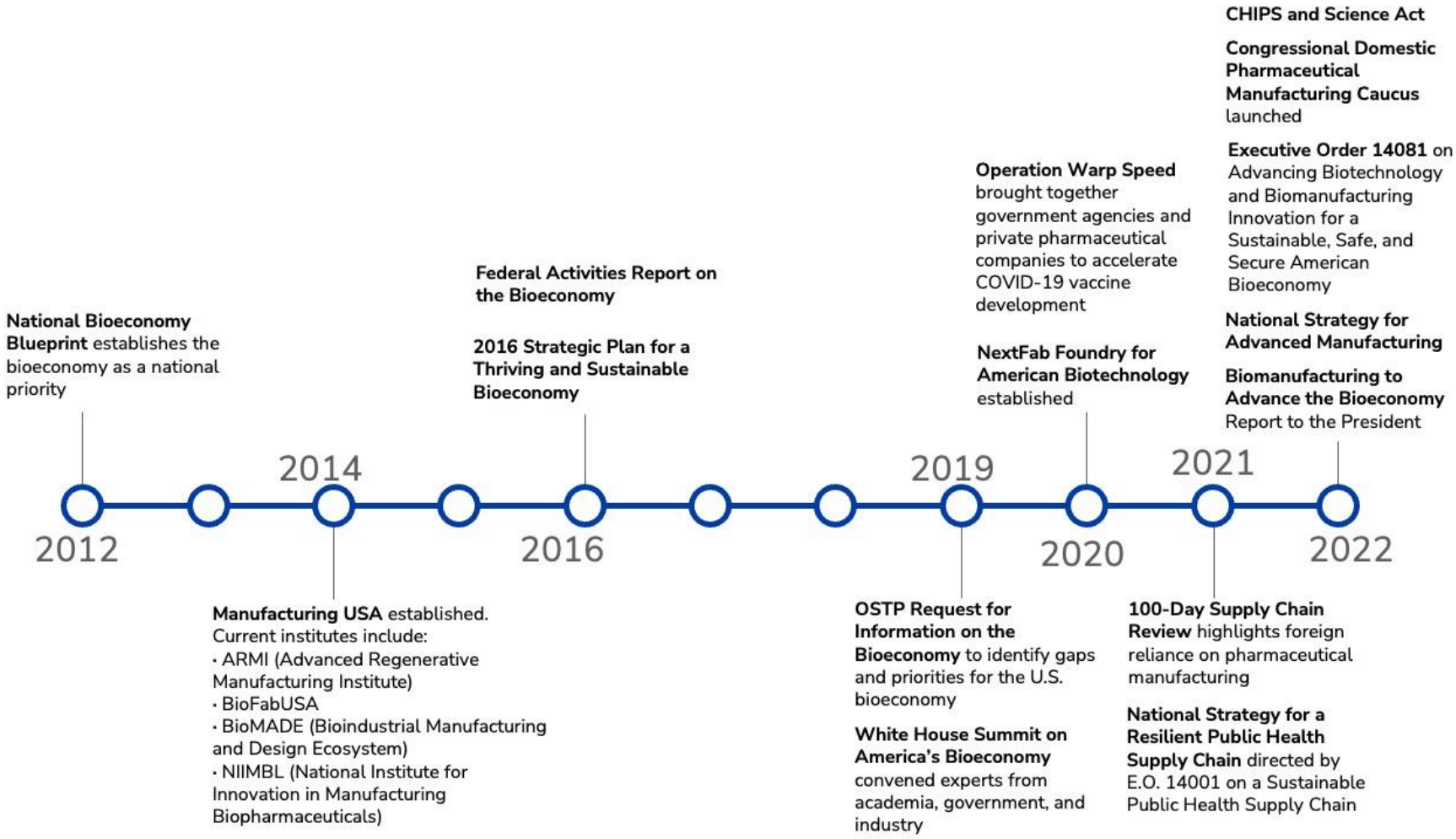
For feedback and assistance, the authors would like to thank Caroline Schuerger, Vikram Venkatram, Catherine Aiken, James Dunham, and Katherine Quinn. The authors are especially grateful to Gerald W. Parker and Ryan Morhard for their comprehensive reviews. Finally, we thank Matt Mahoney for his fact-checking and Lynne Weil and Shelton Fitch for their editorial support.



Document Identifier: doi: 10.51593/20230001

Appendix

Figure A1. A Decade of Advancing the Bioeconomy as a National Strategic Priority



Source: CSET

Table A1. Vaccines Included in Analysis

Vaccine	Indication
ACAM2000**	Smallpox (Vaccinia) Vaccine, Live
ActHIB**	Haemophilus b Conjugate Vaccine (Tetanus Toxoid Conjugate)
Adacel**	Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine, adsorbed
Afluria Quadrivalent	Influenza Vaccine
AUDENZ**	Influenza A (H5N1) Monovalent Vaccine, Adjuvanted
BCG Vaccine	BCG Live
BEXSERO	Meningococcal Group B Vaccine
Biothrax**	Anthrax Vaccine Adsorbed
Boostrix**	Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine, adsorbed
Cervarix*	Human Papillomavirus Bivalent (Types 16, 18) Vaccine, Recombinant
Comirnaty	COVID-19 Vaccine, mRNA
DAPTACEL**	Diphtheria & Tetanus Toxoids & Acellular Pertussis Vaccine Adsorbed
DENGVAXIA**	Dengue Tetravalent Vaccine, Live
Engerix-B	Hepatitis B Vaccine (Recombinant)
ERVEBO**	Ebola Zaire Vaccine, Live
Fluad Quadrivalent	Influenza Vaccine, Adjuvanted
Fluarix Quadrivalent	Influenza Virus Vaccine (Quadrivalent, Types A and Types B)
Flublok Quadrivalent	Influenza Vaccine (Quadrivalent)
Flucelvax Quadrivalent	Influenza Vaccine
Flulaval Quadrivalent	Influenza Vaccine
FluMist Quadrivalent	Influenza Vaccine, Live, Intranasal (Quadrivalent, Types A and Types B)
Fluzone High-Dose Quadrivalent	Influenza Virus Vaccine (Trivalent, Types A and B)

Fluzone Quadrivalent	Influenza Virus Vaccine (Quadrivalent, Types A and Types B)
Gardasil*	Human Papillomavirus Quadrivalent (Types 6, 11, 16, 18) Vaccine, Recombinant
Gardasil 9	Human Papillomavirus 9-valent Vaccine, Recombinant
Havrix	Hepatitis A Vaccine, Inactivated
HEPLISAV-B	Hepatitis B Vaccine (Recombinant), Adjuvanted
Hiberix**	Haemophilus b Conjugate Vaccine (Tetanus Toxoid Conjugate)
Imovax**	Rabies Vaccine
Infanrix**	Diphtheria & Tetanus Toxoids & Acellular Pertussis Vaccine Adsorbed
IPOL	Poliovirus Vaccine Inactivated
Ixiaro**	Japanese Encephalitis Virus Vaccine, Inactivated, Adsorbed
JYNNEOS**	Smallpox and Monkeypox Vaccine, Live, Non-Replicating
Kinrix**	Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed and Inactivated Poliovirus Vaccine
Menactra	Meningococcal (Groups A, C, Y, and W-135) Polysaccharide Diphtheria CRM197 Conjugate Vaccine
Menomune-A/C/Y/W-135*	Meningococcal Polysaccharide Vaccine, Groups A, C, Y and W-135 Combined
MenQuadfi	Meningococcal (Groups A, C, Y, W) Conjugate Vaccine
Menveo	Meningococcal (Groups A, C, Y, and W-135) Oligosaccharide Diphtheria CRM197 Conjugate Vaccine
MMR II	Measles, Mumps, and Rubella Virus Vaccine, Live
No Trade Name**	Adenovirus Type 4 And Type 7 Vaccine, Live
No Trade Name**	Diphtheria & Tetanus Toxoids Adsorbed
No Trade Name**	Influenza A (H5N1) Virus Monovalent Vaccine, Adjuvanted
No Trade Name**	Influenza Virus Vaccine H5N1 for National Stockpile
No Trade Name**	Plague Vaccine
No Trade Name**	Rabies Vaccine Adsorbed

No Trade Name**	Tetanus Toxoid Adsorbed
Pediarix**	Diphtheria & Tetanus Toxoids & Acellular Pertussis Vaccine Adsorbed, Hepatitis B (recombinant) and Inactivated Poliovirus Vaccine Combined
PedvaxHIB	Haemophilus b Conjugate Vaccine (Meningococcal Protein Conjugate)
Pentacel**	Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed, Inactivated Poliovirus and Haemophilus b Conjugate (Tetanus Toxoid Conjugate) Vaccine
Pneumovax 23	Pneumococcal Vaccine, Polyvalent
Poliovax*	Poliovirus Vaccine Inactivated (Human Diploid Cell)
PREHEVBRIO	Hepatitis B Vaccine (Recombinant)
Prevnar 13	Pneumococcal 13-Valent Conjugate Vaccine
Prevnar 20	Pneumococcal 20-Valent Conjugate Vaccine
Priorix	Measles, Mumps and Rubella Vaccine, Live
ProQuad	Measles, Mumps, Rubella and Varicella Virus Vaccine, Live
Quadracel**	Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed and Inactivated Poliovirus Vaccine
RabAvert**	Rabies Vaccine
Recombivax HB	Hepatitis B Vaccine (Recombinant)
ROTARIX	Rotavirus Vaccine, Live, Oral
RotaTeq	Rotavirus Vaccine, Live, Oral, Pentavalent
SHINGRIX	Zoster Vaccine Recombinant, Adjuvanted
Spikevax	COVID-19 Vaccine, mRNA
TDVAX**	Tetanus & Diphtheria Toxoids, ADsorbed
TENIVAC**	Tetanus & Diphtheria Toxoids, ADsorbed for Adult Use
TICE BCG	BCG Live
TICOVAC	Tick-Borne Encephalitis Vaccine
TRUMENBA	Meningococcal Group B Vaccine
Twinrix	Hepatitis A Inactivated & Hepatitis B (Recombinant) Vaccine

TYPHIM Vi**	Typhoid Vi Polysaccharide Vaccine
Vaqta	Hepatitis A Vaccine, Inactivated
Varivax	Varicella Virus Vaccine, Live
Vaxchora**	Cholera Vaccine Live Oral
Vaxelis**	Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed, Inactivated Poliovirus, Haemophilus b Conjugate and Hepatitis B Vaccine
VAXNEUVANCE	Pneumococcal 15-Valent Conjugate Vaccine
Vivotif**	Typhoid Vaccine Live Oral Ty21a
YF-Vax**	Yellow Fever Vaccine
Zostavax*	Zoster Vaccine, Live, (Oka/Merck)

** Excluded from analysis.*

*** Included in the FDA's List of Essential Medicines, Medical Countermeasures, and Critical Inputs.*[24]

Source: FDA[25]

Endnotes

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