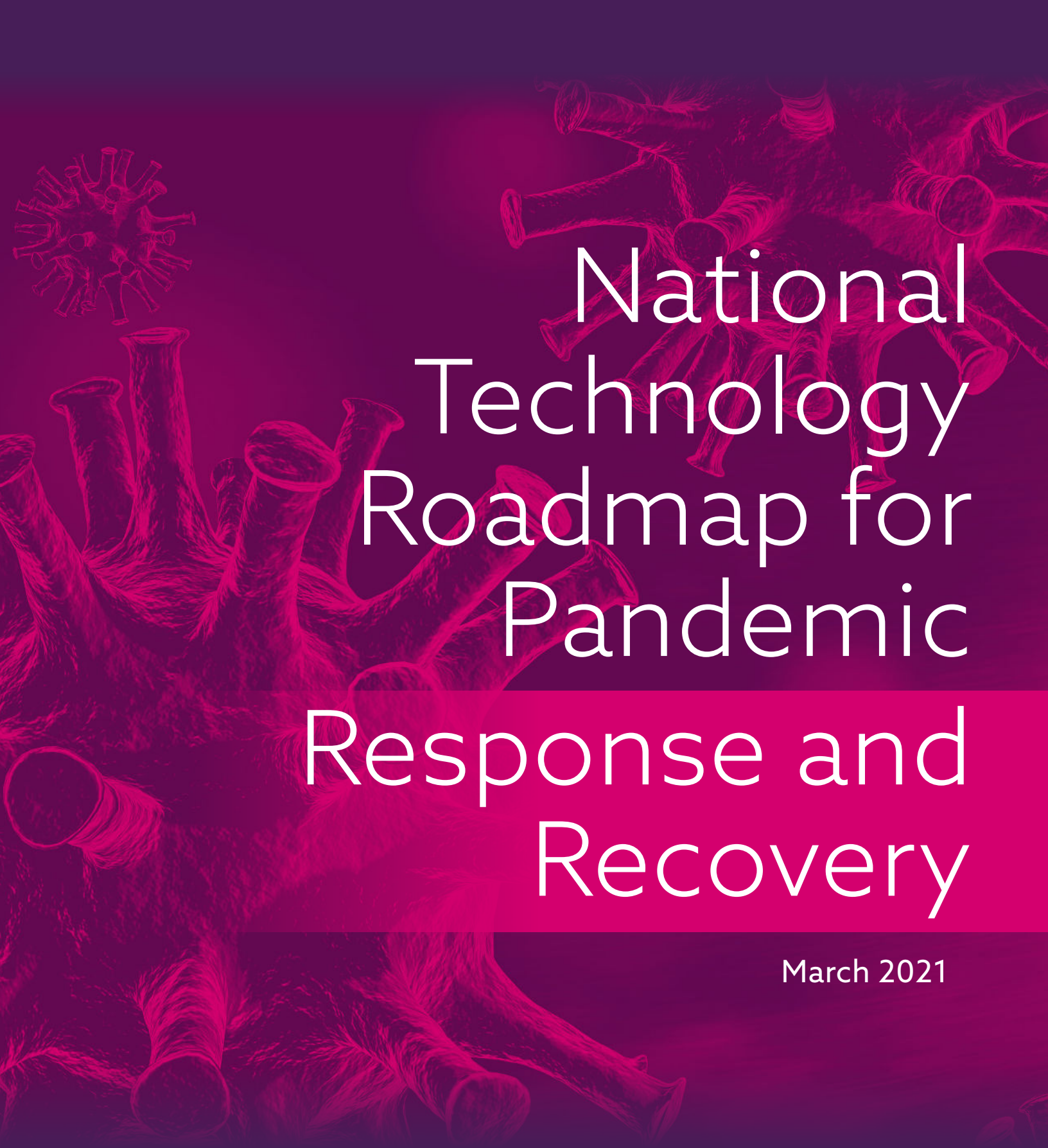

National Technology Roadmap for Pandemic Response and Recovery

March 2021

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NEXIGHT GROUP

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About this Roadmap

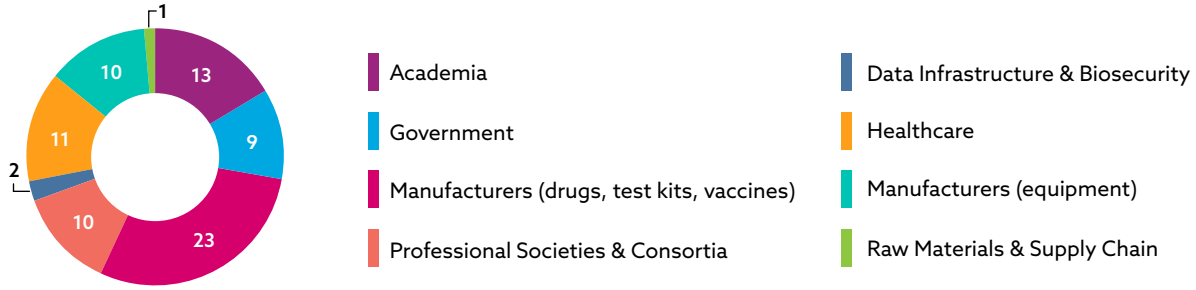
Roadmap Vision

Establish a national initiative that identifies priorities and outlines pathways that can drive the transformative change needed to **significantly accelerate the timeline for U.S. pandemic response and recovery**.

The devastating effects of the COVID-19 pandemic have demonstrated that United States currently lacks the necessary, sustained preparedness to respond to wide-reaching public health crises such as pandemics.

Recognizing the need for a coordinated national strategy to address the COVID-19 pandemic and future pandemics, the Advanced Regenerative Manufacturing Institute (ARMI) sought funding from the National Institute of Standards and Technology (NIST) to develop this *National Technology Roadmap for Pandemic Response and Recovery*. ARMI is a nonprofit, Manufacturing USA Institute focused on the scale-up of advanced therapy manufacturing. ARMI and its members sit at the nexus of sectors—including healthcare, manufacturing, biosecurity, and government—involved in COVID-19 response and recovery. The roadmap draws on **input from ARMI's multidisciplinary community of experts and other invited stakeholders with critical subject matter expertise; more than 75 experts and senior leaders from the frontlines of pandemic response contributed to the roadmap** (see Appendix A: Roadmap Contributors). ARMI partnered with Nexight Group, a consultancy that has completed more than 100 technology roadmaps, including many in the health and medicine space and several for other Manufacturing USA Institutes.

Contributors



Roadmap Scope

The roadmap will equip stakeholders with guidance on the technologies, platforms, and infrastructure needed to accelerate their response and recovery during this critical juncture in the COVID-19 pandemic, and just as critically drive response and recovery times down in future pandemics.

Because of this targeted technology focus, there are additional aspects of the current and future pandemics that this roadmap does not address. These include elements of the healthcare system, such as payment structures and governance, and broader economic and social issues sparked by the pandemic (e.g., economic closures, school re-openings).

Similarly, while the roadmap identifies a variety of types of challenges to responding to COVID-19 and future pandemics, not all are addressed by a directly corresponding activity, as the recommended research and development efforts are focused on technology-related solutions.

The priorities outlined in the roadmap, however, must be supported by a strong and organized national response framework. To that end, the roadmap presents a set of cross-cutting needs that, if addressed by national authorities, will provide the solid foundation needed to support the activities within each technology focus area.

Who Should Read this Roadmap

The roadmap intends to help not only organizations involved in pandemic response and recovery, so they may better coordinate their activities to accelerate progress, but also those in technology sectors that will play a role in building capacity and resiliency for future pandemics. These audiences include:

Healthcare providers

Medical researchers

Government

Academia

Manufacturers of personal protective equipment (PPE), vaccines, drugs, devices, and test equipment

Biosecurity experts

Raw materials suppliers

Automation and artificial intelligence experts

Public and private clinical laboratories

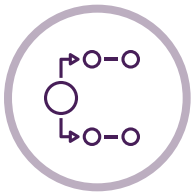
Executive Summary

The United States has struggled to successfully manage the COVID-19 pandemic. The unique characteristics of COVID-19—including high rates of contagion due to aerosolized transmission, asymptomatic infections, and variability in infection onset—have demanded coordination, on a massive and unprecedented scale, from stakeholders across nearly all sectors of the United States. This coordination was often inadequate, exposing gaps in the nation's capacity to respond with the speed and effectiveness that a disaster of this magnitude requires. As the COVID-19 crisis has demonstrated, there **is an ongoing need to move faster** as the United States scales up testing, allocates medical supplies and treatments to where they are needed most, and ramps up production and deployment of millions of vaccine doses. At the same time, it is also critical to learn from experiences with COVID-19 to **prepare for the next pandemic**.

Historically, sustained funding has not been dedicated to U.S. pandemic response. Rather than considering pandemic response a pillar of national defense, responses to previous pandemics have been episodic, largely focused on potential influenza-based outbreaks, and more regional than national, as was the case with the 2009 H1N1 influenza virus. Key barriers encountered during the H1N1 response—including a lack of investment in public health infrastructure, logistical and distribution challenges, and the importance of clear and timely messaging to the public—were not addressed in preparation for the next pandemic. While there is no way to be adequately prepared for all possible scenarios, the United States must **act more aggressively and pointedly to accelerate preparedness against a variety of important pandemic drivers**.

Benefits of More Rapid Pandemic Response and Recovery

The profound loss of life and steep social and economic costs of the COVID-19 pandemic have underscored the pressing need for increased preparedness and resiliency across all public and private sectors involved in pandemic response. A faster and more coordinated response in the early days of a pandemic could greatly reduce public health and economic impacts in five major ways:

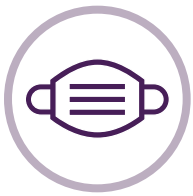


Addressing the initial spread of disease through faster ramp-up of testing, improved data infrastructure for contact tracing and trend analysis, and enhanced epidemiological prediction tools

Enabling rapid production and delivery of vaccines at scale by rethinking manufacturing and distribution strategies to meet urgent and widely distributed demand

Accelerating identification, testing, and regulatory review of potential treatments and vaccines through better tools for disease analysis and innovative clinical trial approaches and regulatory approval pathways

Supporting and augmenting the healthcare workforce by leveraging technology tools and strategies to reduce worker risk while developing supplemental community reserves and civil disaster response



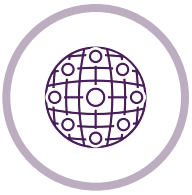
Equipping medical staff to safely and effectively treat patients through supply chain improvements and innovative manufacturing and deployment strategies for personal protective equipment (PPE), medical devices, therapeutics, vaccines, and other critical medical supplies

These goals can be achieved through **investment in technological and infrastructure improvements in six key technical focus areas**.

Subsequent roadmap sections for each of the above six technical focus areas:

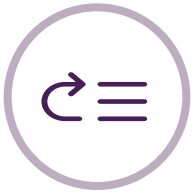
Characterize technology challenges to responding to the COVID-19 and future pandemics

Identify technologies, platforms, and infrastructure necessary to drive down response time



Recommend specific technology development and commercialization efforts that can be immediately implemented to respond to COVID-19

Define longer-term research and development priorities needed to improve readiness to respond to future pandemics



Cross-Cutting Foundational Requirements of a Strong Pandemic Response

While the innovations in technology and infrastructure outlined in this roadmap will be critical to accelerating pandemic response and recovery, they must be **supported by a strong and organized national response framework**. Drawing on the lessons learned from the COVID-19 pandemic, the following cross-cutting needs should also be addressed by national authorities.

National Leadership and Coordination

+ Develop a culture of readiness for public health crises, including clear plans for response activities, guided by state governments and the federal government working in concert

Clear Command and Control Structure Across All Stakeholders

+ Define a clear framework of roles and responsibilities and communications mechanisms to help more effectively leverage the myriad capabilities of federal agencies and departments, state/tribal/local/regional governments, the public health sector, clinical and research laboratories, and private industry throughout the United States

Sustained Funding for Pandemic Preparedness

+ Proactively recognize the threats that pandemics pose and invest in sustained rather than episodic preparedness and mitigation through continued funding, building on lessons learned from past pandemics/pathogens, providing leadership and financial support for solution development, and modernizing basic health infrastructure

Strong Public Education and Information Sharing

+ Provide communication during a pandemic that is consistent, transparent, accurate, and digestible; monitor and counter the spread of misinformation; communicate scientific methods to instill trust; and ensure industry has early access to trusted information

Harnessing the Power of Crowdsourcing and Collaboration

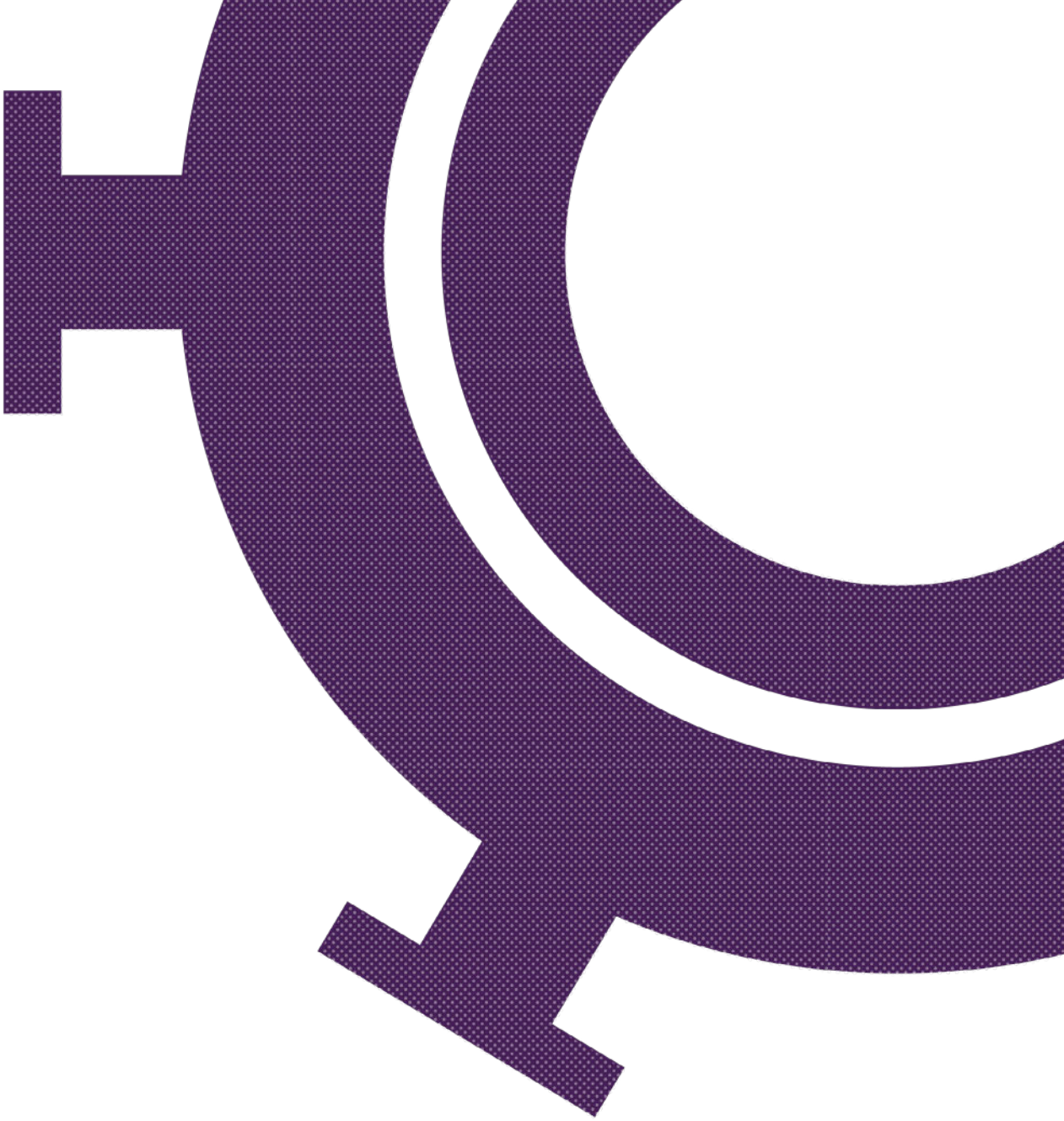
+ Better leverage good will and the desire to help during a crisis by clearly communicating needs to help focus on relevant solutions, mapping expertise across all stakeholders to reduce unnecessary competition, and encouraging collaboration across sectors and research areas

Developing Pathogen-Specific Countermeasure Toolkits

+ Develop a toolkit that includes public health measures for infection control (e.g., PPE, social distancing); biosurveillance (e.g., contact tracing); tests for diagnosis and surveillance that are accessible, affordable, effective, and able to deliver rapid results; therapeutics to treat resulting disease; and vaccines to build immunity

Planning for Long-Term Post-Pandemic Effects

+ Address specific mitigation measures required for long-term pandemic effects, including economic repercussions; long-term health impacts of those infected (e.g., long COVID); impacts on advancement of research, diagnosis, and treatments for other medical conditions; and delays of routine healthcare



Call to Action

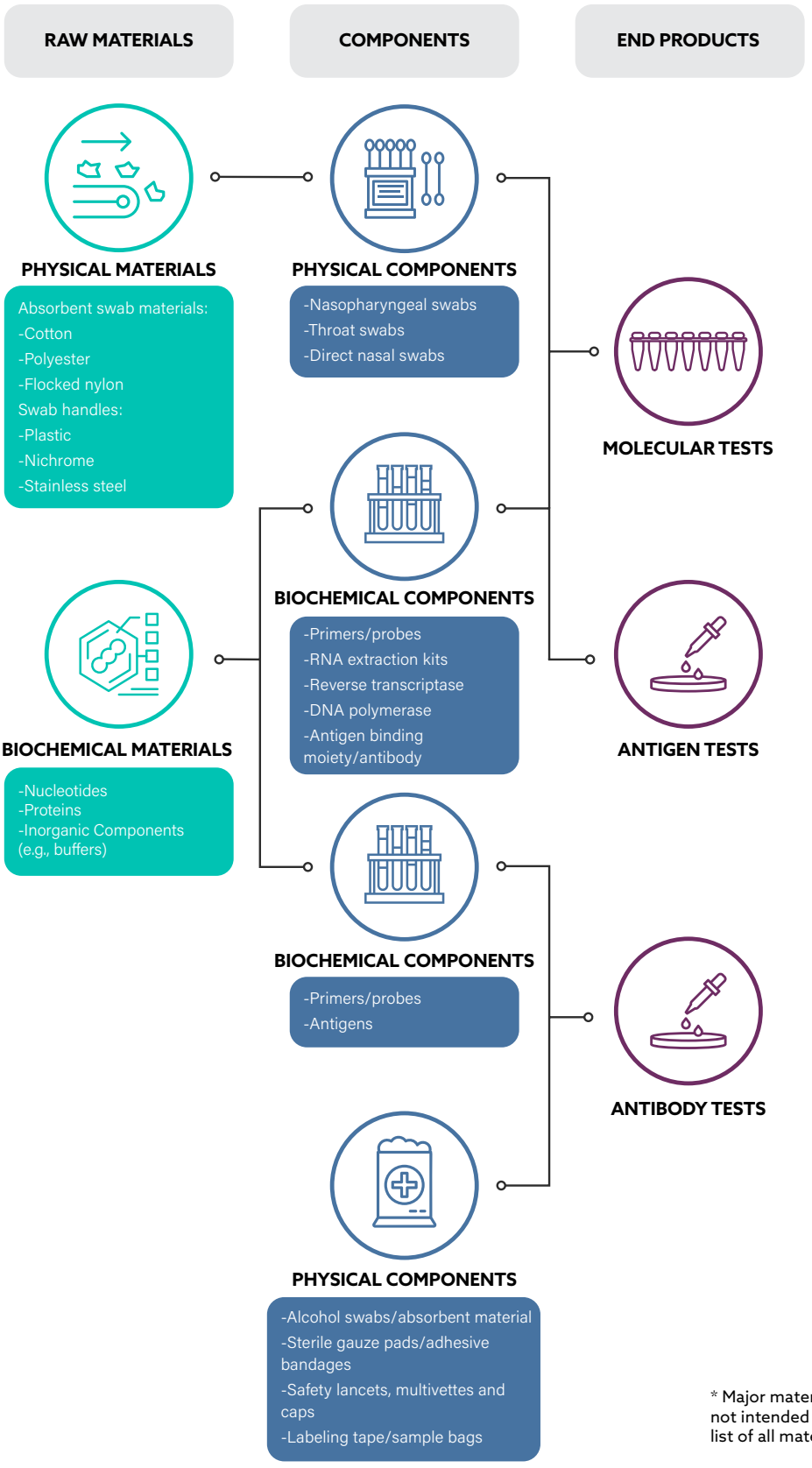
The COVID-19 pandemic has painfully demonstrated how critical sustained pandemic planning is—and how devastating its absence can be. **Industry and government must act on the lessons learned and the rapidly deployable action plans presented in this roadmap before the next pandemic occurs**.

This *National Technology Roadmap for Pandemic Response and Recovery* is the first pandemic roadmap driven by the manufacturing sector—a key perspective that must be at the core of a response and recovery strategy. And while the anticipated impacts of this roadmap are substantial and will have significant benefit to the private sector, the ultimate impact depends on federal funding. Private sector support cannot fully leverage the federal convening power which this effort requires to be successful. **Aligning public- and private-sector funding priorities and collaboration efforts toward the shared goal of sustained pandemic preparedness will have far greater impacts than either sector can achieve on its own.**

Supply Chains

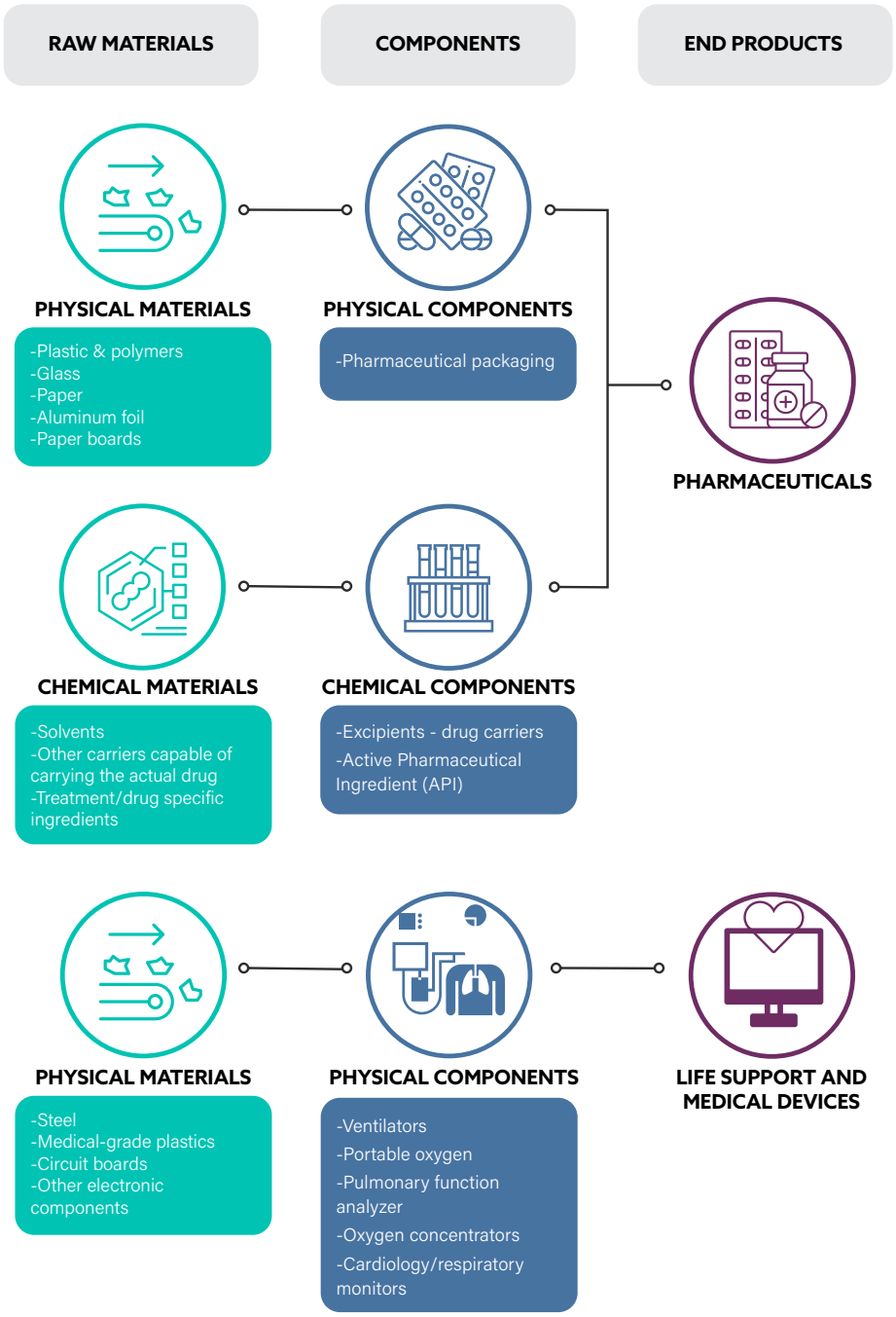
Medical supply chains are a cornerstone of effective pandemic response and recovery. The raw materials and components necessary for critical PPE, medical devices (e.g., diagnostics), vaccines, and therapeutics must be readily accessible during a pandemic to bolster a nation's response capabilities. Any disruption in the supply chain—including regional lockdowns, travel restrictions, labor shortages, or international trade restrictions—has the **potential to delay or entirely halt the accessibility of supplies and resulting end products.**

Current State Overview of Medical Supply Chains: **Diagnostics and Trials***



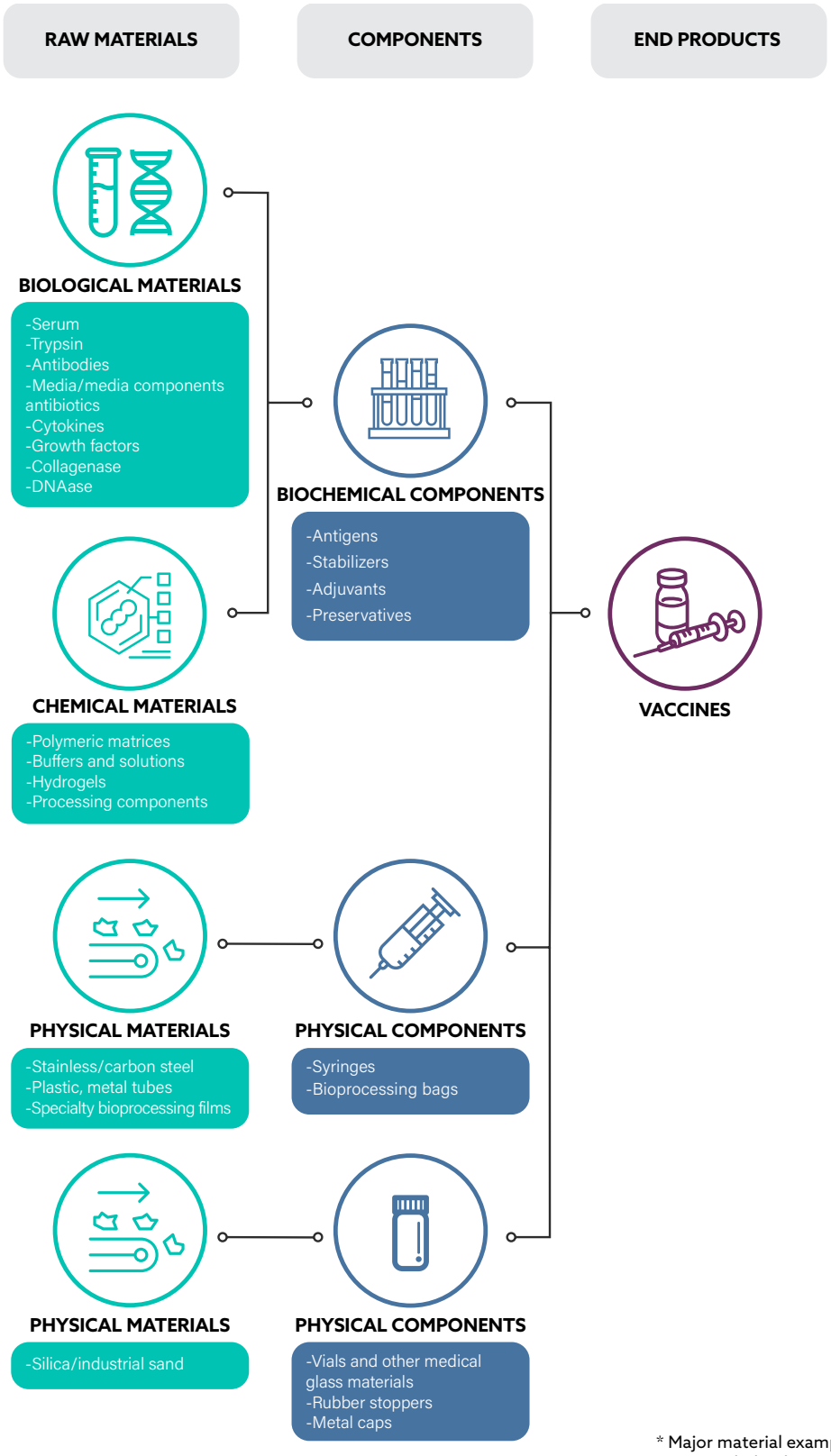
* Major material examples shown; not intended to be a comprehensive list of all materials required

Current State Overview of Medical Supply Chains: **Pharmaceuticals and Life Support and Medical Devices***



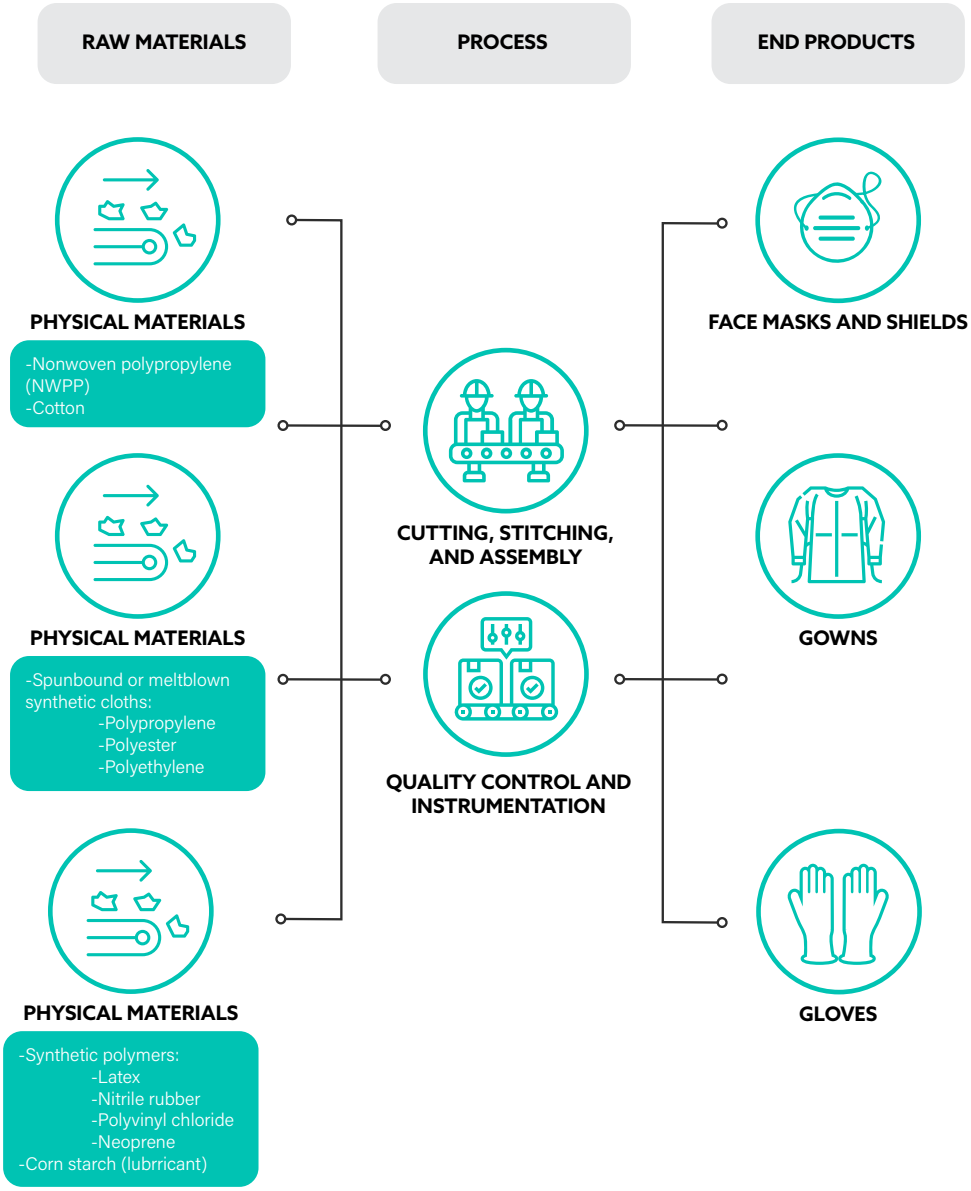
* Major material examples shown; not intended to be a comprehensive list of all materials required

Current State Overview of Medical Supply Chains: **Vaccines***



* Major material examples shown; not intended to be a comprehensive list of all materials required

Current State Overview of Medical Supply Chains: **PPE***



* Major material examples shown; not intended to be a comprehensive list of all materials required

Desired Future State Objectives

To improve the United States' ability to more rapidly and effectively respond to and recover from a pandemic, its medical supply chains must be robust, resilient, reliable, and characterized by:

Adaptability to ramp up and down production of critical raw materials and components in response to fluctuating and anticipated needs across the country

Availability of adequate stockpiles of necessary, non-expired medical supplies, including PPE, diagnostic tests, medical devices, vaccines, and therapeutics

Equitable access to medical supplies by facilities of all sizes, regardless of purchasing power (i.e., prevent price gouging or competition)

Thorough vetting procedures to prevent investment in fraudulent or ineffective supplies

An optimized supply chain will ensure that relevant stakeholders can access all necessary raw materials and components and that key components efficiently flow into the manufacturing process. **Key characteristics include:**

Resilient

Safeguards, redundancies, and contingencies mitigate supply chain vulnerability

Flexible

Resource production can ramp up or down as needed

Interconnected

All relevant stakeholder groups can maintain or modify operations based on real-time changes and updates regarding medical supply chain disruptions and improvements

Transparent

Reliable, real-time access to accurate and up-to-date information provides end-to-end transparency of available stockpiles and movement of resources

Standardized

Common manufacturing processes using industry standard raw materials and components are integrated into production wherever possible

Current Challenges

Current "just-in-time" supply chain model limits pandemic preparedness

The current U.S. medical supply chain operates on a just-in-time model versus a just-in-case model: raw material and product components are produced and/or procured as the need for these supplies arise. Though this practice reduces costs, it also means these leaner supply stockpiles can be easily strained or depleted during emergency situations.

Limited supply chain transparency can impact crisis decision making

Medical supply chain stakeholders often do not have a complete understanding of the sources of raw materials and/or components, leaving them unprepared to deal with supply chain disruptions.

+ Labs and medical facilities have low visibility into their sources for raw materials and components (e.g., cotton swabs for test kits). This low visibility **prevents U.S. stakeholders from being able to proactively and efficiently pivot to alternate sources** in the event of a shortage, supplier shutdown, or other urgent need.
+ At the outset of the COVID-19 pandemic, access to patient samples and other critical materials needed for clinical protocols was **impeded by a lack of sources of materials and, at times, a lack of established material transfer agreements (MTAs)**. MTAs are designed to facilitate the exchange of these items among academia, industry, and other research institutions; establishing new MTAs can take weeks, delaying critical vaccine or other countermeasure development.
+ COVID-19 supply chains require collaboration among stakeholders from different sectors that may use different terminology or potentially have varying definitions for the same term. Without a common ontology, **misunderstandings or miscommunication could occur and create disruptions for an entire region**.

Over-reliance on global sources of raw materials and components creates vulnerabilities

As U.S. medical supply chains are heavily dependent on raw materials and components from abroad, unexpected trade restrictions or localized shutdowns can have enormous consequences.

- Approximately 80% of active pharmaceutical ingredients (API) supplying the United States are sourced from abroad,[1] with **heavy reliance on China and India.**
- At least 80 countries—including China and India—**implemented lockdowns or export bans** during the COVID-19 pandemic, which interrupted the supply of raw materials and components needed to produce drugs, devices, and PPE as demand was rapidly rising.[2]
- At the time of the COVID-19 pandemic, about 65% of all single-use gloves were made in Malaysia with almost no U.S. cutting, stitching, or assembly capacity. COVID-related manufacturer shutdowns dramatically impacted glove availability.
- U.S. dependence on foreign suppliers can create situations in which foreign nations hold or withhold critical supplies as political leverage.

Complexity of components used in critical products can hinder scale-up

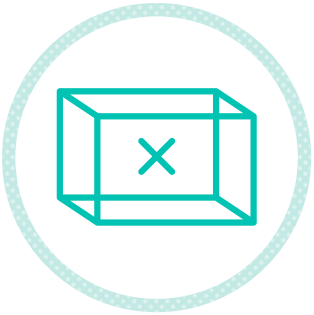
The complexity of proprietary, specialized parts (e.g., for ventilators) can inhibit the mass production and scale-up of crucial technologies and equipment.

- **Some ventilators use bespoke components** rather than interchangeable parts, making it difficult to scale capacity.
- Specialized, complex machinery used to produce raw materials and components for end products are often designed to run continuously; **pandemic-related stoppages have resulted in maintenance delays that can damage specialized production parts**, compounded by the lack of spare parts to repair such equipment.
- Complex custom materials for growth media and bioprocessing bags can also limit vaccine production.

Lean supply chains are vulnerable to disruption

To control costs, medical supply chains have become increasingly lean, with companies frequently sourcing critical raw materials for commodity goods from as few as one or two suppliers. This **limited diversity and redundancy** makes them highly vulnerable to disruption.

1. "Grassley Urges HHS, FDA to Implement Unannounced Inspections of Foreign Drug Manufacturing Facilities: The United States Senate Committee on Finance," United States Senate Committee On Finance, August 7, 2019, https://www.finance.senate.gov/chairmans-news/grassley-urges-hhs-fda-to-implement-unannounced-inspections-of-foreign-drug-manufacturing-facilities.
2. "WTO report finds growing number of export restrictions in response to COVID-19 crisis", World Trade Organization, April 23, 2020, https://www.wto.org/english/news_e/news20_e/rese_23apr20_e.htm.



Insufficient supplies of critical materials can significantly impede production efforts

Specific materials and supplies have the potential to become bottlenecks in U.S. attempts to ramp up testing kit and vaccine production. For example:

+ Supply chain disruptions and a lack of coordination between vaccine manufacturers and suppliers can result in **inefficient use of vaccine vials**. For example, vaccine doses could potentially be wasted if **healthcare providers and professionals do not have access to specialty syringes** (e.g., low-dead volume syringes) that extract the maximum number of available doses.[3]
+ **A shortage of critical reagents used in test analysis** can lead to recurring shortages of diagnostic kits and testing related supplies.
+ **Demand-based shortages of key laboratory supplies** (e.g., swabs, pipette tips) can slow vital testing kit processing, impacting the ability to slow the spread of infection.
+ Biopharma firms use **single-use technology such as bioreactor bags** to manufacture protein-based drugs (e.g., monoclonal antibodies used to treat COVID-19) because they help reduce risk of contamination and eliminate vat re-sterilization between drug batches.
  - But their popularity in growing fields such as gene therapy have already resulted in a supply shortage; **even pre-pandemic, there was a 4-month stock backorder**. Similarly, the **chromatography resins** used for the purification of monoclonal antibodies are also in short supply, due to pre-pandemic demand for their use in fields such as oncology and autoimmune diseases.
  - Because each vaccine and biotech manufacturer uses slightly different custom configurations of bioprocessing bags and resins, component suppliers must provide small orders to many customers, which prevents leveraging economies of scale or large-volume production.

Prohibitively expensive, difficult, and/or time-consuming for new suppliers to enter the market

U.S. medical supply chains lack diversity among suppliers—including small or non-traditional suppliers—that could offset the risk of relying on only a few sources for the majority of supplies.

+ **High levels of regulation** make it difficult for new suppliers to compete and innovate.
+ **Switching suppliers for pharmaceuticals and therapeutics can take up to a year** due to complex requirements involving process qualifications and regulatory approval.[4]

3. Sussannah Luthi and Rachel Roubein, "Hospitals say syringes supplied by feds waste vaccine doses," Politico, January 10, 2021, https://www.politico.com/news/2021/01/10/hospitals-syringes-vaccine-waste-doses-457017.
4. Emma Easthope, "What Impact Will Coronavirus Have on Pharma Supply Chains?," Global Pharma Insights, April 23, 2020, https://www.globalpharmainsights.com/analysis/what-impact-will-coronavirus-have-pharma-supply-chains.

Recommended Actions & Timelines to Achieve Future State Objectives

Bold indicates a high-priority activity

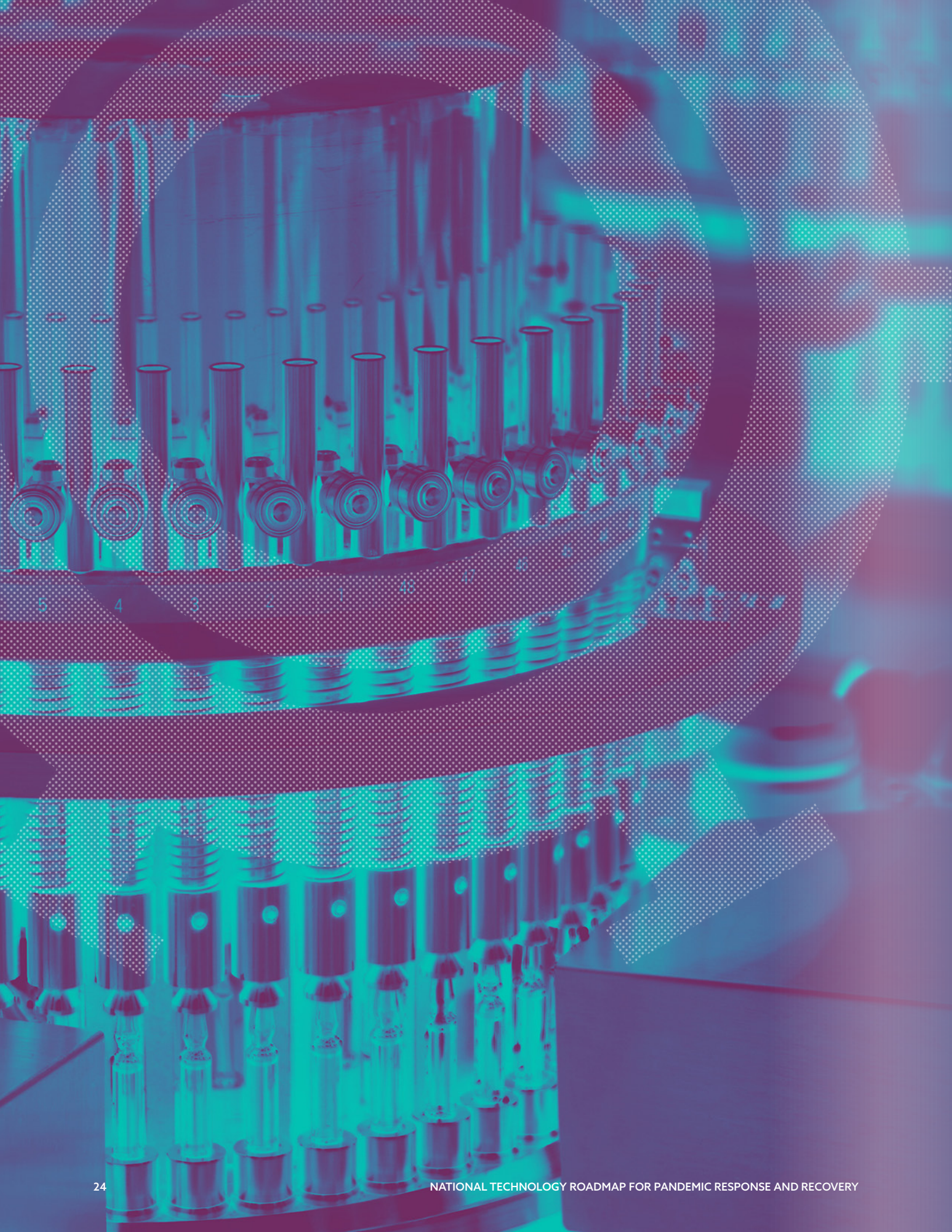
Establish Supply Chain Partnership Networks	2021-2023	2024-2026	2027-2030
Establish a robust public-private partnership to serve as a supply chain maintenance task force—composed of a multidisciplinary team of stakeholders focused on research and development, transportation, and logistics—that can help to guide and improve the stability of the national medical supply chain			
Improve capabilities to respond to supply chain shortages by leveraging emerging and novel production capabilities (e.g., additive manufacturing) that alleviate or eliminate bottlenecks			
Establish national supply chain data exchange network across business sectors that would allow for real-time information flow about product demand to allow for more targeted response to needs from suppliers			

Develop Supply Chain Standards and Best Practices	2021-2023	2024-2026	2027-2030
Develop pandemic/emergency material handling agreements to allow for more efficient transport of increased amounts of critical patient samples both internationally and across state lines			
Develop standards to ensure the consistent quality of raw materials and components across suppliers, enabling more reliable manufacturing across U.S. manufacturing sites			
Establish supply chain cybersecurity best practices—for mitigating threats from both external and internal malicious actors—to enhance supply chain security			
Establish a network to anticipate the need for and make patient samples readily available early in a pandemic, including ensuring the necessary material transfer agreements are in place between government, commercial entities, and academic institutions			
Create uniform/standardized components that can be used interchangeably in any type of relevant product			

Advance Supply Chain Management Systems	2021-2023	2024-2026	2027-2030
Revitalize domestic chemical sourcing to ensure more ready access to components needed to develop drugs critical to patient survival in intensive care and emergency response			
Create an accurate inventory of all types of raw material and component suppliers critical to pandemic response to better understand interdependencies and impacts on the production of various end products across sectors			

Bold indicates a high-priority activity

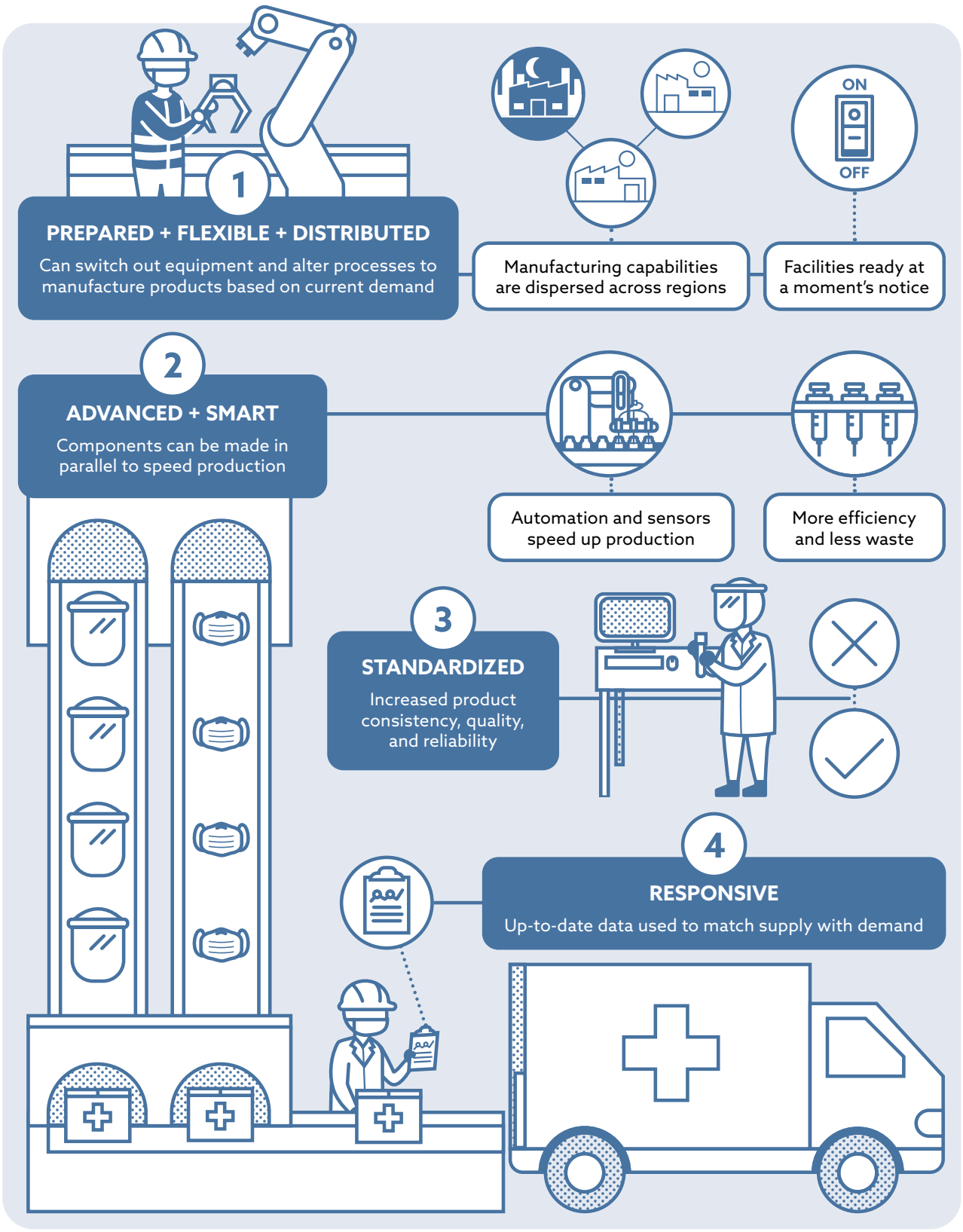
Advance Supply Chain Management Systems, continued	2021-2023	2024-2026	2027-2030
Create financial incentives to motivate private industry to invest in more accessible, robust, and innovative supply chain management systems and to collect and share supply chain data			
Increase domestic production of the raw materials used for PPE (e.g., nitrile butadiene rubber [NBR] for single-use gloves), as well as automation techniques to incorporate cutting, stitching, and assembly into domestic production lines			
Invest in one interconnected content management system (CMS) to digitally document supply chain management and maintain supply records of raw materials and components across healthcare facilities, government, private business, and universities to ensure national supply chain resiliency, nimbleness, and agility			



Manufacturing

The increased and urgent demand for vaccines, drugs, PPE, and medical devices during a pandemic **requires U.S. manufacturing to scale up well beyond ordinary capabilities and capacity**. Equipping manufacturers to carry out this ramp-up effectively will mean the difference between high-quality products reaching the people who need them or long delays and potential production of unsafe or faulty products.

Overview of an Optimized Manufacturing Ecosystem



Desired Future State Objectives

Improved infrastructure and supportive technologies—applying best practices and lessons learned from COVID-19 Operation Warp Speed—will enable manufacturers to rapidly scale operations to meet the enormous demand for medical supplies and countermeasures during a pandemic. This support will help manufacturers:

Establish effective production processes within accelerated timeframes

Rapidly scale up or down production as demand changes

Ensure product safety, quality, and reliability

Key characteristics of an optimized manufacturing ecosystem include:

Advanced

Manufacturers apply novel technologies and innovative, streamlined processes to speed production and availability of new treatments and countermeasures

Smart

Features like automation and digital in-line monitoring help detect and correct problems in real time, avoid waste, and improve efficiency

Flexible

Facilities can be repurposed quickly to produce other needed or new products

Responsive

Production is driven by data, more closely coupling supply and demand

Prepared

Resources such as an on-call crisis workforce of volunteers help manufacturers prepare for a sudden surge in demand

Standardized

Manufacturing automation platforms use standardized designs, control software, and processes to speed ramp-up and facilitate cross-facility collaboration

Distributed

Manufacturing facilities at different locations are ready to come online in response to regional needs

Current Challenges

Risk limits the potential extent of vaccine innovation

Uncertainty around developing and scaling up vaccine manufacturing capacities has prevented timely progress from being made by existing companies and discouraged new companies from entering the market.

+ **Vaccine manufacturing is often not profitable,** and it is challenging, if not impossible for pharmaceutical companies to assess the return on investment of developing a vaccine in response to a pandemic.[5]
+ **Only five companies** currently manufacture vaccines for the U.S. market, down from 20+ in the 1970s.[6]
+ To meet projected capacity needs, **manufacturers need to produce vaccines at risk** (i.e., before the candidate is shown to work via clinical trials). Vaccine candidates may fail, so manufacturers will be investing significant effort developing upfront capacity and product that may never be used.
+ Past epidemics (e.g., SARS, Zika) ended before vaccine development finished, **leaving manufacturers with not only direct financial losses but also opportunity costs** of taking resource offline to focus on potential pandemics. These decisions can cause setbacks to other vaccine development programs and have long-lasting implications on company pipelines and competitive positioning.
+ Investments in immunobiology and regenerative medicine predominantly target chronic disease. The extent to which these investments could be altered or leveraged to also target infectious disease is unclear.

Increased manufacturing flexibility and responsiveness may impact manufacturer profitability

The **costs associated with switching or scaling up** existing production lines to make products needed during a pandemic may not yield a return on investment, harming manufacturers' profits and discouraging them from joining efforts to address capacity challenges.

+ For example, retooling or building dedicated manufacturing capacity to make COVID-19 tests requires significant investment to **serve a market need that is likely to disappear when the pandemic ends**, likely before the investment can be recovered.
+ Manufacturers must adjust pre-pandemic vaccine development efforts to focus on COVID-19 vaccine development without **compromising production of other vital vaccines** (e.g., for measles).
+ Non-medical manufacturers shifting production lines to manufacture PPE interrupts their prior business plan.

5. Arlene Weintraub, "Bio: What's the ROI on a COVID-19 vaccine? We have no idea, says Pfizer", Fierce Pharma, June 11, 2020, https://www.fiercepharma.com/pharma/bio-what-s-roi-a-covid-19-vaccine-we-have-no-idea-says-pfizer.
6. Jay Hancock, "They Pledged to Donate Rights to Their COVID Vaccine, Then Sold Them to Pharma", Kaiser Health News, August 25, 2020, https://khn.org/news/rather-than-give-away-its-covid-vaccine-oxford-makes-a-deal-with-drugmaker/.

Scale-up capacity is constrained by current systems and processes

Limits within current manufacturing systems and processes can **delay scale up of crucial products**.

- Technology transfer (i.e., moving technology from development to production) for production scale-up typically takes anywhere from 18-30 months. Within the vaccine market, many small developers are unexperienced with technology transfer, which creates additional risk and could further lengthen this timeline.[7]
- Test kit manufacturers may not be able to scale up test kit readers or other necessary collateral equipment on the same scale as the test kits themselves.
- The final filling and finishing step of vaccine development is usually done by small, specialized companies, in small batches, for clinical trials. If a new vaccine progresses beyond trials, larger companies will need to take over to produce the volume of doses needed. Several of the candidate COVID-19 vaccines are based on novel vaccine platforms, which will require new processes for scale-up.

Limits in manufacturers' ability to scale up production impact the adoption of advanced manufacturing techniques and can adversely affect product quality

Manufacturers **may not be able to quickly scale up and incorporate advanced manufacturing techniques into existing processes** or may try to speed scale-up too quickly and for products that have limited usefulness.

- Non-medical manufacturers attempting to develop appropriate PPE may not have access to materials or processes that can enable proper sterilization for medical use; this **wastes effort on items that are of limited usefulness**.
- Current 3D printing centers (e.g., MIT) are designed more for **demonstrating proof-of-concept designs than manufacturing to scale**.
- Manufacturers are rushing to build capacity and may buy/build plants without adequate oversight to ensure everything is working properly and the plant can scale up to match needed capacity.

7. Cormac O'Sullivan, Paul Rutten, and Caspar Schatz, "Why Tech Transfer May Be Critical to Beating COVID-19", McKinsey & Co., July 23, 2020, https://www.mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/why-tech-transfer-may-be-critical-to-beating-covid-19.

Regulatory and reporting requirements for manufacturing are not widely understood

Many manufacturers, particularly those shifting to manufacturing of other products in response to need, may not be fully aware of or understand **relevant compliance requirements and regulations**.

+ Manufacturers' liability for the PPE they make under emergency use authorizations (EUAs) is unclear.
+ Laboratories connected to hospitals or research centers, which can manufacture their own test kits for private use, now **must receive an EUA from the FDA** before using them, which slows down their ability to make kits and test samples.
+ **Manufacturing may need to be moved to other facilities or sites** in response to delays with Good Manufacturing Practices (GMP) inspections or disruptions due to the pandemic (e.g., lockdowns); additional data will be required for product applications (e.g., biologics license application) due to these changes.

Recommended Actions & Timelines to Achieve Future State Objectives

Bold indicates a high-priority activity

Optimize Manufacturing Processes	2021-2023	2024-2026	2027-2030
Develop and encourage adoption of standards and measurement tools (e.g., assay development and interpretation, sterility approaches) that ensure product quality across manufacturing sites, including for diagnostics and vaccines			
Identify approaches for more continuous, in-line monitoring and quality testing (e.g., advanced sensors) to accelerate speed of production and identify quality issues early, reducing the potential for unusable products; ensure that instrumentation required for quality control and production remains up-to-date with current manufacturing approaches			
Assess existing and novel vaccine platforms to understand the potential for manufacturing scale-up and efficiency			
Continue government support for novel, emerging vaccine platforms (beyond current designs) through at least Phase 1 testing			
Invest in advanced manufacturing technologies that can facilitate scale-up of biologics manufacturing (e.g., new cell expansion approaches, more efficient cell separation technologies, synthetic biology to reduce dependence on natural raw materials)			
Leverage single-use technology platforms for biologics manufacturing (i.e., using large poly bags to culture cells) to eliminate or reduce cleaning and sterilization between batches and allow for increased batch specialization			
Apply digitization approaches to enable more product to be manufactured with a smaller footprint in existing facilities, rather than building new facilities to meet demand			
Advance continuous-flow chemical synthesis processes that leverage computational tools to accelerate manufacturing of therapeutics			
Research and develop new methods for large-scale sterile fill finish for vaccine production			
Advance real-time release assays to accelerate transfer from cell processing to final products			

Design More Resilient Manufacturing Networks	2021-2023	2024-2026	2027-2030
Form a Resilient Manufacturing Advisory Council to communicate industry-generated recommendations on improving current and future manufacturing processes to the U.S. government			

Bold indicates a high-priority activity

Design More Resilient Manufacturing Networks, continued	2021-2023	2024-2026	2027-2030
Connect with and/or survey small- and medium-sized manufacturers (both within and outside the medical field) to determine capacity or ability to pivot their manufacturing capabilities to support production of critical medical supplies (e.g., PPE)			
Maintain and clearly communicate liability protections for manufacturers shifting to produce medical supplies or other critical products needed for pandemic response to help mitigate risk averseness (e.g., establish limited liability that is proportional to the value of the product segment for "emergency products")			
Develop modular manufacturing systems that connect wirelessly, which allow for continuous, flexible manufacturing to meet fluctuating demand			
Design equipment that can be temporarily incorporated into existing manufacturing processes to allow for manufacturing of products in critical need			
Develop rapid market assessment tools to help both individual manufacturers and the manufacturing network better understand true demand amid a pandemic (e.g., avoid developing products with insufficient market penetration)			
Establish end-to-end manufacturing of critical products at multiple sites (both globally and in the United States) to combat impacts of local lockdowns and travel restrictions			
Form a National Manufacturing Guard – a network of volunteers who convene to share best practices and train to strengthen manufacturing and respond to local and national crises			
Leverage modeling and simulation to increase understanding of manufacturing processes that can be adapted for other uses			
Develop technology clusters/regional hubs that are primed for requisition or awarded contracts to manufacture designs and infrastructure where needed (i.e., could leverage Manufacturing USA network)			

Enhance Product Designs and Specifications	2021-2023	2024-2026	2027-2030
Develop more sustainable PPE that can be reprocessed, reused, or has replaceable components			
Create an oversight committee that would vet new specifications to guide national investment toward reliable, consistent designs			
Form a Technology Corps that builds on the strengths of Manufacturing USA Institutes to develop a diverse and networked national talent pool and introduce the next generation of the workforce to impactful manufacturing careers			

Bold indicates a high-priority activity.

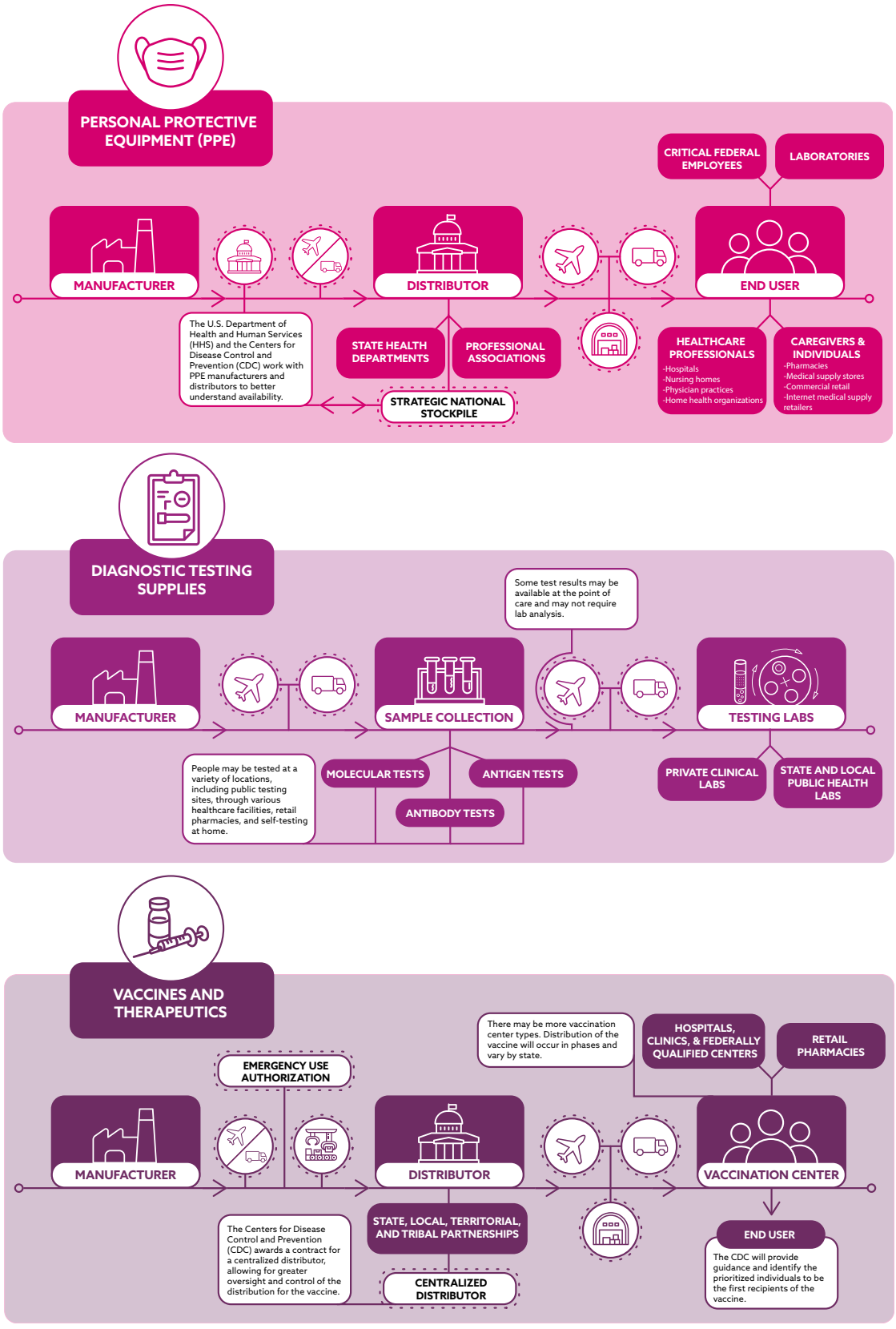
Enhance Product Designs and Specifications, continued	2021-2023	2024-2026	2027-2030
Establish digital stockpiles of product designs and accompanying instructions and quality control measures to facilitate proper use of designs for distributed manufacturing			
Invest in the science needed to develop "universal vaccines" or vaccines for classes of pathogens			
Develop broader, rapidly interoperable vaccine platforms that can leverage existing manufacturing processes and infrastructure to accelerate manufacturing scale-up and increase capacity			
Establish platforms for diagnostic testing (e.g., leveraging CRISPR) to enable rapid rollout of viable, low-cost diagnostics			

Build a Skilled Manufacturing Workforce	2021-2023	2024-2026	2027-2030
Develop validated sample banks to enable developers to test sensitivity and specificity of diagnostics			
Provide educational services about quality system regulation requirements and the regulatory pathway prior to and during the early stages of a pandemic			
Help manufacturers understand and mitigate cyber threats to facilitate secure exchange of data			

Deployment & Access

Pandemics require effective mobilization of medical supplies and countermeasures—including PPE, medical devices, drugs, and vaccines—to meet sudden and dramatic increases in demand. Optimized deployment involves the rapid and efficient distribution of these supplies from the manufacturing site to the end user. **To optimize deployment logistics, the United States must gain greater insight into resource availability, as well as when, where, and by which populations resources are most needed**.

High-Level Overview of Deployment of PPE, Diagnostic Testing Supplies, and Vaccines and Therapeutics



Desired Future State Objectives

To improve the United States' ability to respond to and recover from a pandemic, deployment of and access to needed supplies and products must be rapid, effective, efficient, and reliable. Achieving such a robust deployment methodology involves:

Developing a clear understanding of current supply inventory and manufacturing capacity across states and regions

Identifying populations with the greatest need for medical supplies and countermeasures both in advance and in near-real time to design and optimize transportation and distribution systems

Rapidly and efficiently distributing PPE, medical devices, drugs, and vaccines to healthcare facilities and patient populations where and when they are needed

Understanding the implications of cross-border delivery restrictions (both national and international) so they can quickly be addressed (e.g., via exemptions and fast-tracking), during pandemic scenarios

Key characteristics of optimized deployment and access include:

Coordinated

Activities of different companies fulfilling medical supply needs are centrally monitored and coordinated to ensure efficient and complete coverage

Flexible

Insights into shifts in demand inform allocations of medical supplies and countermeasures to ensure they are delivered where they are needed most

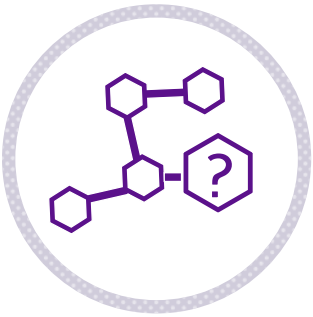
Equitable

Medical supplies and countermeasures can reach those who need them, regardless of individual or organizational buying power; distribution plans exist to account for remote or low-population-density areas or areas with at-risk populations

Transparent

Systems can track in detail inventory, locations, and availability of medical supplies and countermeasures, as well as where they have already been administered or distributed

Current Challenges



Limited or inaccurate diagnostic data for informing supply distribution

A **lack of adequate testing and/or inaccurate testing data** leads to difficulty in predicting demand for critical medical supplies, especially as virus hotspots rapidly shift. Without this data, it is difficult to accurately and efficiently distribute adequate supplies.

A decentralized coordination system and lack of visibility into supply inventory can impede deployment

The **U.S. deployment system has become increasingly decentralized** based on the vast geographical size of the United States, state control of supply stockpiles and distribution networks, and the complex scope of stakeholders (e.g., provider offices, hospitals, pharmacies, rural areas) that need the supplies and countermeasures. Without coordination between the state and federal governments, **supplies may be either over- or under-stocked**.

Competition for limited supplies can lead to significantly higher costs

With the federal government, states, and hospital systems all competing for the same limited resources, **the price of medical supplies may increase with demand**.

+ For example, a report by the Society for Healthcare Organization Procurement Professionals[8] found PPE costs increased dramatically at the beginning of the COVID-19 pandemic:
  - **N95 masks** rose from $0.38 to $5.75 **(1,413%)**
  - **Reusable face shields** rose from $0.50 to $4.50 **(800%)**
  - **Hand sanitizer** rose from $0.26 to $0.56 **(115%)**

8. Society for Healthcare Organization Procurement Professionals, April 7, 2020, http://cdn.cnn.com/cnn/2020/images/04/16/shopp.covid.ppd.costs.analysis_.pdf.

Overburdened frontline healthcare workers, as well as shortages of clinicians trained to operate medical devices or administer treatments, can impact patient care and recovery

+ During COVID-19, **extensive training for non-ICU clinicians was required for hospitals** to begin maintaining increased numbers of ventilators and caring for large numbers of critically ill ventilated patients.
+ Many smaller or more rural hospitals may lack either staff adequately trained in the use of these specialized devices or sufficient "back-up" staff should skilled specialists fall ill.
+ Critical care for COVID-19 patients is particularly labor intensive due to protocols needed to control infection spread, as well as the patients' increased need for ICU space and services (e.g., ventilators, respiratory therapists). Case surges are therefore more difficult to manage, impacting staff and facility capacity to treat all patients adequately.

Need for temperature-controlled facilities and equipment can impact transport and allocation of vaccines

Cold-storage requirements for some vaccine formulations will impact the volume and speed of vaccine distribution.

+ mRNA-based vaccines for COVID-19, such as those being produced by Moderna and Pfizer/BioNTech, **require specialized refrigeration equipment** for transportation and storage (-4°F for Moderna, -94°F for Pfizer/BioNTech).
+ To address ultracold shipping requirements, Pfizer developed "thermal shippers," which hold a minimum of 975 doses. Facilities in rural areas may not meet that volume demand, leading to either vaccine waste or allocation only to more urban areas. Similarly, the ultracold freezers required to store the vaccines for up to 6 months are **prohibitively expensive** for small or rural hospitals.
+ Logistics companies required time to **make significant adjustments to cold-chain infrastructure**. For example, UPS created a "freezer farm" of ultracold freezers (each capable of holding 48,000 vials) at its largest hub in Louisville, KY.

Travel restrictions can limit flow of supplies

Travel restrictions can make it more difficult to deploy medical supplies and countermeasures and to service medical equipment.

+ Pandemic-related downturns in air travel can make it difficult to secure sufficient air freight capacity to accommodate the sheer volume of vaccines and other medical supplies needed. For example, **total global air cargo capacity during the COVID-19 pandemic declined 20%** in 2020 compared with 2019.[9]
+ Travel restrictions can delay or limit the ability for field service staff to access hospitals or other care locations to **service and maintain critical medical equipment** (e.g., ventilators).
+ Given that over 80% of global trade by volume is transported by sea, **port closures or other border restrictions could prevent or delay vital supplies** on cargo ships from reaching their intended destinations.

Rapid vaccine deployment will require extensive staffing and facility protocols

Complex site and staffing requirements for **large-scale vaccine administration** must be well defined.

+ Personnel are needed to screen patients to ensure eligibility and safety, as well as administer vaccines.
+ **Multiple-dose vaccines** require public health departments and hospitals to send patients reminders to return for their second dose. For example, Moderna's second dose is administered 28 days after the first; Pfizer/BioNTech's second, in 21 days. Both of these timeframes, coupled with the approach of using second doses to prime more vaccinees while relying on additional vaccine shipments for booster shots, add complexity to record keeping.
+ Facilities that administer vaccines need to adhere to **specific protocols**, such as increased space for reducing exposure, organized traffic flow in and out of facilities, and provisions for medical waste disposal.
+ Ideally, potential vaccine providers should **connect their records to an immunization information system** (IIS). Those not already connected to such an IIS may need qualified data entry personnel to manually input patient information, with new IIS connection requests often taking weeks or months to fill. The Center for Disease Control's (CDC's) Vaccine Administration Management System (VAMS) addresses some of these concerns yet also creates others; for example, certain information required by the CDC is not allowed to be shared in some states.

9. "COVID-19: Effects on Air Cargo Capacity," Accenture, October 19, 2020, accessed October 23, 2020.

Vaccine allocation and prioritization decisions can be ethically complex

In the United States, state-level public health agencies are responsible for **quickly and fairly allocating vaccines**, as they become available, to the populations prioritized to receive them. Given the high demand for these vaccines and limited supplies, a **staged rollout** is necessary.

+ Those most in need should be targeted for early receipt of a vaccine. These populations include public health and frontline healthcare providers, emergency services personnel, deployed and mission-essential personnel, manufacturers of vaccines and antivirals, teachers and childcare providers, and pregnant women.
+ Identifying the most vulnerable populations to **determine supply needs and ensure optimal distribution** requires consideration of both state and federal priorities. More accurate and current data will improve understanding of the demographic factors (e.g., race, income) that can inform how and where to distribute supplies.

Eligible patients may be reluctant to be vaccinated

When vaccines are available, many Americans may be reluctant or at least concerned about getting immunized.

+ **General vaccine hesitancy**—whether based on complacency, lack of convenient access, misinformation, or lack of confidence—was identified in 2019 by the World Health Organization as one of the top 10 threats to global health.
+ **Government distrust is a key driver for resistance to vaccination**, particularly for marginalized communities, and can compromise the ability to reach herd immunity across the population.
+ Cultural **values of privacy** and concern about unprotected medical information can exacerbate distrust.
+ The accelerated regulatory approval of vaccines may lead the public to **question vaccine safety**.

Vaccine nationalism may restrain global response

Potential stockpiling ("future-proofing") of vaccines in the United States risks a worsening of the pandemic in other countries, which ultimately risks a pandemic recurrence and a re-infection of the population.

+ The potential risk of the United States adopting export control (e.g., refusing to export a vaccine) could result in retaliatory measures/countermeasures from other countries.
+ The United States must increase its ability to guard against cybersecurity breaches and technical espionage (e.g., intentional phishing for vaccine technology).

Recommended Actions & Timelines to Achieve Future State Objectives

Bold indicates a high-priority activity

Implement Novel Distribution Strategies and Approaches	2021-2023	2024-2026	2027-2030
Ensure testing is deployed to marginalized communities (e.g., through mobile testing sites)			
Leverage the food-agriculture space for distribution strategies to improve nimbleness of delivery across geographies			
Leverage guidance from previous vaccination campaigns to identify and reach early access groups			
Digitize parts of the transport process that are currently manual (e.g., checking temperatures on refrigerators) to accelerate timelines and improve quality (i.e., reduce potential for human error)			
Ensure deployment of critical interventions, including vaccines, through mobile delivery units that bring resources directly to affected communities to ensure timely and efficient patient access to treatment (e.g., avoid queues of patients for a limited number of vaccines, accommodate areas without easily accessible distribution centers)			
Develop a challenge competition to inexpensively build extreme-cold-capable refrigerators, with tested winning designs that could be fielded to make-shift hospitals during pandemics			
Develop algorithms to inform distribution of specific medical products			
Consider use of autonomous drones to deliver medical products such as test samples to hard-to-reach rural and urban areas			

Advance Product Tracing and Tracking Systems	2021-2023	2024-2026	2027-2030
Establish a certification or tracking system for resources and supplies deemed vital to patient survival to accelerate their clearance at ports, customs, or other checkpoints			
Leverage Internet of Things [IoT] capabilities to improve ability to trace and track product inventory/storage, transport, and delivery			
Establish standards/tiers for deployment of products with varying levels of medical-grade materials (e.g., ventilators and PPE made by non-traditional manufacturers of those products)			

Bold indicates a high-priority activity

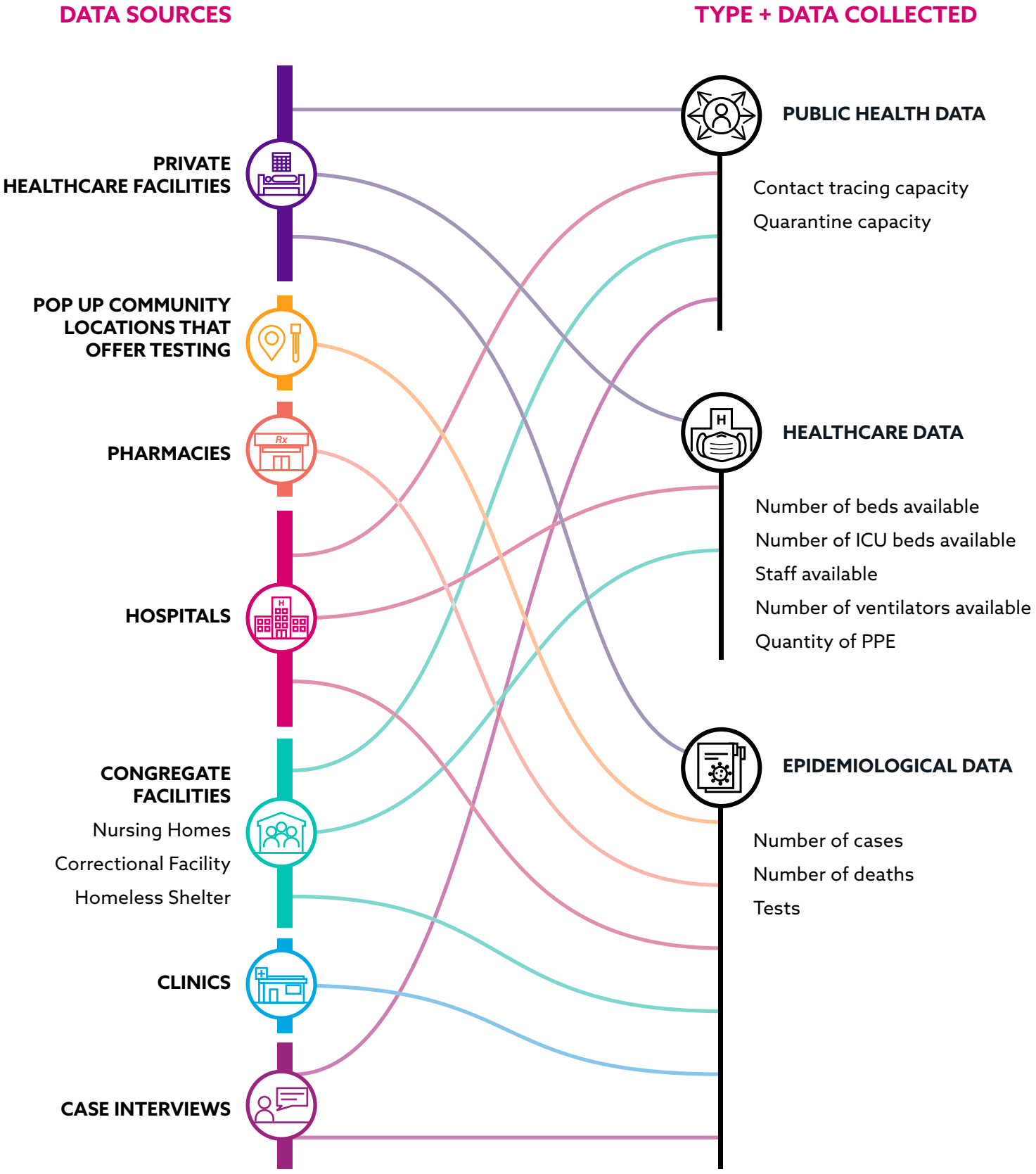
Maintain Distributed Supply Stockpiles	2021-2023	2024-2026	2027-2030
Establish distributed, locally managed stockpiles of critical non-pathogen-specific medical supplies (e.g., PPE, ventilators) that would allow for reallocation/transfer of resources in response to surges in demand			
Implement processes for cycling and maintenance of product stockpiles to guarantee their readiness for deployment, ensuring products are not beyond their shelf life, all components are packaged together, and any batteries are charged			
Establish an information-sharing network to track capacity of medical supplies and staffing in critical areas (hospitals, lower income areas with the lowest buying power)			

Ensure Workforce and Community Readiness	2021-2023	2024-2026	2027-2030
Increase capacity of trained personnel and establish personnel sharing protocols (e.g., award emergency credentials to reposition health workers to serve in surge capacities) across state lines so they can more easily support response in areas of critical need			
Assess personnel and training resources needed to provide education for operating medical devices for diagnosis and treatment (e.g., ventilators), ensuring resources are readily available when needed			
Conduct tabletop exercises to test deployment processes, helping to identify and address weaknesses and bottlenecks to improve preparedness			
Increase healthcare automation or other strategies (e.g., ventilators that can be adjusted digitally rather than manually, self-administered vaccines) that reduce the need for human intervention to reduce worker exposure risk and extend workforce capacity			
Create locally and/or regionally based Community Healthcare Reserves of trained volunteers, using a federated model, that can be called upon to provide assistance to career professionals during critical care surges			
Create localized Civil Disaster Response Groups that can develop community-based strategies to effectively marshal and administer local resources to aid in disaster response (e.g., leverage local hotels or large community facilities as triage centers or field hospitals to alleviate hospital overcrowding)			
Establish a mechanism to facilitate widespread training of non-ICU clinicians and other primary functions arising during pandemics, including specialized training for teams being deployed to rural hospitals			
Build greater resilience for a potential surge in the need for ICUs through community data gathering and investments (e.g., city planners incorporating addition sterilization into new or refurbished buildings to identify them as pandemic-ready)			

Data Infrastructure

Data infrastructure is a critical component of pandemic response and recovery efforts. Epidemiological data—cases, infection rate, testing—provides insight into the spread and severity of the pandemic, which is integral to both informing decision makers and helping the public understand risk. Other forms of data, such as the results of research and clinical trials or real-world data on patient experiences, can be used to inform the development of tests, treatments, and vaccines. **Creating structures and mechanisms that ensure necessary data is accurate and consistent, as well as easy to collect, share, retrieve, and interpret are essential to enabling successful data infrastructure.**

Data Needed for Pandemic Response



Data-Driven Actions and Decisions for Pandemic Response

ACTIONS & DECISIONS	DATA NEEDED: EPIDEMIOLOGICAL DATA	HEALTHCARE DATA	PUBLIC HEALTH DATA
Measure the impact of the pandemic on local communities (e.g., urban, suburban, and rural populations; multi-generational households; K-12 and post-secondary educational settings)	●	●	●
An early-warning system to prevent explosions of cases by scaling back physical connections as soon as cases begin to rise	●	●	●
Improve the turnaround times of tests, which is crucial to stop spread	●	○	○
The opportunity to better understand and reverse the unequal burden the pandemic is placing on Black, Hispanic, Native American, and other communities	●	●	●
Understanding community risk and preventing deaths in vulnerable populations	●	○	●
Rapidly isolate cases and quarantine contacts for outbreak control	●	○	●
Measure government response	●	●	●
Healthcare, education practitioners, and policymakers track measures being taken by various countries and institutions in response to the pandemic	●	●	●
Inform reopening strategies or decide to reopen	●	●	●
Inform and understand health system capacity to respond to COVID-19. Also informs safety of workforce, facilities, and patients.	○	●	○

Desired Future State Objectives

To improve pandemic response and recovery, the United States needs a robust data infrastructure capable of accurately, efficiently, and securely linking data across multiple sources critical to public health response. National data infrastructure must be well designed and integrated to track this data from a pandemic's outset and translate it into clear metrics to inform decisions. Elements of a robust data infrastructure that can facilitate and improve pandemic response and recovery include:

HIPAA-compliant data-sharing practices that ensure personally identifiable information (PII) remains confidential

Highly automated and interoperable systems that can link epidemiological data, clinical data, genomic data, and other relevant data across national, state, and local levels

Easily usable systems designed to be accessed, updated, and leveraged by public health professionals and key decision makers, not just data experts

Sustained investment in identifying and implementing advanced data systems and tools to ensure readiness for future pandemics

Common data collection, analysis, and reporting standards that represent the needs of all key stakeholders, as well as regular review of these standards to identify gaps, promote process improvement, and accommodate input from additional supporting entities (e.g., private healthcare systems) that may collect or provide data

Key characteristics of an optimized U.S. data infrastructure include:

Interoperable

Record-keeping systems and procedures use a common framework; data can be shared and accessed easily by stakeholders across government agencies, states, regions, public health facilities, and insurers; and incentives exist to share data

Automated

Processes such as data collection, aggregation, cleaning, and analysis are automated to the greatest extent possible to ensure speed and avoid overburdening the workforce

Accurate

Records are subject to de-duplication and other verification measures to ensure they are accurate and meaningful

Well Managed

Systems can detect breakdowns in data sharing or data gaps and create an alert so these issues can be addressed

Consistent

All pertinent case data (e.g., which patients are hospitalized, comorbidities, and risk factors) is captured and reported in a standardized manner and format

Secure

The integrity of data, including PII, is scrupulously maintained, and data-sharing infrastructure is digitally secure and protected from intentional or unintentional manipulation

Current Challenges

Decentralized information and lack of data sharing

Currently, **no central repository exists for the collection and curation of infectious disease outbreak data** from multiple sources, including federal, state, and local public health agencies; healthcare networks; public health and clinical laboratories; private healthcare facilities; and research organizations.

Data inaccuracy caused by lack of consistency in collection and reporting

Public health data—including testing, claims and clinical data, electronic health record information (EHR), patient-generated information, sociodemographic data, and others—is **not collected, managed, or reported in a consistent, standardized way**, nor is there a consistent process for data verification and validation.

+ Data variability makes positivity rates and case counts unreliable, and often **not comparable** across geographies or demographic groups.
+ Public health authorities **do not receive standardized data** to inform community-level analysis and facilitate immediate follow-up or contact tracing.
+ States **develop their data collection methods independently**, with no two identical in terms of information presented, usability, or structure.
+ Basic **demographic data is not standardized**, resulting in epidemiological sampling that is not representative of populations at risk (e.g., often only includes geographical considerations, not gender, race, ethnicity, living situation, or occupation).
+ As more is understood about a pandemic, data collection processes may periodically change (e.g., redirecting data delivery from CDC to HHS), resulting in **potentially inconsistent data**.
+ Healthcare systems are **overburdened by data collection requirements** (e.g., regarding patient histories and underlying conditions).

Legal and privacy concerns related to data sharing

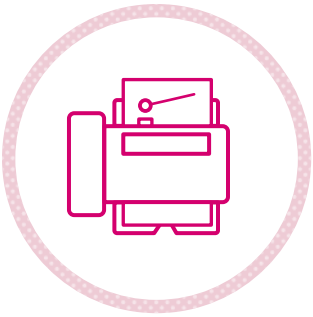
Federal laws and regulations that govern data sharing and privacy, as well as local interpretations of those same laws, can impact data sharing.

+ While the Health Insurance Portability and Accountability Act **(HIPAA) Privacy Rule establishes rules for the use and disclosure of protected health information** held by "covered entities" (e.g., physician practices, hospitals, clinics, laboratories, pharmacies, health plans, electronic medical record vendors, and health information exchanges), **state laws may also govern the ability of data sources** to share data (e.g., California Consumer Privacy Act).
+ Applicability of privacy laws and policies may depend on the data source (e.g., whether test results coming from a lab are anonymous or contain PII).
+ Confusion about these laws and conservative interpretations—due to fear of running afoul of the law—can create **barriers to sharing, managing, reporting, and describing data**.

Unreliable testing data due to insufficient testing and slow results

Testing is a major source of data in a pandemic and crucial to understanding the spread and impact of the pathogen. Yet, **insufficient levels of testing and slow results** can hinder decision making.

+ At the start of the COVID-19 pandemic, a **shortage of available tests** delayed the ability to conduct meaningful analysis.
+ **Without fast, affordable, and abundant testing**, it is difficult to identify individuals in their infectious window.
+ **Slow test response**—often up to 5 days to report a result—**delays contact tracing, patient treatment and recovery**, and overall ability to control the rate of infection.
+ Test responses are often slow because **clinical and reference laboratories are overburdened** and lack adequate capacity to process testing data.
+ There is **no process for collecting or reporting results** of point-of-care, and particularly at-home, testing to public health entities.
+ A **disconnect between rapid diagnostic testing and follow-up procedures** prevents physicians from using this information to better manage their patients; no protocol exists for linking rapid test diagnostics to EHRs.



Outdated approaches/mechanisms for collecting, aggregating, cleaning, and analyzing data

Many public health authorities, hospitals, labs, private healthcare providers, and clinics are hampered by either **a lack of access to up-to-date data-related technology (e.g., EHR systems) or a reluctance to embrace advanced technologies**.

+ Some health professionals and hospitals still rely on fax machines as well as extensive manual data entry and analysis, preventing interoperability with digital systems.

Insufficient system interoperability

Pandemic-relevant data is often collected and shared in a range of different formats. **Variabilities across existing databases** (e.g., input field labels, data types, data formats) can lead to data integration inaccuracies or inconsistencies that hamper the ability to record, analyze, or share a full range of relevant data.

+ **EHR systems are siloed/proprietary and designed for electronic billing**, rather than interoperability and data sharing.
+ Data on viral genomic sequences from infected individuals can answer questions related to the origin of novel viral pathogens, transmission dynamics during an outbreak, and relationships between viral genetic variants and disease severity. However, currently **no network or system exists to auto-integrate patient clinical data and genomic sequence data**.

Recommended Actions & Timelines to Achieve Future State Objectives

Bold indicates a high-priority activity

Improve Processes for Data Generation	2021-2023	2024-2026	2027-2030
Identify approaches to facilitate improved contact tracing (e.g., geo-tracking) while also protecting privacy (e.g., anonymous notification if near an individual with a positive diagnosis)			
Identify nontraditional resources for processing test results (e.g., veterinary labs, academic labs)			
Build testing labs that can process thousands of additional tests a day to ensure testing results are available more quickly			

Build Robust Data Management and Integration Systems	2021-2023	2024-2026	2027-2030
Define data management guidelines at the local, state, and federal levels to effectively and legally address requirements for managing consumer data			
Advance algorithms for de-duplication of data, matching data from across data sources			
Develop a data infrastructure that can integrate phone services needed for contact tracing and coordinating with medical centers and health providers			
Identify a third party that can vet and manage data, while ensuring its timely access to all relevant stakeholders			
Build and staff a data repository that establishes national reporting relationships across all levels to ensure consistent data; leverage advanced analytical methods (e.g., machine learning and artificial intelligence analyses) to inform disease and epidemiology models			
Collaborate with software companies to develop data management systems that use built-in monitoring tools to ensure data consistency and data visualization to facilitate streamlined communication to decision makers and the public			
Improve electronic health recording and provide integration with proximity tracking apps for contact tracing			

Encourage Information Sharing and Collaboration	2021-2023	2024-2026	2027-2030
Design an automatic system to alert health departments when there is a positive test result at a point of care, allowing for faster initiation of contact tracing and other measures needed to break the chain of transmission			
Incentivize stakeholders (e.g., hospitals) to share data, potentially leveraging existing Medicare and Medicaid financial incentives			

Bold indicates a high-priority activity

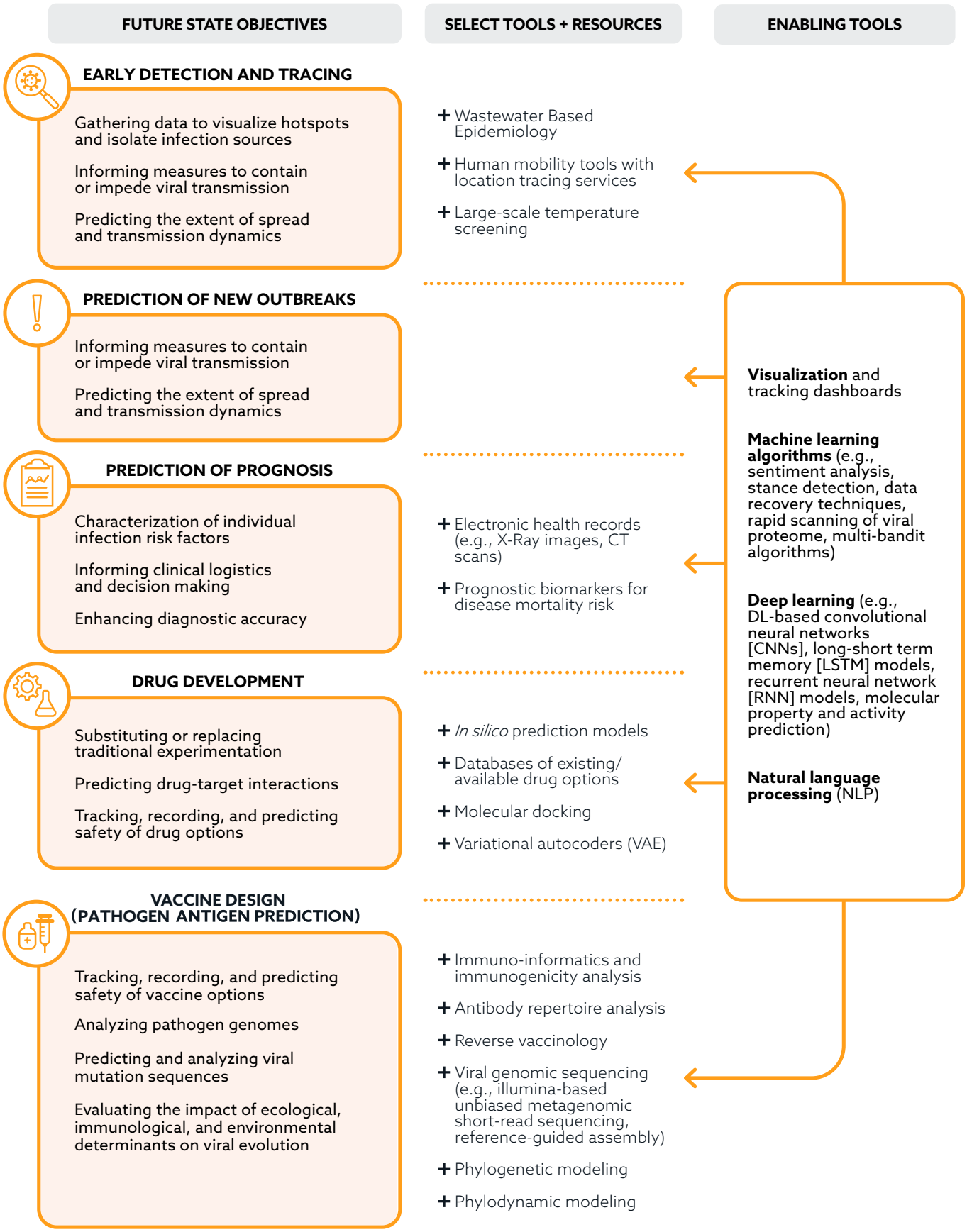
Encourage Information Sharing and Collaboration, continued	2021-2023	2024-2026	2027-2030
Establish a national-level leadership group to instill principles of good governance for data sharing, such as: **+ Clear accountability processes that clarify authorities and responsibilities** **+ Principles of transparency, equity, and participation** **+ Clear legal protections for public health agencies, researchers, and individuals' rights**			
Develop formalized voluntary agreements contingent on state consent or through Congressional legislation to support data sharing during a public health emergency			
Develop public-private partnership between the U.S. Department of Health and Human Services and private industry focused on establishing best practices for data integration while protecting data privacy (e.g., using cryptographic techniques such as one-way hashing)			
Establish integrated information-sharing networks among hospitals and medical systems to track, in real time, capacity of medical supplies, staffing, ICU beds, etc.			
Establish multilateral agreements among scientific institutions, private industry, and local government to develop a system that can enable synchronization of digital and physical contact tracing with people's other activities			
Establish a standardized pandemic emergency data capture system that can be easily modified by health experts based on the unique characteristics of each pandemic			

Enhance Data Security	2021-2023	2024-2026	2027-2030
Public health authorities should communicate their commitment to abiding by applicable privacy, confidentiality, security, non-discrimination, and civil rights laws, to assure the public that their data is protected			
The HHS Office for Human Research Protections should issue written guidance to confirm processes for reporting and disclosure of data to public health authorities during a public health emergency			
Public health authorities, or those acting on their behalf, could make available de-identified (per HIPAA standards) data to support public and private research related to COVID-19 and future pandemics			

Predictive Capabilities

Predictive capabilities are computationally driven forecasting tools for analyzing trends and patterns in large datasets to help enhance preparedness, improve logistical planning, and inform decision making. **Artificial intelligence (AI)-based technologies, including machine learning (ML) and deep learning (DL), have shown enormous promise in providing the pandemic response and recovery community with vital insights** for predicting transmission dynamics, viral evolution, patient prognoses, and potential drug and vaccine options.

How Predictive Capabilities Aid Pandemic Response



Desired Future State Objectives

Biosurveillance, analytics, and prediction modeling are essential forecasting tools that continuously produce new and meaningful insights for decision makers as the conditions of pandemics evolve. Predictive analytics can support pandemic response, recovery, and preparedness through:

Early detection of infected individuals to help reduce disease spread and give healthcare experts more time to establish medical treatments, coupled with tracing contacts to identify "hot spots" of positive cases to inform viral transmission control and/or deployment of supplies and resources

Computational predictive models that rely on data streams that provide timely, accurate, and relevant information to help predict the course of infectious disease outbreaks and guide measures to prevent and control viral spread

AI forecasting tools that not only anticipate future outbreaks but also help enhance disease diagnostics and predict prognostic outcomes (e.g., disease severity, patient susceptibility) to inform decision making related to infected patients and prevention measures

Application of ML and DL algorithms to drastically reduce the cost and time for discovering, repurposing, and testing therapeutic drug candidates

Immunoinformatics, reverse vaccinology, and other AI-driven computational methods that could significantly reduce the cost and time required to identify and develop promising antigen candidates compared with conventional vaccine discovery methods

Key characteristics of predictive capabilities include:

Validated

Accurate and relevant predictive models that represent real-world conditions are validated through comparisons of simulated results to experimental observations and known results of other valid simulation models

Reliable

AI-based systems use well-calibrated algorithms to ensure predicted results are consistent, repeatable, and precise

Interpretable

Useful, relevant knowledge can be extracted from underlying data for practical application of modeling results (e.g., visualizations that clarify complex, high-dimensional outputs)

Transparent

Predictive computational techniques are transparent so peers can audit, verify, and fully understand the reasoning behind predictive modeling methodologies and their impacts on the veracity of prediction results

Current Challenges

Lack of robust methods for data gathering and reporting

Current protocols for gathering and reporting data are inconsistent, immature, or lack interoperability.

+ There are **insufficient diagnostic capabilities** for tracking and tracing, including a lack of infrastructure for tracking travelers, **limited support of *existing* methods for anonymous tracing, lack of point-of-contact rapid testing diagnostics**, and infrequent use of and limited sources available to conduct rapid diagnostic testing.
+ There is **limited use of automated testing checkpoints** for critical or high-traffic locations, with too much reliance on human face-to-face interactions.
+ **Variations in conditions across different experiments** may result in data discrepancies. During genomic sequencing, changes or inconsistencies in the experimental conditions can produce unreliable or inconsistent results needed for subsequent gene expression profiling.
+ Gathering data from disparate sources can introduce **redundancies and discrepancies** (e.g., re-reporting generic interview questions about disease history that could otherwise be accessed through virtual platforms).
+ Predictive algorithms are underutilized for the purpose of **allocating limited resources**. Using AI-based approaches could help determine the most logical regions or facilities to allocate wastewater epidemiological tests.
+ Many scientific studies lack coherent data-gathering approaches, which leads to a **lack of quality control of information in published works** (e.g., critical information on limits of detection from wastewater epidemiology).

Quality of data impacts its usefulness

Poor quality datasets—those that are small, biased, incomplete, or in need of peer review—lack usefulness for many predictive applications.

+ Researchers require sufficient high-quality (or "gold-standard") experimental datasets to evaluate predictive modeling performance and to train AI-based algorithms (e.g., sufficient data to train algorithms to recognize features from medical images).
+ **Poor-quality structural data**—such as insufficiently recorded epidemiological information, viral phenotypic characteristics, and host characteristics—limits the ability to identify potential drug-target interactions.
+ Unoptimized allocation of global and local resources can cause **unequal data sampling of geographical regions**.

Complex biological systems limit or slow the application of predictive methodologies

Biological systems, intermolecular interactions, and viral transmission dynamics are highly complex and difficult to characterize or simulate.

+ The tremendous complexity of biological systems **complicates comprehensive understanding of disease and drug mechanisms**, as well as discovery of new uses for existing drugs.
+ **Transmission dynamics are highly difficult to characterize**; insights during earlier stages of pandemics could allow for proper mitigation strategies.
+ The **continuous evolution of certain viruses** complicates conducting rigorous experimental measurements of viral infectivity.
+ Failure to synthesize information across the host, pathogen, and environment (i.e., models that incorporate epidemiological, immunological, and ecological factors) leads to **major information gaps** needed for vaccine development.

Viral infectiousness impacts working conditions

The infectiousness of viral pathogens can affect working conditions and physically prevent researchers and practitioners from conducting R&D, using or gathering data for predictive analytics, or providing patient care.

+ **Testing requires a high training standard and laboratory containment measures**, making it difficult to study the presence of infectious virus in wastewater.
+ There is concern among radiologists that using CT-scans and X-rays to generate training data for computer-aided diagnostic predictions **may contaminate equipment and spread the disease**.
+ Some containment measures may be too restrictive for researchers and healthcare workers, such as **limitations in the duration and frequency of work shifts**, thereby creating further **scheduling challenges** for supervisors.
+ Access to clinical samples—particularly for the 2019 novel coronavirus (SARS-CoV-2)—has not been possible for biosafety level 2 (BSL-2)-rated laboratories, making cell sourcing a major challenge.

Data privacy and mishandling concerns limits the potential of predictive capabilities

Growing **tensions between public health imperatives and privacy concerns** can prevent researchers from taking full advantage of AI-based tools for tracing, tracking, outbreak forecasting models, drug discovery, and vaccine development.

+ There is resistance by public agencies to use smartphone-based geo-tracking, including systems developed by private companies such as Google and Apple.
+ Control over contact tracing data may be limited, with certain countries' apps having violated privacy laws.

Recommended Actions & Timelines to Achieve Future State Objectives

Bold indicates a high-priority activity

Implement Tracking and Tracing Technologies	2021-2023	2024-2026	2027-2030
Develop HIPAA-compliant anonymized tracking solutions to monitor population densities and movements of individuals and enable tracking of those infected, vaccinated, etc.			
Pursue the use of proximity-based smart device applications that provide notifications or emergency alerts to individuals who may have been exposed to infectious populations			
Examine cyber vulnerabilities of existing smartphone-based geo-tracking platforms; encourage widespread use of those deemed cyber secure in support of contact tracing			
Integrate viral genomic data into tracking to accelerate tracing of transmission networks relative to traditional contact tracing			

Optimize Early Detection and Diagnostic Testing Approaches	2021-2023	2024-2026	2027-2030
Deploy pool testing to support early and accurate detection of regional hotspots for emerging disease outbreaks			
Create and optimize methodological frameworks for community-based wastewater testing of municipal sewage collection systems to detect the presence of infected individuals			
Establish performance benchmarks to guide development of gold-standard diagnostic testing approaches with high analytic sensitivities			
Explore the use of AI-driven smart thermometers, pulsometers, and other handheld devices for physiological monitoring and surveillance (including real-time notification capabilities) in early diagnoses of disease conditions and onset of symptoms to facilitate a more proactive response			
Establish and maintain relationships with international researchers to identify early-stage zoonotic threats			
Support efforts to train AI-based predictive algorithms by developing a data management framework for large datasets that are generated by disease tracking smart devices and sensors			
Leverage observational studies at the regional level to identify public health anomalies and inform development of clear and consistent public health guidelines			

Bold indicates a high-priority activity

Employ Strategies for Real-Time Forecasting and Surveillance	2021-2023	2024-2026	2027-2030
Apply predictive approaches to estimate the limits of production capacities for manufacturing equipment and supplies required for different stages of pandemic response			
Conduct ongoing sampling of blood products around the world (e.g., in hospitals, blood banks, clinics) to identify novel pathogens circulating throughout the population			
Establish a global immunological observatory to continuously monitor novel pathogens around the world with the potential to infect humans (e.g., USAID PREDICT program)			
Establish a centralized interagency institution, similar in nature to the National Weather Service, to pursue foundational efforts in forecasting infectious disease activity at the regional, state, and national levels			
Identify key data streams (see Data Infrastructure) needed to use real-time analytical tools to inform decision making			
Launch a robust real-time biosurveillance system and a strategy for quickly scaling up the development of rapid diagnostic tests and screening tests to support disease detection, targeted treatments, and sustained barriers to disease transmission			
Advance Data-Generation Platforms for AI-Driven Analytics	**2021-2023**	**2024-2026**	**2027-2030**
Support AI-based drug discovery platforms, tools, and in silico prediction models that reduce the need for physical experiments, including use of animal models			
Standardize the data and reporting structures for genomic, clinical, and epidemiological data to support laboratories and educational institutions in producing multivariate prediction models (e.g., real-time epidemic forecasting, transmission patterns, protective immune response)			
Coordinate a broad virus DNA sequencing effort, particularly at hospitals and in wastewater, with the goal of training DL-based algorithms (e.g., generative adversarial networks [GANs]) to generate short DNA sequence variants for studying viral mutation rates and identifying drug candidates			
Enhance Clinical Outcomes and Product Development	**2021-2023**	**2024-2026**	**2027-2030**
Use AI to improve clinical trial design, including identifying effects observed in randomized controlled trials			
Use prognostic-focused tests to identify and help mitigate potential long-term health impacts in individuals who have been infected with COVID-19			

Bold indicates a high-priority activity

Enhance Clinical Outcomes and Product Development, continued	2021-2023	2024-2026	2027-2030
Engage vendors of EHRs to find ways to make EHRs securely available for collecting and analyzing pandemic-related data			
Establish regional mega-labs with high-throughput laboratory testing capabilities and pair with rapid, high-performance, point-of-care testing			
Advance serology testing efficacy and conduct serology studies to understand disease incidence, immunological history, and stability of immune memory against different pathogens			
Invest in accelerated testing and vaccine development that uses in silico methods, in which the immune system of a virtual patient population is replicated for computational testing of vaccines			
Promote the development of modeling and simulation standards for medical imaging devices to support AI-based predictive analytics for diagnostics, drug development, and vaccine discovery			

Regulatory Processes

There is an urgent need for effective new devices, drugs, and vaccines during a pandemic. Streamlining regulatory processes to enable approvals on an accelerated timeline—while still ensuring product safety and efficacy—can help ensure the public has access to these life-saving products in months, or even weeks, rather than years. **Providing guidance to help developers more easily navigate regulatory pathways will be key to ensuring this streamlining success.**

Accelerated Regulatory Timeline for Vaccines: Overlapping Phases

Traditional Timeline

Accelerated Timeline

[1]The U.S. Food and Drug Administration can rescind emergency use authorization (EUA) status. Product developers are recommended to seek complete regulatory approval through traditional regulatory pathways like the new drug application (NDA), biologics licensing application (BLA), Premarket Approval (PMA) and 510(k) Premarket Notification.

Desired Future State Objectives

Optimized regulatory processes, leveraging lessons learned from COVID-19, can significantly improve the United States' ability to more rapidly and effectively respond to and recover from a pandemic by:

Enabling previously approved therapeutics to be authorized for emergency use for a new application within weeks, and facilitating the testing and approval of new treatments and vaccines within months to a year

Providing rapid approval pathways for devices, drugs, and vaccines that responsibly balance risks and opportunities, ensuring product safety and efficacy

Supporting innovative clinical trial designs and approaches to reduce lengthy process steps

Developing clear guidance for pharmaceutical and biotechnology companies on available fast-track options

Establishing standards and regulatory guidance to help streamline development processes and improve quality

Key characteristics of optimized regulatory processes include:

Proactive

Government agencies (e.g., U.S. Department of Health and Human Services) approach companies to encourage potential emergency product development, rather than waiting for them to step forward

Innovative

Product sponsors use novel clinical trial models, technology platforms (e.g., in vitro, in vivo, microphysiological), and AI to design more efficient, accelerated studies

Targeted

Product sponsors deploy and facilitate mobile and targeted clinical trials in areas most affected by the pandemic to ensure trial populations are representative of the patients sponsors aim to treat

Collaborative

Data sharing and transparency (with appropriate intellectual property protections) among product developers and with regulators can help accelerate progress by increasing understanding of a pathogen's biological/immunological mechanisms

Responsible

Reasonable scientific support for benefit-risk decisions ensures product safety and efficacy

Guided

Regulatory agencies invest in education and communication efforts to ensure product developers understand available approval pathways and options for expedited approval

Current Challenges

The general public may perceive rapid regulatory timelines as unsafe

Product developers and regulatory agencies can coordinate to safely accelerate the development and approval of a vaccine candidate and have it brought to market, but **vaccine hesitancy can delay the widespread herd immunity needed for vaccines to slow disease spread**. While some polls may report that the majority of the U.S. public plans to get the COVID-19 vaccine, aggregating a range of positive responses (e.g., "very likely," "somewhat likely," or "probably"), evidence indicates that some people are still considering information related to the vaccine and its distribution to make a decision on whether to be vaccinated.[10]

+ Similarly, the 2009 H1N1 vaccine was perceived to be unsafe due to its rapid approval and production. **Only 24%-27% of Americans were vaccinated**, leaving over a million vaccine dosages unused.[11]

Regulatory pathways with less rigorous standards for evidence can lead to ineffective solutions

Easing evidence standards for regulatory pathways can result in manufacturers developing products that are less effective:

+ The FDA discovered that out of 125 EUA requests for COVID-19 diagnostic tests, **82 were found to have efficacy concerns** after easing evidence standards in February 2020. Some of these tests were still denied authorization after working with the FDA.[12]

Some vaccine technology platforms require more regulatory review, limiting the extent to which regulatory timelines can be accelerated

+ Because they are not yet part of licensed products in the United States, **new and novel vaccine platforms** (e.g., DNA and messenger RNA) used for COVID-19 vaccine candidates may require longer review compared to proven technologies.

10. Gillian K. SteelFisher, Robert J. Blendson, and Hannah Caporello, "An Uncertain Public — Encouraging Acceptance of Covid-19 Vaccines," The New England Journal of Medicine, March 3, 2021, https://www.nejm.org/doi/full/10.1056/NEJMp2100351.
11. "How to Steward Medical Countermeasures and Public Trust in an Emergency: A Communication Casebook for FDA and its Public Health Partners", UPMC Center for Health Security, November 2016, https://www.centerforhealthsecurity.org/our-work/events/2016%20FDA%20MCM/FDA_Casebook.pdf.
12. Jeffrey Shuren and Timothy Stenzel, "Covid-19 Molecular Diagnostic Testing — Lessons Learned", New England Journal of Medicine, October 22, 2020, https://www.nejm.org/doi/full/10.1056/NEJMp2023830.

Regulatory agencies' limited operational capacity during a pandemic may delay approval of non-pandemic related products

FDA has received an unprecedented amount of inquiries and applications during the COVID-19 pandemic that must be processed by its limited staff. Prioritizing pandemic-related technologies over other technologies and projects may delay development of medical products crucial for treating other diseases and conditions.

Updates to regulatory guidance to accommodate new pandemic information may disrupt potential studies or delay ongoing studies

Clinical trial designs must be adjusted to accommodate new guidance about the pandemic virus, introducing challenges for developers as well as for regulatory evaluations.

+ FDA has updated and clarified its guidance for potential EUA applications for COVID-19 vaccine candidates to ensure study sponsors provide an appropriate level of evidence to verify safety and efficacy.

COVID-19 and future infectious diseases may impact adherence to study protocols for other diseases and conditions

The COVID-19 pandemic disrupted ongoing and potential clinical trials due to its characteristics (e.g., airborne spread) and associated public health concerns. Study sponsors have experienced challenges, including patient recruitment, protocol deviation/violation, patient compliance, coinciding illness and medication, delay of treatment, delayed site activation, and site closures.[13]

+ According to the Cancer Research Institute (CRI) and IQVIA, **only 14%-20% of active oncology clinical trials were enrolling patients at normal rates** from March 23 to April 3.[14]

+ Study protocols can be revised to adapt to new circumstances, but study sponsors must notify FDA and justify the proposed changes. While FDA has issued guidance to support this process, it can still be burdensome for study sponsors to make adjustments that may impact the cost and duration of a study.

13. Shein-Chung Chow and Wei Zhang, "Statistical Evaluation of Clinical Trials Under COVID-19 Pandemic", Therapeutic Innovation & Regulatory Science, June 24, 2020, https://link.springer.com/article/10.1007/s43441-020-00182-8.
14. Samik Upadhaya, Jia Xin Yu, Cristina Oliva, Megan Hooton, Jeffrey Hodge, and Vanessa M. Hubbard-Lucey, "Impact of COVID-19 on Oncology Clinical Trials", Nature, May 18, 2020, https://www.nature.com/articles/d41573-020-00093-1.

Complexity of local and mobile clinical trials limits efficient recruitment of representative populations

Mobile clinical trials provide the opportunity to efficiently target and examine infected populations that sponsors aim to treat to inform product development. However, the **significant resources they required (e.g., funding, logistics, time) prevent this model from being scalable**.

Lack of standardized animal model studies limits their use for understanding human disease outcomes related to infectious diseases

Identifying an animal model is time-consuming, which can **slow down study processes**. Additionally, translating data from animal models to human disease outcomes is challenging because animal models may not replicate the pathology and post-response symptoms of COVID-19 patients.

Product developers may be unfamiliar with regulatory pathways designed for an accelerated process

Product developers and sponsors are not sufficiently educated on the regulatory landscape and the processes involved in applying for regulatory pathways like the EUA.

+ **Incomplete or poor-quality applications** could lengthen the regulatory review process.
+ Product sponsors **may not pursue regulatory approval if they are unsure of the process** and how to navigate it.
+ Developers may have an insufficient understanding that **EUAs can be rescinded when an emergency is over** and they must fulfill additional requirements for full authorization. The healthcare community could become stymied if certain products or product features in use are then rescinded.

Recommended Actions & Timelines to Achieve Future State Objectives

Bold indicates a high-priority activity

Optimize Clinical Trials	2021-2023	2024-2026	2027-2030
Allow alternative clinical trial operations (i.e., tele-health visits to collect data and off-site testing), easing administration and follow-up requirements to reduce pandemic infection risks			
Establish a clinical trial network dedicated to pandemic response and recovery efforts to quickly secure thousands of volunteers for clinical trials examining vaccine candidates and therapeutics seeking regulatory approval *Examples include: COVID-19 Prevention Trials Network (CoVPN), HIV Vaccine Trials Network (HVTN), HIV Prevention Trials Network (HPTN), Infectious Disease Clinical Research Consortium (IDCRC), and the AIDS Clinical Trials Group (ACTG)*			
Establish a central entity to orchestrate all clinical trials, helping to identify standards for success and ensure the sharing of lessons learned that could inform other trials			
Identify systematic approach for assessing the potential benefits of all clinical trials, ensuring resources are not being wasted on devices, therapeutics, and vaccines with low value and prioritizing the approaches that create the most benefit with the least complications			
Design mobile and efficient clinical trial models that can be facilitated and deployed in areas experiencing outbreaks to ensure medical products successfully treat the infected population			
Advance microphysiological systems (i.e., organ-on-a-chip technologies) to help alleviate time delays and shortages for identifying appropriate animal models, facilitate high-throughput screening of therapeutics and vaccines, and increase understanding of the latent effects of pathogens			

Expand Frameworks for Expedited Product Approvals	2021-2023	2024-2026	2027-2030
Develop additional guidance and case studies on the EUA and other regulatory pathways to ensure developers understand how to navigate the review process, allowing for further expedited approvals and product availability and ensuring developers understand that the limited data requirements for an EUA will not be sufficient for full product approval			
Grant local institutional review boards (IRB) with an appropriate level of authority to make regional decisions (e.g., lifting some restrictions on short form consent limits to be able to enroll a greater number of non-English speakers in treatment)			
Establish an adaptive regulatory framework for novel digital product designs that leverages digital manufacturing capabilities (i.e., software, sensors, and smart machines) for rapid approval and manufacturing during a pandemic			
Capture the clinical outcomes of an investigational medical product if it is used through Expanded Access (Compassionate Use) outside of an ongoing clinical trial			

Bold indicates a high-priority activity

Uphold Commitments to Product Safety and Efficacy	2021-2023	2024-2026	2027-2030
Clearly outline and communicate quality control measures in the regulatory process to instill public trust in products as they become available			
Communicate the roles and responsibilities of regulatory agencies, including the role of the U.S. Environmental Protection Agency in regulating chemicals			
Provide regulatory guidance on the shelf life of PPE for developers and end users			
Establish stop-gap or countermeasure processes that allow, within emergency experimental therapeutics or EUA, an ability to simultaneously study and inform on effective adverse event reduction, mitigation, or treatment strategies and approaches			
Use existing and expanded safety monitoring systems to track adverse events related to pandemic-related medical products *Examples include: CDC's V-SAFE app, CDC's National Healthcare Safety Network (NHSN), CDC and FDA's Vaccine Adverse Event Reporting System (VAERS), CDC's Vaccine Safety Datalink (VSD), CDC's Clinical Immunization Safety Assessment (CISA) Project*			

Cross-Cutting Foundational Requirements of a Strong Pandemic Response

While the innovations in technology and infrastructure recommended in this roadmap will be critical to accelerating pandemic response and recovery, these innovations must be supported by a strong and organized national response framework. Drawing on the lessons learned from the COVID-19 pandemic, **the following cross-cutting needs should be addressed by national authorities to provide a solid foundation for activities within each technology focus area.**

National Leadership and Coordination

+ State governments should work, with the direct support of the federal government, to **cultivate a culture of readiness for public health crises**, including clear plans for response activities such as ramping up testing, contact tracing, and manufacturing.
+ There is an opportunity to undertake various preparedness measures that could strengthen future pandemic response and recovery, including sustained support for the Pandemic Response Team, conducting exercises to test response capabilities, and routinely assessing stockpiles at the national and state levels.
+ During a pandemic, it is vital to communicate, collaborate, and coordinate across different agencies and sectors, which requires strong leadership and a centralized plan. State government leadership should work in concert with the federal government to develop and maintain the consistently well-funded and trained public health corps and structures needed to provide the best national defense against future pandemics.
+ National coordination also prevents unnecessary competition between stakeholders and offers structure, transparency, and consistency in recovery and response efforts.

Clear Command and Control Structure Across All Stakeholders

+ A lack of defined roles for government agencies during a pandemic leads to overlapping activities, inefficiency, and confusion among stakeholders about who to approach with problems or potential solutions.
+ A clear command and control structure with a **clear framework of roles and responsibilities, particularly across government agencies, can help more effectively leverage capabilities in the United States**.
+ Authorities, processes, and policies must be aligned across federal agencies, state governments, regional/county/local governments, the public health sector, laboratories, and private industry. The health sector has the potential to leverage the stakeholder structure of the Federal Reserve System, which is composed of both public and private components to govern U.S. monetary policy.
+ A consistent or common taxonomy/ontology—particularly among different levels of government, businesses, and the public health sector—can prevent miscommunication that may slow progress.

Sustained Funding for Pandemic Preparedness

- Inconsistencies in funding and policy, particularly between government administrations with differing priorities, can lead to wasted preparedness efforts and a failure to meet long-term public health goals.
- The United States must **proactively recognize the threats that pandemics pose and invest in preparedness and mitigation, rather than responding to crises** as they arise. Continued R&D will allow for accelerated development and deployment of on-the-shelf technologies during emergencies.
- It is critical to leverage and build on lessons learned from past pandemics/pathogens, including those related to prediction and data modeling, vaccine development, and targeted therapeutics. For example, previous research and vaccine/therapeutic development on SARS1 and MERS stopped/slowed once the immediate threat passed. Similarly, funding cannot stop for COVID-19 now that vaccines are available; therapeutics will be needed to treat long-term health impacts.
- While some solutions to public health challenges may have clear financial incentives to encourage private organizations to contribute solutions (e.g., drugs or vaccines), those with little or no built-in incentives such as diagnostics are harder to advance and rapidly scale. National authorities must identify the problems that are unlikely to be addressed by the private sector and be prepared to provide leadership and financial support for the development of solutions.
- To implement the technology and infrastructure innovations recommended in this roadmap, **there is a need to modernize basic health infrastructure**. Making modernization improvements will require sustained increases to funding of public health infrastructure.

Strong Public Education and Information Sharing

- Misinformation has been a major threat throughout the COVID-19 pandemic that has undermined public education efforts and trust in national health guidance.
- The public needs to be able to trust the information they are receiving and know how to use it to inform their own behavior (e.g., what to do with the results of an at-home test). **Communication to the public during a pandemic must be consistent, transparent, accurate, and digestible**. Authorities must clearly communicate the scientific method to instill trust and provide the rationale behind any changes in messaging as new information emerges.
- Since widespread misinformation can detract from progress, national authorities should **monitor and counter the spread of misinformation** and reactions within the community to adapt and respond in real time.
- Industry in particular needs early access to trusted information—particularly genetic sequencing of pathogen and epidemiology of resulting disease—to inform decision-making and drive development of diagnostics, therapeutics, and vaccines.

Harnessing the Power of Crowdsourcing and Collaboration

To better leverage good will and the desire to help and collaborate when there is a significant need, such as a pandemic, the United States should identify and establish dedicated entities that will:

+ Clearly communicate needs from leadership (i.e., countermeasures needed in response to the pathogen—such as ventilators for a respiratory virus) to help **focus on solutions most relevant to the key challenges/problems**.
+ Map expertise—across academia, private, and public sectors—to reduce unnecessary competition and improve preparedness for a wider variety of situations.
+ **Encourage collaboration across sectors and research areas**, leveraging organizations with concentrations of problem solvers—even those outside the traditional medical research community (e.g., NASA). The medical community can help define technology and infrastructure requirements to encourage innovative solutions.
+ Prioritize the most impactful efforts, creating a step-based process to assess technology/solution proposals against credible standards.

Developing Pathogen-Specific Countermeasure Toolkits

Effective **pandemic response and recovery requires a multi-faceted response effort**. Key elements of such a toolkit include:

+ Public health measures for infection control: handwashing, PPE, social distancing, travel restrictions, quarantine
+ Biosurveillance: screening and contact tracing
+ Tests for monitoring and diagnosis that are accessible, affordable, effective, and able to deliver results within an actionable timeframe
+ Therapeutics: both prophylactic and to treat resulting disease
+ Vaccines to build immunity

Planning for Long-Term Post-Pandemic Effects

Many pandemics are likely to have **long-term effects that will require specific mitigation measures**. Anticipated key impacts from COVID-19 that must be addressed include:

+ Economic repercussions: A long-term recovery program will be necessary to recover from high unemployment rates, the bankruptcies of companies, etc.
+ Long-term health impacts of those who were infected, as well as disproportionate access to healthcare
+ Impacts on research, technology development, and advancement of treatments for other diseases and medical conditions
+ Delays of routine healthcare (e.g., childhood vaccinations, preventative care, disease screenings)

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Appendix B **Sources Consulted**

Accenture. "COVID-19: Impact on Air Cargo Capacity." November 3, 2020. https://www.accenture.com/us-en/insights/travel/coronavirus-air-cargo-capacity.aspx.

Actifio and Sentry Data Systems. "Flexibility, Speed Enabling Actifio to Help in Pursuit of COVID-19 Treatments." *PR Newswire,* September 2020. https://www.wfmz.com/news/pr_newswire/pr_newswire_business/flexibility-speed-enabling-actifio-to-help-in-pursuit-of-covid-19-treatments/article_a04010fa-00a0-55f9-b3c7-73d06fc13b89.html

Additive Manufacturing Center of Excellence. "COVID-19 - Design for Additive Manufacturing." w.

Agbehadji, Israel Edem, Bankole Osita Awuzie, Alfred Beati Ngowi, and Richrd C. Millham. "Review of Big Data Analytics, Artificial intelligence and Nature-Inspired Computing Models towards Accurate Detection of COVID-19 Pandemic Cases and Contact Tracing." *International Journal of Environmental Research and Public Health* Vol. 17 No. 15 (July 2020). https://www.mdpi.com/1660-4601/17/15/5330

Agrawal, Gaurav, Michael Conway, Jennifer Heller, Adam Sabow, and Gila Tolub. "On pins and needles: Will COVID-19 vaccines 'save the world'?" McKinsey & Company. July 29, 2020. https://www.mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/on-pins-and-needles-will-covid-19-vaccines-save-the-world#.

Allam, Zaheer and David S. Jones. "On the Coronavirus (COVID-19) Outbreak and the Smart City Network: Universal Data Sharing Standards Coupled with Artificial Intelligence (AI) to Benefit Urban Health Monitoring and Management." *Healthcare* Vol. 8 No. 1 (2020). https://www.mdpi.com/2227-9032/8/1/46/htm

Alpert, Bill. "Scaling Up Output of a Covid Vaccine Is Costly, Says Moderna." *Barron's*. Accessed November 17, 2020. https://www.barrons.com/articles/scaling-up-output-of-a-covid-vaccine-is-costly-says-moderna-51596655582.

Arshadi, Arash Keshavarzi, Julia Webb, Milad Salem, Emmanuel Cruz, Stacie Calad-Thomson, Niloofar Ghadirian, Jennifer Collins, Elena Diez-Cecilia, Brendan Kelly, Hani Goodarzi, and Jiann Shiun Yuan. "Artificial Intelligence for COVID-19 Drug Discovery and Vaccine Development." *Frontiers in Artificial Intelligence.* August 18, 2020. https://www.frontiersin.org/articles/10.3389/frai.2020.00065/full

Arshadi, Arash Keshavarzi, Milad Salem, Jennifer Collins, Jiann Shiun Yuan, and Debopam Chakrabarti. "DeepMalaria: Artificial Intelligence Driven Discovery of Potent Antiplasmodials." *Frontiers in Pharmacology*. November 26, 2019. https://www.frontiersin.org/articles/10.3389/fphar.2019.01526/full.

Associated Press. "COVID-19 and Red Tape Is Keeping Thousands of Mariners Stuck at Sea." Euronews, October 19, 2020. https://www.euronews.com/2020/09/25/covid-19-and-red-tape-is-keeping-thousands-of-mariners-stuck-at-sea.

Association of State and Territorial Health Officials. *Assessing Policy Barriers to Effective Public Health Response in the H1N1 Influenza Pandemic: Project Report to the Centers for Disease Control and Prevention*, June 2010. https://www.astho.org/Programs/Infectious-Disease/H1N1/H1N1-Barriers-Project-Report-Final-hi-res/.

Ayyoubzadeh, Seyed Mohammad, Seyed Mehdi Ayyoubzadeh, Hoda Zahedi, Mahnaz Ahmadi, and Sharareh R Niakan Kalhori. "Predicting COVID-19 Incidence Through Analysis of Google Trends Data in Iran: Data Mining and Deep Learning Pilot Study." *JMIR Public Health and Surveillance* 6, no. 2 (2020). https://doi.org/10.2196/18828.

Bai, Zhihua, Yue Gong, Xiaodong Tian, Ying Cao, Wenjun Liu, and Jing Li. "The Rapid Assessment and Early Warning Models for COVID-19" *Virologica Sinica*. 35, 272–279 (2020). https://doi.org/10.1007/s12250-020-00219-0.

Baird, Robert P. "What Went Wrong with Coronavirus Testing in the U.S." *The New Yorker*, March 16, 2020. https://www.newyorker.com/news/news-desk/what-went-wrong-with-coronavirus-testing-in-the-us.

Bansal, Agam, Rana Prathap Padappayil, Chandan Garg, Anjali Singal, Mohak Gupta, and Allan Klein. "Utility of Artificial Intelligence Amidst the COVID 19 Pandemic: A Review." *Journal of Medical Systems* 44, no. 9 (2020). https://doi.org/10.1007/s10916-020-01617-3.

Barda, Noam, Dan Riesel, Amichay Akriv, Joseph Levy, Uriah Finkel, Gal Yona, Daniel Greenfield, et al. "Developing a COVID-19 mortality risk prediction model when individual-level data are not available." *Nature Communications* 11, 4439 (2020). https://doi.org/10.1038/s41467-020-18297-9.

Barker, Joanne. "Online Ventilator Training Addresses COVID-19 Clinician Shortage." Boston Children's Discoveries, April 23, 2020. https://discoveries.childrenshospital.org/ventilator-training-covid-19/.

Bazzoli, Fred. "COVID-19 Emergency Shows Limitations of Nationwide Data Sharing Infrastructure." *Healthcare IT News,* June 2, 2020. https://www.healthcareitnews.com/news/covid-19-emergency-shows-limitations-nationwide-data-sharing-infrastructure

Behnam, Mohammad, Arnav Dey, Tony Gambell, and Vaibhav Talwar. "COVID-19: Overcoming Supply Shortages for Diagnostic Testing." McKinsey, July 15, 2020. https://view.ceros.com/mckinsey/coronavirus-promo-video-desktop.

Blanc, Florentin. "Regulatory Delivery Lessons From COVID-19 Responses." *The Regulatory Review*. May 28, 2020. https://www.theregreview.org/2020/05/28/blanc-regulatory-delivery-lessons-covid-19-responses/.

Boburg, Shawn, Robert O'Harrow Jr., Neena Satija, and Amy Goldstein. "Inside the Coronavirus Testing Failure: Alarm and Dismay among the Scientists Who Sought to Help." *The Washington Post*, April 3, 2020. https://www.washingtonpost.com/investigations/2020/04/03/coronavirus-cdc-test-kits-public-health-labs/.

Borio, Luciana and Jesse L. Goodman. "A vaccine alone won't stop Covid-19. We also need a trusted plan for it." STAT. September 17, 2020. https://www.statnews.com/2020/09/17/vaccine-alone-wont-stop-covid-19-we-also-need-a-plan-for-it/.

Brandom, Russel and Adi Robertson. "Apple and Google are Building a Coronavirus Tracking System into iOS and Android." *The Verge,* April 10, 2020. https://www.theverge.com/2020/4/10/21216484/google-apple-coronavirus-contact-tracing-bluetooth-location-tracking-data-app.

Branswell, Helen and Adam Feuerstein. "Sanofi, a Straggler in the Covid-19 Vaccine Race, Accelerates Its Plans." *STAT+ Biopharma* (blog), June 23, 2020. https://www.statnews.com/2020/06/23/sanofi-a-straggler-in-the-covid-19-vaccine-race-accelerates-its-plans/.

Bregu, Migena, Simon J. Draper, Adrian V. S. Hill, and Brian M. Greenwood. "Accelerating Vaccine Development and Deployment: Report of a Royal Society Satellite Meeting." *Philosophical Transactions of the Royal Society B: Biological Sciences* 366, no. 1579 (2011): 2841–49. https://doi.org/10.1098/rstb.2011.0100.

Bronstein, Scott, Curt Devine, and Drew Griffin. "How the government delayed coronavirus testing." Cable News Network. April 10, 2020. https://edition.cnn.com/2020/04/09/politics/coronavirus-testing-cdc-fda-red-tape-invs/index.html.

Camillo, Jim. "Manufacturers Shift to PPE Production to Fight COVID-19 Pandemic." *Assembly*, June 17, 2020. https://www.assemblymag.com/articles/95741-manufacturers-shift-to-ppe-production-to-fight-covid-19-pandemic?v=preview.

Carey, Benedict. "Can an Algorithm Predict the Pandemic's Next Moves?" *The New York Times*. July 2, 2020. https://www.nytimes.com/2020/07/02/health/santillana-coronavirus-model-forecast.html.

Centers for Disease Control and Prevention. "Bridging Public Health and Health Care: Better Exchange, Better Data." October 27, 2020. https://www.cdc.gov/surveillance/projects/bridging-public-health-and-health-care-better-exchange-better-data.html.

Centers for Disease Control and Prevention. *COVID-19 Vaccination Program Interim Playbook for Jurisdiction Operations*. October 29, 2020. https://www.cdc.gov/vaccines/imz-managers/downloads/COVID-19-Vaccination-Program-Interim_Playbook.pdf.

Centers for Disease Control and Prevention. Ebola Virus Disease. "Considerations for U.S. Healthcare Facilities to Ensure Adequate Supplies of Personal Protective Equipment (PPE) for Ebola Preparedness," January 5, 2016. https://www.cdc.gov/vhf/ebola/healthcare-us/ppe/supplies.html.

Centers for Disease Control and Prevention. "'Excess Death' Data Point to Pandemic's True Death Toll." October 30, 2020. https://www.cdc.gov/nchs/covid19/articles/excess-death.htm

Centers for Disease Control and Prevention. *Interim Updated Planning Guidance On: Allocating and Targeting Pandemic Influenza Vaccine During an Influenza Pandemic*. https://www.cdc.gov/flu/pandemic-resources/pdf/2018-Influenza-Guidance.pdf.

Centers for Disease Control and Prevention, Public Health Surveillance and Data. "Data Modernization Initiative." https://www.cdc.gov/surveillance/surveillance-data-strategies/data-IT-transformation.html

Centers for Disease Control and Prevention. "Reporting and Coding Deaths Due to COVID-19." May 20, 2020. https://www.cdc.gov/nchs/covid19/coding-and-reporting.htm

Chen, Elaine. "From 'Freezer Farms' to Jets, Logistics Operators Prepare for a Covid-19 Vaccine." *The Wall Street Journal*, August 28, 2020. https://www.wsj.com/articles/from-freezer-farms-to-jets-logistics-operators-prepare-for-a-covid-19-vaccine-11598639012?mod=flipboard.

Chen, Jiahui, Rui Wang, Menglun Wang, and Guo-Wei Wei. "Mutations Strengthened SARS-CoV-2 Infectivity." *Journal of Molecular Biology*, Volume 432, Issue 19, 2020, Pages 5212-5226, ISSN 0022-2836, https://doi.org/10.1016/j.jmb.2020.07.009.

Cheng V.C., S. Wong, and K. Yuen. "Estimating Coronavirus Disease 2019 Infection Risk in Health Care Workers." *JAMA Network Open*. 2020;3(5):e209687. https://doi.org/10.1001/jamanetworkopen.2020.9687.

Chow, Shein-Chung and Wei Zhang. "Statistical Evaluation of Clinical Trials Under COVID-19 Pandemic." *Therapeutic Innovation & Regulatory Science* (June 2020). https://doi.org/10.1007/s43441-020-00182-8.

Cormac O'Sullivan, Paul Rutten, and Caspar Schatz. "Why Tech Transfer May Be Critical to Beating COVID-19." McKinsey, July 23, 2020. https://view.ceros.com/mckinsey/coronavirus-promo-video-desktop.

COVID-19 Prevention Network. "About Us." Accessed November 12, 2020. https://www.coronaviruspreventionnetwork.org/about-covpn/.

"COVID-19 Related Guidance Documents for Industry, FDA Staff, and Other Stakeholders." U.S. Food and Drug Administration. Accessed November 12, 2020. https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-related-guidance-documents-industry-fda-staff-and-other-stakeholders.

COVIDExitStrategy.org. "Tracking Our COVID-19 Response." Accessed November 11, 2020. https://www.covidexitstrategy.org/

Daley, Jim. "How to Decide Who Should Get a COVID-19 Vaccine First." *Scientific American*, September 3, 2020. https://www.scientificamerican.com/article/how-to-decide-who-should-get-a-covid-19-vaccine-first/.

De Benedetti, Juan E. *CPRD COVID-10 Synthetic Data Specification*. National Institute for Health Research, June 18, 2020. https://www.cprd.com/sites/default/files/CPRD%20Covid%20Data%20Specification%20V1.pdf

DiMasi, Joseph A., Maria I. Florez, Stella Stergiopoulos, Yaritza Peña, Zachary Smith, Michael Wilkinson, and Kenneth A. Getz. "Development Times and Approval Success Rates for Drugs to Treat Infectious Diseases." *Clinical Pharmacology & Therapeutics* 7, no. 2: (September 2019). https://doi.org/10.1002/cpt.1627.

Donohue, Thomas J. "Why Intellectual Property Protection Matters in the Time of Coronavirus." U.S. Chamber of Commerce. June 1, 2020. https://www.uschamber.com/series/above-the-fold/why-intellectual-property-protection-matters-the-time-of-coronavirus.

Ejaz, Hasan, Abdullah Alsrhani, Aizza Zafar, Humera Javed, Kashaf Junaid, Abualgasim E. Abdalla, Khalid O.A. Abosalif, Zeeshan Ahmed, and Sonia Younas. "COVID-19 and Comorbidities: Deleterious Impact on Infected Patients." *Journal of Infection and Public Health*. Elsevier, August 4, 2020. https://www.sciencedirect.com/science/article/pii/S1876034120305943.

Ekins, Sean, Daniel Mietchen, Megan Coffee, Thomas P Stratton, Joel S Freundlich, Lucio Freitas-Junior, Eugene Muratov, Jair Siqueira-Neto, Antony J Williams, and Carolina Andrade. "Open Drug Discovery for the Zika Virus." *F1000Research* 5 (2016): 150. https://doi.org/10.12688/f1000research.8013.1.

Euchi, Jalel. "Do Drones Have a Realistic Place in a Pandemic Fight for Delivering Medical Supplies in Healthcare Systems Problems?" *Chinese Journal of Aeronautics* (2020). https://doi.org/10.1016/j.cja.2020.06.006.

Extance, Andy. "Scrambling and Gambling to Scale up Covid-19 Medicines." *Chemistry World*, July 2, 2020. https://www.chemistryworld.com/news/scrambling-and-gambling-to-scale-up-covid-19-medicines/4012085.article.

Fairbanks, Katie. "COVID-19 Data Sharing Pits Privacy Against Public Safety." *Government Technology,* July 23, 2020. https://www.govtech.com/health/COVID-19-Data-Sharing-Pits-Privacy-Against-Public-Safety.html

Finlay, Brett B., Raymond H. See, and Robert C. Brunham. "Rapid response research to emerging infectious diseases: lessons from SARS." *Nature Reviews Microbiology 2, 602–607 (2004)*. https://dx.doi.org/10.1038%2Fnrmicro930.

Fisher, Kiva A., Mark W. Tenforde, Leora R. Feldstein, Christopher J. Lindsell, Nathan I. Shapiro, D. Clark Files, Kevin W. Gibbs, et al. "Community and Close Contact Exposures Associated with COVID-19 Among Symptomatic Adults ≥18 Years in 11 Outpatient Health Care Facilities — United States, July 2020." CDC Morbidity and Mortality Weekly Report 69, no. 36 (September 11, 2020). https://www.cdc.gov/mmwr/volumes/69/wr/mm6936a5.htm

Ford, Dee, Jillian B. Harvey, James McElligott, Kathryn King, Kit N. Simpson, Shawn Valenta, Emily H. Warr, et al. "Leveraging Health System Telehealth and Informatics Infrastructure to Create a Continuum of Services for COVID-19 Screening, Testing, and Treatment." *Journal of the American Medical Informatics Association,* June 30, 2020. https://academic.oup.com/jamia/advance-article/doi/10.1093/jamia/ocaa157/5865271

Fulton, Denise. "FDA Touts Advanced Manufacturing to Address COVID Shortfalls." RAPS Regulatory Focus, August 4, 2020. https://www.raps.org/news-and-articles/news-articles/2020/8/fda-touts-advanced-manufacturing-to-address-covid.

Galford, Chris. "House Health STATISTICS Act Introduced to Improve COVID-19 Data Sharing Efforts." *Homeland Preparedness News,* August 25, 2020. https://homelandprepnews.com/stories/54492-house-health-statistics-act-introduced-to-improve-covid-19-data-sharing-efforts/

Gallagher, Mary Beth. "The Risks of Using 3-D Printing to Make Personal Protective Equipment." Medical Xpress, March 27, 2020. https://medicalxpress.com/news/2020-03-d-personal-equipment.html

Gavi: The Vaccine Alliance. *Cold Chain Equipment Optimisation Platform*. October 2019. https://www.gavi.org/sites/default/files/publications/Cold-chain-equipment-technology-guide.pdf.

Gelles, David. "How to Ship a Vaccine at –80°C, and Other Obstacles in the Covid Fight." *The New York Times*. September 18, 2020. https://www.nytimes.com/2020/09/18/business/coronavirus-covid-vaccine-cold-frozen-logistics.html.

Gilroy, Rebecca. "Covid-19 Ventilator Appeal 'Pointless' without Staff and Other Kit." Nursing Times, March 31, 2020. https://www.nursingtimes.net/news/coronavirus/covid-19-ventilator-appeal-pointless-without-staff-and-other-kit-16-03-2020/.

Grimes, Howard D., Thomas R. Kurfess, Gabriela F. Ciocarlie, Dongyan Xu, and Lisa Strama. "Pandemic Adaptive Supply Chains Need a Future-Proof Approach." UTSA Today, June 12, 2020. https://www.utsa.edu/today/2020/06/story/pandemic-adaptive-supply-chain.html.

Haendel, Melissa, Christopher G. Chute, and Kenneth Gersing. "The National COVID Cohort Collaborative (N3C): Rationale, Design, Infrastructure, and Deployment." *Journal of the American Medical Informatics Association* (2020). https://academic.oup.com/jamia/advance-article/doi/10.1093/jamia/ocaa196/5893482

Hamasaki, Toshimitsu, Frank Bretz, Freda Cooner, Lisa M. LaVange, and Martin Posch. (2020) "Statistical Challenges in the Conduct and Management of Ongoing Clinical Trials During the COVID-19 Pandemic." *Statistics in Biopharmaceutical Research* 12:4, pages 397-398. https://doi.org/10.1080/19466315.2020.1828692

Hancock, Jay. "They Pledged to Donate Rights to Their COVID Vaccine, Then Sold Them to Pharma." Kaiser Health News, August 25, 2020. https://khn.org/news/rather-than-give-away-its-covid-vaccine-oxford-makes-a-deal-with-drugmaker/.

Hasel, Joe, Edouard Mathieu, Diana Beltekian, Bobbie Macdonald, Charlie Giattino, Esteban Ortiz-Ospina, Max Roser, and Hannath Ritchie. "A cross-country database of COVID-19 testing." Our World in Data, October 30, 2020. https://ourworldindata.org/coronavirus-testing

Hessel, Luc. "Pandemic Influenza Vaccines: Meeting the Supply, Distribution and Deployment Challenges." *Influenza and Other Respiratory Viruses* 3, no. 4 (2009): 165–70. https://doi.org/10.1111/j.1750-2659.2009.00085.x.

Hopkins, Jared S. "A Covid-19 Vaccine Problem: People Who Are Afraid to Get One." *The Wall Street Journal*, August 28, 2020. https://www.wsj.com/articles/covid-19-vaccine-hesitancy-is-a-growing-concern-for-researchers-health-officials-11598607002?mod=flipboard.

Hosangadi, Divya, Kelsey Lane Warmbrod, Elena K. Martin, Amesh Adalja, Anita Cicero, Thomas Inglesby, Crystal Watson, Matthew Watson, and Nancy Connell. "Enabling Emergency Mass Vaccination: Innovations in Manufacturing and Administration during a Pandemic." *Vaccine* 38, no. 26 (2020): 4167–69. https://doi.org/10.1016/j.vaccine.2020.04.037.

Hu, Yipeng, Joseph Jacob, Geoffrey J. M. Parker, David J. Hawkes, John R. Hurst, and Danail Stoyanov. "The Challenges of Deploying Artificial Intelligence Models in a Rapidly Evolving Pandemic." *Nature Machine Intelligence* 2 no. 6 (2020): 298–300. https://doi.org/10.1038/s42256-020-0185-2.

Huang, Hsin-Chan, Bismark Singh, David P. Morton, Gregory P. Johnson, Bruce Clements, and Lauren Ancel Meyers. "Equalizing Access to Pandemic Influenza Vaccines through Optimal Allocation to Public Health Distribution Points." Edited by David L. Swerdlow. *PLOS ONE* 12, no. 8 (2017). https://doi.org/10.1371/journal.pone.0182720.

Institute of Medicine (US) Committee on the Evaluation of Vaccine Purchase Financing in the United States. *Financing Vaccines in the 21st Century: Assuring Access and Availability*. National Academies Press (US), 2003. https://www.ncbi.nlm.nih.gov/books/NBK221811/.

Iskander, John, Eva McLanahan, Jennifer D. Thomas, J. Brian Henry, David Byrne, and Holly Williams. "Public Health Emergency Response Lessons Learned by Rapid Deployment Force 3, 2006–2016." *American Journal of Public Health* 108, no. S3 (2018): S179–82. https://doi.org/10.2105/AJPH.2018.304496.

Japsen, Bruce. "U.S. Approves Abbott Labs $5 Rapid Covid-19 Test For 'Mass Scale' Use." *Forbes*, August 26, 2020. https://www.forbes.com/sites/brucejapsen/2020/08/26/us-approves-abbott-labs-5-mass-scale-covid-19-test/.

Jarada, T.N., J.G. Rokne, and R. Alhajj. "A review of computational drug repositioning: strategies, approaches, opportunities, challenges, and directions." *Journal of Cheminformatics* 12, 46 (2020). https://doi.org/10.1186/s13321-020-00450-7.

Johns Hopkins Bloomberg School of Public Health, Center for Health Security. "Serology-based Tests for COVID-19." October 27, 2020. https://www.centerforhealthsecurity.org/resources/COVID-19/serology/Serology-based-tests-for-COVID-19.html

Johns Hopkins Bloomberg School of Public Health, Center for Health Security. *Developing a National Strategy for Serology (Antibody Testing) in the United States*. April 22, 2020. https://www.centerforhealthsecurity.org/our-work/pubs_archive/pubs-pdfs/2020/200422-national-strategy-serology.pdf

Johns Hopkins University & Medicine. "Coronavirus Resource Center." Johns Hopkins University & Medicine. Updated Daily. https://coronavirus.jhu.edu/

Johns Hopkins University & Medicine. "Coronavirus Testing Hub." Johns Hopkins University & Medicine. Updated Daily. https://coronavirus.jhu.edu/testing

Kanno-Youngs, Zolan and Jack Nicas. "'Swept Up by FEMA': Complicated Medical Supply System Sows Confusion." *The New York Times*, April 6, 2020. https://www.nytimes.com/2020/04/06/us/politics/coronavirus-fema-medical-supplies.html.

Karako, Kenji, Peipei Song, Yu Chen, and Wei Tang. "Analysis of COVID-19 Infection Spread in Japan Based on Stochastic Transition Model." *BioScience Trends*. International Research and Cooperation Association for Bio & Socio-Sciences Advancement, May 21, 2020. https://www.jstage.jst.go.jp/article/bst/14/2/14_2020.01482/_article.

Kimmel, Stephen E., Robert M. Califf, Natalie E. Dean, Steven N. Goodman, Elizabeth L. Ogburn. "COVID-19 Clinical Trials: A Teachable Moment for Improving Our Research Infrastructure and Relevance." *Annals of Internal Medicine,* October 20, 2020. https://www.acpjournals.org/doi/pdf/10.7326/M20-2959

Kis, Zoltán, Cleo Kontoravdi, Antu K. Dey, Robin Shattock, and Nilay Shah. "Rapid Development and Deployment of High‐volume Vaccines for Pandemic Response." *Journal of Advanced Manufacturing and Processing* 2, no. 3 (2020). https://doi.org/10.1002/amp2.10060.

Koons, Cynthia and Susan Decker. "Inovio Tells Court Supplier Is Holding Covid Vaccine 'Hostage.'" *Bloomberg*, June 3, 2020. https://www.bloomberg.com/news/articles/2020-06-03/inovio-tells-court-supplier-is-holding-covid-vaccine-hostage.

Kotlikoff, Laurence J. and Michael Mina. "Opinion: A Cheap, Simple Way to Control the Coronavirus." *The New York Times*, July 3, 2020. https://www.nytimes.com/2020/07/03/opinion/coronavirus-tests.html.

Krouse, Sarah and Brianna Abbot. "Covid-19 Tests: Answers on Cost, Accuracy and Turnaround Time." *The Wall Street Journal*, September 3, 2020. https://www.wsj.com/articles/covid-19-tests-answers-on-cost-accuracy-and-turnaround-time-11599134378.

Labpulse Staff. "Johns Hopkins Launches COVID-19 Testing Database." *LabPulse,* May 1, 2020. https://www.labpulse.com/index.aspx?sec=sup&sub=gen&pag=dis&ItemID=801136

Lakdawala, Seema S. and Vineet D. Menachery. "The search for a COVID-19 animal model." *Science* 368, no. 6494 (May 29, 2020): 942-943. https://science.sciencemag.org/content/368/6494/942.

Lalmuanawma, Samuel, Jamal Hussain, and Lalrinfela Chhakchhuak. "Applications of machine learning and artificial intelligence for Covid-19 (SARS-CoV-2) pandemic: A review." *Chaos, Solitons & Fractals*, Volume 139, 2020, 110059, ISSN 0960-0779, https://doi.org/10.1016/j.chaos.2020.110059.

Lavecchia, Antonio. "Deep Learning in Drug Discovery: Opportunities, Challenges and Future Prospects." *Drug Discovery Today*. Elsevier Current Trends, August 1, 2019. https://www.sciencedirect.com/science/article/abs/pii/S135964461930282X.

Lemieux, Jacob, Katherine J. Siddle, Bennett M. Shaw, Christine Loreth, Stephen F. Schaffner, Adrianne Gladden-Young, Gordon Adams, et al. "Phylogenetic Analysis of SARS-CoV-2 in the Boston Area Highlights the Role of Recurrent Importation and Superspreading Events." *MedRxiv* Vol. 1 (August 2020). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7457619/

Lipsitch M. and M. Santillana. (2019) Enhancing Situational Awareness to Prevent Infectious Disease Outbreaks from Becoming Catastrophic. In: *Current Topics in Microbiology and Immunology*. Springer, Berlin, Heidelberg. https://doi.org/10.1007/82_2019_172.

Liu, Xiaoxuan, Samantha Cruz Rivera, David Moher, Melanie J. Calvert, Alastair K. Denniston, The SPIRIT-AI and CONSORT-AI Working Group. "Reporting guidelines for clinical trial reports for interventions involving artificial intelligence: the CONSORT-AI extension." *Nature Medicine* 26, 1364–1374 (2020). https://doi.org/10.1038/s41591-020-1034-x.

Loiacono, Matthew M., Nicholas Mitsakakis, Jeffrey C. Kwong, Gabriela B. Gomez, Ayman Chit, and Paul Grootendorst. "Development and Validation of a Clinical Prediction Tool for Seasonal Influenza Vaccination in England." *JAMA Network Open* 3, no. 6 (2020). https://doi.org/10.1001/jamanetworkopen.2020.7743.

Lu, Fred S., Andre T. Nguyen, Nicholas B. Link, Jessica T. Davis, Matteo Chinazzi, Xinyue Xiong, Alessandro Vespignani, Marc Lipsitch, and Mauricio Santillana. "Estimating the Cumulative Incidence of COVID-19 in the United States Using Four Complementary Approaches" medRxiv 2020.04.18.20070821. https://doi.org/10.1101/2020.04.18.20070821

Lurie, Nicole, Melanie Saville, Richard Hatchett, and Jane Halton. "Developing Covid-19 Vaccines at Pandemic Speed." *New England Journal of Medicine*, March 30, 2020. https://doi.org/10.1056/NEJMp2005630.

Macdonald, Gareth John. "Single-Use Tech Key for Capacity Hike Required for COVID-19." Genetic Engineering and Biotechnology News, May 4, 2020. https://www.genengnews.com/topics/bioprocessing/single-use-tech-key-for-capacity-hike-required-for-covid-19/.

Malone, Brandon, Boris Simovski, Clément Moliné, Jun Cheng, Marius Gheorghe, Hugues Fontenelle, Ioannis Vardaxis, et al. "Artificial Intelligence Predicts the Immunogenic Landscape of SARS-CoV-2: toward Universal Blueprints for Vaccine Designs." bioRxiv. Cold Spring Harbor Laboratory, January 1, 2020. https://www.biorxiv.org/content/10.1101/2020.04.21.052084v1.

Malone, Katie. "Pandemic Advances Cybersecurity Efforts at HHS as Agency Becomes Bigger Target, CISO Says." MeriTalk. August 19, 2020. https://www.meritalk.com/articles/pandemic-advances-cybersecurity-efforts-at-hhs-as-agency-becomes-bigger-target-ciso-says/.

Mandavilli, Apoorva. "Your Coronavirus Test is Positive. Maybe it Shouldn't Be." *The New York Times,* August 29, 2020. https://www.nytimes.com/2020/08/29/health/coronavirus-testing.html

McGinley, Laurie and Carolyn Y. Johnson. "FDA poised to announce tougher standards for a covid-19 vaccine that make it unlikely one will be cleared by Election Day." *The Washington Post*. September 22, 2020. https://www.washingtonpost.com/health/2020/09/22/fda-covid-vaccine-approval-standard/.

Mervosh, Sarah and Manny Fernandez. "Months into Virus Crisis, U.S. Cities Still Lack Testing Capacity." *The New York Times*, July 15, 2020. https://www.nytimes.com/2020/07/06/us/coronavirus-test-shortage.html.

Meyer, Robinson and Alexis C. Madrigal. "How to Test Every American for COVID-19, Every Day." *The Atlantic*, August 14, 2020. https://www.theatlantic.com/health/archive/2020/08/how-to-test-every-american-for-covid-19-every-day/615217/.

Meyer, Robinson and Alexis C. Madrigal. "The Plan That Could Give Us Our Lives Back." *The Atlantic,* August 14, 2020. https://www.theatlantic.com/health/archive/2020/08/how-to-test-every-american-for-covid-19-every-day/615217/

Michael-Kordatou, I., P. Karaolia, and D. Fatta-Kassinos. "Sewage analysis as a tool for the COVID-19 pandemic response and management: the urgent need for optimised protocols for SARS-CoV-2 detection and quantification." *Journal of Environmental Chemical Engineering*, Volume 8, Issue 5, 2020, 104306, ISSN 2213-3437, https://doi.org/10.1016/j.jece.2020.104306.

Miller, Joe and Hannah Kuchler. "Drugmakers Race to Scale up Vaccine Capacity." Financial Times, April 28, 2020. https://www.ft.com/content/87d1170a-78bc-11ea-bd25-7fd923850377

Mina, Michael J., Roy Parker, and Daniel B. Larremore. "Rethinking Covid-19 Test Sensitivity — A Strategy for Containment." *New England Journal of Medicine*. Perspective. (2020). https://doi.org/10.1056/NEJMp2025631.

Miri, Aaron, and Daniel P. O'Neill. "Accelerating Data Infrastructure For COVID-19 Surveillance and Management." *Health Affairs,* April 14, 2020. https://www.healthaffairs.org/do/10.1377/hblog20200413.644614/full/

Morens, David M. and Anthony S. Fauci. "Emerging Pandemic Diseases: How We Got to COVID-19." *Cell* 182, no. 5 (2020): 1077-92. https://doi.org/10.1016/j.cell.2020.08.021.

Mostaghimi, Arash, Marc-Joseph Antonini, Deborah Plana, Philip D. Anderson, Brandon Beller, Edward W. Boyer, Amber Fannin, et al. "Regulatory and Safety Considerations in Deploying a Locally Fabricated, Reusable Face Shield in a Hospital Responding to the COVID-19 Pandemic." *Med*, June 19, 2020. https://doi.org/10.1016/j.medj.2020.06.003.

Murray, Brendan and Riley Griffin. "The Supply Chain to Save the World Is Unprepared for a Coronavirus Vaccine." ET HealthWorld. *The Economic Times*. July 25, 2020. https://health.economictimes.indiatimes.com/news/diagnostics/the-supply-chain-to-save-the-world-is-unprepared-for-a-coronavirus-vaccine/77166407.

The National Academies of Sciences, Engineering, Medicine. *Genomic Epidemiology Data Infrastructure Needs for SARS-CoV-2: Modernizing Pandemic Response Strategies*. The National Academic Press, 2020. https://www.ncbi.nlm.nih.gov/books/NBK562770/

National Institutes of Health. "Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)." Accessed November 12, 2020. https://www.nih.gov/research-training/medical-research-initiatives/activ.

National Institutes of Health. "NIH leadership details unprecedented initiative to ramp up testing technologies for COVID-19." July 22, 2020. https://www.nih.gov/news-events/news-releases/nih-leadership-details-unprecedented-initiative-ramp-testing-technologies-covid-19.

National Institutes of Health. "Rapid Acceleration of Diagnostics (RADx)." Accessed November 12, 2020. https://www.nih.gov/research-training/medical-research-initiatives/radx.

Naude, Wim. "Artificial Intelligence vs COVID-19: Limitations, Constraints and Pitfalls." *Ali & Society* (April 2020). https://www.researchgate.net/publication/340982362_Artificial_intelligence_vs_COVID-19_limitations_constraints_and_pitfalls

Neisloss, Liz. "Vaccine Manufacturing at Pandemic Speed." WGBH News, May, 28, 2020. https://www.wgbh.org/news/local-news/2020/05/27/vaccine-manufacturing-at-pandemic.speed .

New York Times Staff. "Almost 500 Million Children Are Cut Off from School in Pandemic." *The New York Times,* August 26, 2020. https://www.nytimes.com/2020/08/26/world/covid-19-coronavirus.html?referringSource=articleShare

Nicola, Maria, Zaid Alsafi, Catrin Sohrabi, Ahmed Kerwan, Ahmed Al-Jabir, Christos Iosifidis, Maliha Agha, and Riaz Agha. "The Socio-Economic Implications of the Coronavirus Pandemic (COVID-19): A Review." *International Journal of Surgery* 78 (2020): 185–93. https://doi.org/10.1016/j.ijsu.2020.04.018.

Oakes, Kari. "NIH kicks off COVID-19 vaccine, monoclonal antibody research network." Regulatory Affairs Professionals Society. July 8, 2020. https://www.raps.org/news-and-articles/news-articles/2020/7/nih-kicks-off-covid-19-vaccine-and-monoclonal-anti.

O'Leary, Colin, Amritha Jayanti, and Michael Mina. "Considering Public Purpose in the Time of COVID-19." Harvard Kennedy School of Government, Belfer Center for Science and International Affairs, April 2020. https://www.belfercenter.org/publication/considering-public-purpose-time-covid-19.

Ong, Edison, Mei U. Wong, Anthony Huffman, and Yongqun He. "COVID-19 Coronavirus Vaccine Design Using Reverse Vaccinology and Machine Learning." *Frontiers in Immunology*, June 15, 2020. https://www.frontiersin.org/articles/10.3389/fimmu.2020.01581/full.

Open Source Medical Supplies. "Frequently Asked Questions." Accessed November 17, 2020. https://opensourcemedicalsupplies.org/about/faq/.

Pagliusi, Sonia , Stephen Jarrett, Benoit Hayman, Ulrike Kreysa, Sai D. Prasad, and Martin Reers, Pham Hong Thai, et al. "Emerging Manufacturers Engagements in the COVID –19 Vaccine Research, Development and Supply." *Vaccine* 38, no. 34 (July 22, 2020): 5418–23. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7287474/ .

Panda, Pritam Kumar, Murugan Natarajan Arul, Paritosh Patel, Suresh K. Verma, Wei Luo, Horst-Günter Rubahn, Yogendra Kumar Mishra, Mrutyunjay Suar, and Rajeev Ahuja. "Structure-Based Drug Designing and Immunoinformatics Approach for SARS-CoV-2." *Science Advances*. American Association for the Advancement of Science, July 1, 2020. https://advances.sciencemag.org/content/6/28/eabb8097.

Parvathaneni, Vineela and Vivek Gupta. "Utilizing drug repurposing against COVID-19 – Efficacy, limitations, and challenges." *Life Sciences*, Volume 259, 2020, 118275, ISSN 0024-3205, https://doi.org/10.1016/j.lfs.2020.118275.

Patel, Anita, Maryann M. D'Alessandro, Karen J. Ireland, W. Greg Burel, Elaine B. Wencil, and Sonja A. Rasmussen. "Personal Protective Equipment Supply Chain: Lessons Learned from Recent Public Health Emergency Responses." *Health Security* 15, no 3 (2017): 244–52. https://doi.org/10.1089/hs.2016.0129.

Pathan, Refat Khan, Munmun Biswas, and Mayeen Uddin Khandaker. "Time series prediction of COVID-19 by mutation rate analysis using recurrent neural network-based LSTM model." *Chaos, Solitons & Fractals*, Volume 138, 2020, 110018, ISSN 0960-0779, https://doi.org/10.1016/j.chaos.2020.110018.

Pfizer. "Scaling Up to Manufacture and Supply a COVID-19 Vaccine, If Approved." Accessed November 17, 2020. https://www.pfizer.com/news/hot-topics/scaling_up_to_manufacture_and_supply_a_covid_19_vaccine_if_approved.

Pittsburgh Press Releases. "Covid-19 Affinity Chromatography Resins Market: Soaring Demand Assures Motivated Revenue Share During 2028."September 19, 2020. http://pittsburghpressreleases.com/2020/09/covid-19-affinity-chromatography-resins-market-soaring-demand-assures-motivated-revenue-share-during-2028/.

Pollack, Andrew and Donald G. McNeil, Jr. "A Nation Battling Flu, and Short Vaccine Supplies." *The New York Times*, October 25, 2009. https://www.nytimes.com/2009/10/26/health/26flu.html?ref=todayspaper&pagewanted=print.

Pollicino, Oreste and Marco Bassini. "Intellectual Property Resilience in the Era of COVID-19." Filodiritto. May 2020. https://www.filodiritto.com/intellectual-property-resilience-era-covid-19.

Prevent Epidemics. *Tracking COVID-19 in the United States: From Information Catastrophe to Empowered Communities.* July 23, 2020. https://preventepidemics.org/wp-content/uploads/2020/07/RTSL_Tracking-COVID-19-in-the-United-States_-7-23-2020.pdf

Qiu, Xueting, Venkata R. Duvvuri, and Justin Bahl. 2019. "Computational Approaches and Challenges to Developing Universal Influenza Vaccines." *Vaccines* 7, no. 2: 45. https://pubmed.ncbi.nlm.nih.gov/31141933/

Quinn, Sandra Crouse, Supriya Kumar, Vicki S. Freimuth, Kelley Kidwell, and Donald Musa. "Public Willingness to Take a Vaccine or Drug Under Emergency Use Authorization during the 2009 H1N1 Pandemic." *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science* 7, no. 3 (October 2009): 275-290. https://dx.doi.org/10.1089%2Fbsp.2009.0041.

Ragoza, Matthew, Joshua Hochuli, Elisa Idrobo, Jocelyn Sunseri, and David Ryan Koes. "Protein–Ligand Scoring with Convolutional Neural Networks." *Journal of Chemical Information and Modeling* 57, no. 4 (April 3, 2017): 942–57. https://pubs.acs.org/doi/abs/10.1021/acs.jcim.6b00740

Rastelli, Giulio, and Luca Pinzi. "Refinement and Rescoring of Virtual Screening Results." *Frontiers in Chemistry* 7 (2019). https://doi.org/10.3389/fchem.2019.00498.

Reader, David, Jiabin Li, Anthony McDonnell, and Prashant Yadav. "Modelling the Manufacturing Process for COVID-19 Vaccines: Our Approach." Center for Global Development. August 19, 2020. https://www.cgdev.org/blog/modelling-manufacturing-process-covid-19-vaccines-our-approach

Réda, Clémence, Emilie Kaufmann, and Andrée Delahaye-Duriez. "Machine Learning Applications in Drug Development." *Computational and Structural Biotechnology Journal* 18 (2020): 241–52. https://doi.org/10.1016/j.csbj.2019.12.006.

Reuters Staff. "U.S. Plans to Distribute COVID-19 Vaccine Immediately after Regulators Authorise It." Reuters, September 16, 2020. https://uk.reuters.com/article/uk-health-coronavirus-usa-vaccine-idUKKBN2672FY.

Rivas, Ana, Peter Loftus, and Alberto Cervantes. "Covid-19 Vaccines: What's Coming and When?" *The Wall Street Journal*, October 22, 2020. https://www.wsj.com/articles/covid-19-vaccines-whats-coming-and-when-11598882964.

Roberson, Bill. "Health Officials Say 'Ventilators' Donated By Tesla Are Wrong Type And Not Powerful Enough." *Forbes*, April 4, 2020. https://www.forbes.com/sites/billroberson/2020/04/04/health-officials-say-ventilators-donated-by-tesla-are-wrong-type-and-not-powerful-enough/.

Romney, Douglas, Hannah Fox, Stephanie Carlson, Daniel Bachmann, Donal O'Mathuna, and Nicholas Kman. "Allocation of Scarce Resources in a Pandemic: A Systematic Review of US State Crisis Standards of Care Documents." *Disaster Medicine and Public Health Preparedness* (2020): 1–7. https://doi.org/10.1017/dmp.2020.101.

Rose, Joel. "Yep, Masks and Protective Gear Are Still Hard to Get — Especially for Small Buyers." National Public Radio. August 19, 2020. https://www.npr.org/2020/08/19/903612006/yep-masks-and-protective-gear-are-still-hard-get-especially-for-small-buyers.

Rowan, Neil J. and John G. Laffey. "Challenges and Solutions for Addressing Critical Shortage of Supply Chain for Personal and Protective Equipment (PPE) Arising from Coronavirus Disease (COVID19) Pandemic – Case Study from the Republic of Ireland." *Science of The Total Environment* 725 (2020): 138532. https://doi.org/10.1016/j.scitotenv.2020.138532.

Sanyaolu, Adekunle, Chuku Okorie, Aleksandra Marinkovic, Risha Patidar, Kokab Younis, Priyank Desai, Zaheeda Hosein, Inderbir Padda, Jasmine Mangat, and Mohsin Altaf. "Comorbidity and its Impact on Patients with COVID-19." *SN Comprehensive Clinical Medicine* 2, 1069–1076 (2020). https://doi.org/10.1007/s42399-020-00363-4.

Saul Ewing Arnstein & Lehr LLP. "Manufacturing and Distributing Personal Protective Equipment in Response to COVID-19: What Higher Education Institutions Need to Know." JD Supra, April 16, 2020. https://www.jdsupra.com/legalnews/manufacturing-and-distributing-personal-43275/.

Schwartz, Jason L. "Evaluating and Deploying Covid-19 Vaccines — The Importance of Transparency, Scientific Integrity, and Public Trust." *New England Journal of Medicine* 2020; 383:1703-1705. https://www.nejm.org/doi/full/10.1056/NEJMp2026393.

Schoch-Spana, Monica, Gigi Kwik Gronvall, Emily Brunson, Tara Kirk Sell, Sanjana Ravi, Matthew P. Shearer, and Hannah Collins. *How to Steward Medical Countermeasures and Public Trust in an Emergency: A Communication Casebook for FDA and its Public Health Partners*. Center for Health Security, Johns Hopkins Bloomberg School of Public Health. November 2016. https://www.centerforhealthsecurity.org/our-work/events/2016%20FDA%20MCM/FDA_Casebook.pdf.

Sengupta, Sohini, Sareeta Mugde, and Garima Sharma. "Covid-19 Pandemic Data Analysis and Forecasting Using Machine Learning Algorithms." medRxiv. Cold Spring Harbor Laboratory Press, January 1, 2020. https://www.medrxiv.org/content/10.1101/2020.06.25.20140004v2.

Servick, Kelly. "'Huge Hole' in COVID-19 Testing Data Makes It Harder to Study Racial Disparities." *Science* (July 10, 2020). https://www.sciencemag.org/news/2020/07/huge-hole-covid-19-testing-data-makes-it-harder-study-racial-disparities.

Shalby, Colleen. "Serious Breakdown in California Systems Causes Inaccurate Coronavirus Numbers." *Los Angeles Times*, August 5, 2020. https://www.latimes.com/california/story/2020-08-05/coronavirus-test-results-collecting-hampering-pandemic-response.

Sheikh, Knvul. "Find a Vaccine. Next: Produce 300 Million Vials of It." *The New York Times*, May 1, 2020. https://www.nytimes.com/2020/05/01/health/coronavirus-vaccine-supplies.html.

Shi, Jun, Yubo Xiao, Yiting Zhang, Donghao Geng, Danhua Cong, Kevin X Shi, and Richard J Knapp. "Challenges of Drug Development during the COVID-19 Pandemic: Key Considerations for Clinical Trial Designs." *British Journal of Clinical Pharmacology* (2020). https://doi.org/10.22541/au.158705386.69295078.

Shokrani, Alborz, Evripides G. Loukaides, Edward Elias, and Alexander J. G. Lunt. "Exploration of Alternative Supply Chains and Distributed Manufacturing in Response to COVID-19; a Case Study of Medical Face Shields." *Materials & Design* 192 (July 1, 2020): 108749. https://doi.org/10.1016/j.matdes.2020.108749.

Shuren, Jeffrey and Timothy Stenzel. "Covid-19 Molecular Diagnostic Testing — Lessons Learned." *New England Journal of Medicine* 2020; 383:e97. https://www.nejm.org/doi/full/10.1056/NEJMp2023830.

Siriwardhana, Yushan, Gürkan Gür, Mika Ylianttila, and Madhusanka Liyanage. "The Role of 5G for Digital Healthcare against COVID-19 Pandemic: Opportunities and Challenges." *ICT Express* (2020). https://doi.org/10.1016/j.icte.2020.10.002.

Society for Healthcare Organization Procurement Professionals. Correspondence. April 7, 2020. http://cdn.cnn.com/cnn/2020/images/04/16/shopp.covid.ppd.costs.analysis_.pdf.

Spiro, Topher and Zeke Emanuel. "A Comprehensive COVID-19 Vaccine Plan." Center for American Progress, July 28, 2020. https://www.americanprogress.org/issues/healthcare/reports/2020/07/28/488196/comprehensive-covid-19-vaccine-plan/.

Steckelberg, Aaron, Carolyn Y. Johnson, Gabriel Florit, and Chris Alcantara. "These Are the Top Coronavirus Vaccines to Watch." *The Washington Post*, November 3, 2020. https://www.washingtonpost.com/graphics/2020/health/covid-vaccine-update-coronavirus/.

Steenhuysen, Julie and Kate Kelland Reuters. "Vaccine Makers Face Biggest Medical Manufacturing Feat in History." *St. Louis Dispatch*, June 25, 2020. https://www.stltoday.com/business/local/vaccine-makers-face-biggest-medical-manufacturing-feat-in-history/article_b350bdd1-d671-5683-baf6-e0d80dc9ca9a.html.

Stein, Robert. "Can the U.S. Use Its Growing Supply of Rapid Tests to Stop the Virus?" National Public Radio. October 1, 2020. https://www.npr.org/sections/health-shots/2020/10/01/915793729/can-the-u-s-use-its-growing-supply-of-rapid-tests-to-stop-the-virus.

Stolberg, Sheryl Gay. "Health Experts Warn About Perils of New Virus Data Collection System." *The New York Times,* August 12, 2020. https://www.nytimes.com/2020/08/12/us/politics/health-experts-warning-coronavirus-data.htm

Strasburg, Jenny. "If Oxford's COVID-19 Vaccine Succeeds, Layers of Private Investors Could Profit." *The Wall Street Journal*. August 2, 2020. https://www.wsj.com/articles/if-oxfords-covid-19-vaccine-succeeds-layers-of-private-investors-could-profit-11596373722.

Tekumalla, Ramya and Juan M. Banda. "Characterizing Drug Mentions in COVID-19 Twitter Chatter." arXiv.org, October 9, 2020. https://arxiv.org/abs/2007.10276.

Thompson, Stuart A. "How Long Will a Vaccine Really Take." Opinion. *The New York Times*. April 30, 2020. https://www.nytimes.com/interactive/2020/04/30/opinion/coronavirus-covid-vaccine.html

Tirrell, Meg and Leanne Miller. "Moderna slows coronavirus vaccine trial enrollment to ensure minority representation, CEO says." CNBC. September 4, 2020. https://www.cnbc.com/2020/09/04/moderna-slows-coronavirus-vaccine-trial-t-to-ensure-minority-representation-ceo-says.html.

Toner, Eric, Anne Barnill, Carleigh Krubiner, Justin Bernstein, Lois Privor-Dumm, Matthew Watson, Elena Martin, et al.. *Interim Framework for COVID-19 Vaccine Allocation and Distribution in the United States*. Baltimore, MD: Johns Hopkins Center for Health Security, 2020. https://www.centerforhealthsecurity.org/our-work/pubs_archive/pubs-pdfs/2020/200819-vaccine-allocation.pdf

Torres, Pedro H. M., Ana C. R. Sodero, Paula Jofily, and Floriano P. Silva Jr. "Key Topics in Molecular Docking for Drug Design." *International Journal of Molecular Sciences* 20, no. 18 (2019): 4574. https://doi.org/10.3390/ijms20184574.

Tromberg, Bruce J., Tara A Schwetz, Eliseo J. Pérez-Stable, Richard J. Hodes, Richard P. Woychik, Rick A. Bright, Rachael L. Fleurence, and Francis S. Collins. "Rapid Scaling Up of Covid-19 Diagnostic Testing in the United States — The NIH RADx Initiative." *New England Journal of Medicine* 2020; 383:1071-1077. https://www.nejm.org/doi/10.1056/NEJMsr2022263.

Upadhaya, Samik, Jia Xin Yu, Cristina Oliva, Megan Hooton, Jeffrey Hodge, and Vanessa M. Hubbard-Lucey. "Impact of COVID-19 on oncology clinical trials." *Nature Reviews Drug Discovery* 19, 376-377 (2020) May 18, 2020. https://www.nature.com/articles/d41573-020-00093-1.

UPS. "UPS Mobilizes Against Coronavirus in Collaboration with Global Customers and U.S. Agencies." March 30, 2020. http://www.globenewswire.com/news-release/2020/03/30/2008355/0/en/UPS-Mobilizes-Against-Coronavirus-In-Collaboration-With-Global-Customers-And-U-S-Agencies.html.

U.S. Department of Health and Human Services. "Data Harmonization and Sharing Are Essential for COVID-19 Research." July 8, 2020. https://www.nia.nih.gov/research/blog/2020/07/data-harmonization-and-sharing-are-essential-covid-19-research

U.S. Department of Health and Human Services. "Fact Sheet: Explaining Operation Warp Speed." August 12, 2020. https://www.hhs.gov/coronavirus/explaining-operation-warp-speed/index.html.

U.S. Department of Health and Human Services. "HIPPA and COVID-19." August 31, 2020. https://www.hhs.gov/hipaa/for-professionals/special-topics/hipaa-covid19/index.html

U.S. Food and Drug Administration. "Development and Licensure of Vaccines to Prevent COVID-19; Guidance for Industry." June 2020. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/development-and-licensure-vaccines-prevent-covid-19.

U.S. Food and Drug Administration. "Manufacturing, Supply Chain, and Drug and Biological Product During COVID-19 Public Emergency and Answers: Guidance for Industry." August 2020. https://www.fda.gov/media/141312/download.

Van Norman, Gail A. "'Warp Speed' Operations in the COVID-19 Pandemic: Moving Too Quickly?" *JACC: Basic to Translational Science* 5, no. 7 (July 2020): 730-734. https://doi.org/10.1016/j.jacbts.2020.06.001.

Wade, R.C. and O.M.H. Salo-Ahen. "Molecular Modeling in Drug Design." Molecules 2019, 24, 321. https://www.mdpi.com/1420-3049/24/2/321

Wallach, Izhar, Michael Dzamba, and Abraham Heifets. "AtomNet: A Deep Convolutional Neural Network for Bioactivity Prediction in Structure-Based Drug Discovery." arXiv.org, October 10, 2015. https://arxiv.org/abs/1510.02855.

Wang, Xu, Xiaoxi Zhang, and Jiangjiang He. "Challenges to the System of Reserve Medical Supplies for Public Health Emergencies: Reflections on the Outbreak of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Epidemic in China." *BioScience Trends* 14, no. 1 (2020): 3–8. https://doi.org/10.5582/bst.2020.01043.

Weintraub, Karen. "Not Just Ventilators: Staff Trained to Run Them Are in Short Supply." *Scientific American*, April 8, 2020. https://www.scientificamerican.com/article/not-just-ventilators-staff-trained-to-run-them-are-in-short-supply/.

World Health Organization. "New WHO Technical Package Health Data for COVID-19 Response." August 27, 2020. https://www.who.int/news-room/detail/27-08-2020-new-who-technical-package-health-data-for-covid-19-response

World Health Organization. Regional Office for Europe. *Strategic Considerations in Preparing for Deployment of COVID-19 Vaccine and Vaccination in the WHO European Region*. October 9, 2020. https://apps.who.int/iris/bitstream/handle/10665/335940/WHO-EURO2020-1148-40894-55356-eng.pdf?sequence=1&isAllowed=y.

World Health Organization. *Report of the WHO Pandemic Influenza A(H1N1) Vaccine Deployment Initiative*. 2012. https://www.who.int/influenza_vaccines_plan/resources/h1n1_deployment_report.pdf.

World Health Organization. "SCORE Data Collection." August 27, 2020. https://www.who.int/data/data-collection-tools/score#enable

World Health Organization. *SCORE for Health Data Technical Package: Essential Interventions*. World Health Organization, August 27, 2020. https://apps.who.int/iris/handle/10665/334005

World Health Organization. *SCORE for Health Data Technical Package: Tools and Standards for SCORE Essential Interventions*. World Health Organization, August 27, 2020. https://apps.who.int/iris/handle/10665/334006

Wu, Katherine J. "'It's Like Groundhog Day': Coronavirus Testing Labs Again Lack Key Supplies." *The New York Times*, July 23, 2020. https://www.nytimes.com/2020/07/23/health/coronavirus-testing-supply-shortage.html.

Wu, Katherine J. "Rapid Coronavirus Testing." *The New York Times,* August 6, 2020. https://www.nytimes.com/2020/08/06/health/rapid-Covid-tests.html

Xo, Bu and Moritz U.G. Kraemer. "Open Access Epidemiological Data from the COVID-19 Outbreak." *The Lancet Infectious Diseases* Vol. 20 Issue 5 (2020). https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30119-5/fulltext

Yan, Li, Hai-Tao Zhang, Jorge Goncalves, Yang Xiao, Maolin Wang, Yuqi Guo, Chuan Sun, et al. "An interpretable mortality prediction model for COVID-19 patients." *Nature Machine Intelligence* 2, 283–288 (2020). https://doi.org/10.1038/s42256-020-0180-7.

Yee, Hannah, Niki Gallo, and Kim Raymer. "What To Expect From the FDA During (And After) COVID-19." Clinical Leader. April 20, 2020. https://www.clinicalleader.com/doc/what-to-expect-from-the-fda-during-and-after-covid-0001.

Zhao S., S.S. Musa, Q. Lin, J. Ran, G. Yang, W. Wang, Y. Lou, L. Yang, D. Gao, D. He, and M.H. Wang. "Estimating the Unreported Number of Novel Coronavirus (2019-nCoV) Cases in China in the First Half of January 2020: A Data-Driven Modelling Analysis of the Early Outbreak." *Journal of Clinical Medicine*. 2020; 9(2):388. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7074332/

Zlojutro, Aleksa, David Rey, and Lauren Gardner. "A Decision-Support Framework to Optimize Border Control for Global Outbreak Mitigation." *Scientific Reports* 9, no. 1 (2019). https://doi.org/10.1038/s41598-019-38665-w.