



Navigating the World that COVID-19 Made

A Strategy for Revamping the Pandemic Research and Development Preparedness and Response Ecosystem

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Contents

Abbreviations.....v

Executive Summary..... vi

Introduction.....1

The Vaccine R&D Preparedness and Response Ecosystem Defined..... 2

The World that COVID-19 Made..... 10

Gaps and Opportunities in the COVID-19 Vaccine R&D and Response15

Conclusion 34

References..... 35

Annex. COVID-19 Vaccine Development Timeline 45

Abbreviations

BARDA	Biomedical Advanced Research and Development Authority
CDC	US Centers for Disease Control and Prevention
CEPI	Coalition for Epidemic Preparedness Innovations
COVAX	COVID-19 Vaccine Global Access
COVID-19	coronavirus disease 2019
DNA	deoxyribonucleic acid
FDA	US Food and Drug Administration
G7	Group of Seven
G20	Group of Twenty
Gavi	Gavi, the Vaccine Alliance
IHR	International Health Regulations (2005)
LMIC	low- and middle-income country
MERS	Middle East respiratory syndrome
mRNA	messenger RNA
NIAID	US National Institute of Allergy and Infectious Diseases
NIH	US National Institutes for Health
OWS	Operation Warp Speed
PIP Framework	Pandemic Influenza Preparedness Framework
R&D	research and development
RNA	ribonucleic acid
SARS-CoV-1	severe acute respiratory syndrome coronavirus 1
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
WHO	World Health Organization

Executive Summary

The COVID-19 pandemic has revealed that a true, end-to-end research and development (R&D) and response ecosystem—meaning, one that develops, produces, and delivers needed vaccines to global populations in a rapid and equitable fashion—remains an elusive goal. Most low- and middle-income countries (LMICs) have been unable to acquire and administer a sufficient supply of COVID-19 vaccines, and the dearth of vaccines and limited capacity to deliver them are prolonging the pandemic and contributing to destabilizing economies and societies around the world. Multilateral initiatives, bilateral aid, and vaccine donations, though useful, have been slow to arrive and insufficient to provide adequate vaccine coverage for LMIC populations. The consequences of this deeply inequitable global response extend beyond the COVID-19 pandemic. Global initiatives to prepare for and respond to future pandemic threats cannot succeed if LMIC governments believe they will be the last to benefit from vaccines produced as a result of improvements in global disease surveillance, increased sample sharing, or expedited vaccine R&D.

In short, the actions being taken to respond to the COVID-19 crisis are writing the opening chapters to the story of how we will prepare for and respond to the next pandemic threat. To prevent the devastation that has accompanied the COVID-19 pandemic from happening again, we must not only identify the successes and failures that have emerged from the global response, we must also anticipate how our response has changed government, industry, and civil society priorities for the pandemic R&D and response ecosystem in order to confront to future threats.

Beyond its human and economic toll, the COVID-19 pandemic has also exposed and redefined the realities of the global vaccine R&D and response ecosystem in the following ways:

- *There is now widespread recognition that safe and effective vaccines provide unparalleled health, social, and economic benefits during a pandemic.* Multiple governments have already announced new and potentially competing plans to invest in pandemic vaccine R&D and response. For example, China, which hardly shipped any vaccines abroad prior to the pandemic, has now become the largest exporter of COVID-19 vaccines to date.
- *COVID-19 has made it clear that most nations will not share scarce supplies of early vaccines and related inputs in a crisis.* From the United States to Europe to the African Union, efforts are underway to domesticate vaccine manufacturing and their associated supply chains. This “me-first” approach to COVID-19 vaccine allocation could also dim countries’ enthusiasm for participating in future global pooled procurement initiatives and access and benefit sharing arrangements, given the reasonable fear that these arrangements might not be able to provide timely, equitable quantities of vaccines for LMICs in future crises.
- *COVID-19 demonstrated that pandemics can be profitable for vaccine manufacturers.* Record revenues for COVID-19 vaccines has drawn new vaccine developers into the market, but also made them less willing to enter into public sector and nongovernmental organization funding arrangements that impose equitable access requirements that could encumber potential profitmaking.
- *Geopolitics constrained COVID-19 response and threaten future global health security.* Global health emergencies have historically been a cause for increased international cooperation, but the response to the COVID-19 pandemic has been constrained by

geopolitical rivalries. In this context, not all nations will be willing to cooperate closely on national security matters, such as pandemic vaccine R&D and response. Cooperation on pandemic R&D and response may be more feasible in groupings of regional partners or like-minded states, with global cooperation instead focused on promoting common standards and scientific collaboration.

Any future pandemic pathogen that emerges will do so in a world changed by and aware of these realities. To ensure that these lessons are heeded and to prevent the devastation of the present crisis from repeating in the next pandemic, governments, international institutions, and private sector actors must immediately act to address gaps and explore opportunities at each step along the vaccine value chain. The measures to be taken should include:

- ***Develop and fund an inclusive strategy for the R&D of prototype vaccine candidates for future pandemics.*** Although highly effective vaccines against COVID-19 were developed in record time, shortening vaccine development time even further could yield substantial benefits in the next pandemic. To shorten the development timeframe *during* a pandemic, research and preliminary trials must be conducted *before* a pandemic may occur. Candidate vaccines for a representative prototype pathogen within each of the roughly 25 viral families most likely to cause the next pandemic could be developed and taken through Phase 1 clinical evaluation. This would allow the collection of early data on safety, dosage, and schedule of vaccine administration with that particular platform, antigenic target, or other design characteristics. Taking those candidate vaccines through Phase 2 clinical trials could help identify and characterize correlates of protection for those viral families. Conducting preclinical and early-stage clinical research in advance could potentially allow for shorter and much smaller-scale Phase 3 trials when a new virus emerges. Proposals by the Coalition for Epidemic Preparedness Innovations and the US Senate, if enacted and funded, could advance this research and enable vaccines to be developed within 100 days of identification of the next pandemic.
- ***Engage local government and donor financing and policy support to enable global vaccine manufacturing scale up.*** Producing a safe and effective vaccine within 100 days of a pandemic threat being detected would save significant time and lives. However, the benefits of ensuring that every country can administer vaccines at the same pace as most high-income countries have done in the COVID-19 pandemic would be even larger. Establishing vaccine manufacturing capacity in LMICs is essential to achieving this goal, but it should be viewed as a complement, not a near-term substitute, for investing in the economies of scale afforded by centralized production capacity. To succeed, donors and local governments will need to provide sustained financing, support the use of flexible business models, invest in manufacturing innovations, and establish mechanisms to facilitate and sustain technology transfer.
- ***Create and support equitable financing, procurement, and allocation mechanisms to help end COVID-19 and prepare for the future.*** Wealthy and vaccine-producing nations governments will always be able to outbid a multilateral procurement body or seize locally produced vaccine doses in a pandemic. Enabling a more equitable allocation of vaccines in the next pandemic requires creating more supply and procurement mechanisms in which vaccine-producing nations are willing to participate on the same level as LMICs. COVID-19 Vaccines Global Access, or COVAX, has achieved much during this pandemic, but concerns about its performance in the present crisis make it unlikely to be trusted in the next one. Regional mechanisms may

offer the most hope, but they must be established in advance and routinely used to be trusted in future crises.

- ***Strengthen cross-border trade, standardization, and supply chain transparency in order to expand vaccine manufacturing and access during a crisis.*** The widespread use of export restrictions during the COVID-19 pandemic has contributed to unnecessary infections, hospitalizations, and deaths and continues to undermine efforts to prepare for future pandemic threats by discouraging international investments in vaccine and input manufacturing capacity. The threat of export restrictions on vaccines and related inputs should be reduced through adoption of regional trade and investment agreements, standardization of the specialized inputs needed for vaccine production, and greater supply chain transparency.
- ***Build the systems needed to enable vaccine distribution, allocation, and uptake for the next pandemic.*** While inadequate supplies may still be the single biggest factor limiting vaccine coverage globally, COVID-19 has also illustrated the need to devote adequate and timely attention to distributing and allocating vaccines and communicating with the public about vaccine-related risks and benefits. Dedicated plans are needed to ensure that high-priority groups can be vaccinated. Operationally feasible plans are also needed to support risk communication and community engagement and to combat the spread of misinformation and disinformation about vaccines.
- ***Plan for global coordination of postmarket research studies.*** Insufficient coordination of postmarket studies is compromising the ability to track COVID-19 vaccine effectiveness, monitor vaccine escape, and assess optimal dosing and the need for boosters. An independent, but government-supported organization, such as the Coalition for Epidemic Preparedness Innovations, could provide this level of international coordination of follow-on clinical investigations, in consultation with national regulatory authorities and research institutes. The World Health Organization could also assume a greater coordinating role on postmarket research studies by adapting its R&D Blueprint for Action to Prevent Epidemics.

Although COVID-19 has been described as a once-in-a-century crisis, another pandemic could occur at any time, including in the not-to-distant future. Other pandemic pathogens could emerge at any time, causing loss of life or quality of life and spillover economic, social, and political effects at the same, if not greater, magnitude than the world has suffered over the past 2 years. No one can say for certain how governments will respond when the next crisis emerges. What is certain is that national, regional, and international responses to COVID-19 are already writing the opening chapters of the next pandemic. Only by translating lessons learned into viable, equitable action can the world change the pandemic narrative in time for the next crisis.

Introduction

Over the past several decades, governments and international agencies commissioned dozens of scenarios, blue ribbon reports, and multiday tabletop exercises that revealed the potential toll and trajectory of a major epidemic and the glaring need for a robust capacity for vaccine research and development (R&D) and response.¹ Despite these warnings, adequate upgrades were not made to most national and international structures, and the COVID-19 pandemic revealed that a true, end-to-end R&D and response ecosystem—meaning, one that both produces and delivers needed vaccines to global populations in a rapid and equitable fashion—remains an elusive goal.

The goals of this report are to: (1) identify the greatest opportunities and workable ideas for shortening the time to vaccine availability and (2) eliminate disparities in access in future pandemics by proposing ways to rework the architecture that supports the end-to-end vaccine R&D and response ecosystem.

This report is comprised of 3 major sections. The first section defines what the pandemic vaccine R&D and response ecosystem is: a network of interacting actors and infrastructure involved in researching, developing, manufacturing, allocating, distributing, financing, and delivering vaccines against pandemic threats. It describes this ecosystem at the national and global levels and assesses its performance in the COVID-19 pandemic. The second section of this report identifies ways in which COVID-19 has changed government, industry, and institutional perceptions and priorities for the pandemic R&D and response ecosystem to confront to future threats. It considers the strategic implications of those changes for efforts to ensure the world is better prepared when the next pandemic threat emerges, as it inevitably will. The third section of this report assesses the major gaps and opportunities revealed along the value chain to the production of COVID-19 vaccines, including the sharing of genetic sequence data, viral specimens, and biological reference materials; prior research on platform technologies and pathogens with pandemic potential; establishment and scale up of manufacturing capacity; equitable distribution and access; and mobilization of financing and resources. Based on those foregoing analyses, a summary table lists our proposals for improving the end-to-end ecosystem that supports pandemic preparedness R&D and response for vaccines during the COVID-19 pandemic and future large-scale health emergencies. In doing so, this report builds on other recent analyses of the R&D and response ecosystems.²

In preparing this report, researchers from Council on Foreign Relations and the Johns Hopkins Center for Health Security assessed the relevant peer-reviewed and grey literature and had informal conversations with 24 international experts, representing the broad scope of the vaccine development ecosystem (see Acknowledgments for names and affiliations) from August to October 2021. The individuals interviewed were selected for their subject matter expertise in 1 or more steps of the pandemic vaccine production value chain, from genetic sequence identification to clinical trials and manufacturing to vaccine distribution and delivery.

Although the focus of this report is on vaccines, its authors are well aware that the COVID-19 pandemic has also revealed significant weaknesses and gaps across the pandemic R&D and response ecosystems for therapeutics and diagnostics. Expanding and adapting the insights and analysis provided in this report for these 2 other product categories is an important area for potential future research.

The Vaccine R&D Preparedness and Response Ecosystem Defined

The ecosystem for vaccine pandemic R&D and response is an interconnected network of *actors* (academic and scientific institutions, private industry, governments, and intergovernmental institutions) and *infrastructure* (governance frameworks, partnerships, laws, treaties, and supply chains) involved with the following vaccine R&D and response activities:

1. *Sharing genomic sequences, virus isolates, and biological reference materials* – The genomic sequences from patient specimens during an emerging epidemic provide some of the earliest opportunities to analyze and understand the pathogen. In the absence of pathogen-specific diagnostic tests, genetic data may be the only way to identify or classify the pathogen. Virus isolates and biological reference materials from patients also support product development and validation. In fact, emerging biotechnology and vaccine development platforms can use genetic sequences to begin R&D for vaccine candidates, even without access to physical specimens.
2. *Prior research on vaccine platform technologies and potential pandemic pathogens* – Vaccines can take years, decades, or longer to develop from scratch, and R&D that is conducted prior to a pandemic can substantially help accelerate vaccine development for novel pathogens. This can include identifying appropriate vaccine platforms and technologies that are more likely to be effective against specific pathogens or demonstrating the safety and efficacy of specific products against closely related pathogens, which can then be adapted to novel threats.
3. *Clinical trials* – The safety and efficacy of vaccine candidates is determined in multiple rounds of clinical trials. Trials start with relatively small numbers of healthy participants to establish the safety of the candidate vaccine as well as whether it triggers the desired immune response. Subsequent stages involve increasingly larger study populations to generate preliminary estimates of safety, efficacy, appropriate dosage, and potentially appropriate timing for multidose regimens. Phase 3 trials require thousands or tens of thousands of participants, who are typically randomly assigned to be administered either the candidate vaccine or a control (eg, a known comparator product, often a placebo). These participants are then tracked over time to determine whether the vaccine is safe and effective. These clinical trials are performed according to protocols approved and overseen by national regulatory agencies and ethics committees. The data collected through clinical trials are critical to regulatory oversight and authorization processes, so these trials must meet stringent standards in terms of the safety and ethical treatment of participants and for data collection and analysis.
4. *Manufacturing and supply chains* – Vaccine manufacturing processes differ according to the type of vaccine, but they generally involve 2 phases. The first phase is the creation of the drug substance and its formulation into a drug product. Scaling up production for the pandemic requires multiple production facilities, each capable of generating tens of millions, if not hundreds of millions, of doses or more a year. The costs of such production facilities include ensuring each individual manufacturing and control step is conducted consistently with the defined process, acquiring specialized capital equipment such as bioreactors and filtration pumps, and employing skilled personnel able to transfer the vaccine technology from a laboratory test tube to dedicated mass-production lines. The process ultimately combines the drug substance with other pharmaceutical ingredients, such as excipients, adjuvants, and preservatives, depending on the vaccine,

for the final formulation. The second step of the entire process typically involves a separate manufacturing facility capable of receiving the drug product to “fill” (squirt doses into vials) and “finish” (cap the vials with stoppers and then label and package) the vaccine for distribution. After a new vaccine is designed and shown to be safe and effective, producing large amounts of a vaccine in a short period of time requires procuring timely, adequate supplies of 100 or more different critical inputs—including capital equipment, such as bioreactors and filtration pumps and single-use materials such as glass vials, filters, tubing, disposable bags, and rubber stoppers as well as cellular and other raw materials and stabilizing agents—produced by different suppliers in dozens of countries.^{3,4}

5. *Regulatory oversight* – Regulatory oversight of a pandemic vaccine is typically a multistage process that must be simultaneously dedicated to patient safety and able to adapt to accelerated review timelines in the midst of a crisis. Most vaccine company sponsors first seek marketing approval by a stringent regulator, such as the US Food and Drug Administration (FDA), in order to minimize the risk of liability and to take advantage of that regulator’s experience in assessment, resources, and clear protocols and rules. Upon receiving marketing approval, the sponsor may then submit the product to the World Health Organization (WHO) prequalification program,⁵ which ensures that drugs, vaccines, and diagnostics meet prescribed quality, safety, and efficacy standards and are appropriate for procurement by United Nations agencies. Although WHO is not a regulatory authority, many low- and middle-income countries (LMICs) use WHO prequalification status to guide their own regulatory processes. After WHO prequalifies a drug or vaccine, sponsors must still seek approval in every country where the vaccine may be used.
6. *Procurement and equitable access* – Procurement of vaccine generally occurs in 1 of 3 ways. First, a state can purchase vaccines directly from manufacturers on the open market, sometimes via purchase agreements, which are contracts between a manufacturer and the government. Advance purchase agreements are made for vaccines to be purchased in the future—often finalized prior to the vaccine receiving authorization for use in that country. Second, nongovernmental and intergovernmental organizations such as Gavi, the Vaccine Alliance (Gavi), the United Nations Children’s Fund, and WHO that act as procurement agents to assist states in acquiring vaccines from manufacturers or other states, either via purchase or donation. Finally, one state government may sell or donate its acquired vaccines directly to another. In combination with the manufacturing capacity, the terms of these agreements, including the volume and timing of delivery, will largely determine the degree to which vaccines are distributed equitably on the global level.
7. *Distribution and administration* – Administering vaccinations to high-priority populations in a pandemic requires well-coordinated global and in-country logistics and public health campaigns to build both confidence and demand for the vaccine. Vaccines may have different distribution requirements (eg, cold chain logistics) and routes of administration (eg, injection or oral), which can compound distribution logistics and vaccine administration operations. WHO and national public health authorities issue target product profiles,⁶ which are guidelines on the desired characteristics of the vaccine needed to expand the suitability for the particular target settings and populations. For low-resource settings, this may include thermostable vaccines that do not require consistent refrigeration or cold chain to be maintained.

8. *Finance and resource mobilization* – For nearly every element of vaccine R&D and response, adequate and predictable financing is needed, from basic research to early-stage development and testing to manufacturing to purchase and distribution. Funding provided at-risk—prior to the successful completion of the R&D process for a candidate vaccine—can help to more rapidly scale up manufacturing, establish more robust supply chains, and facilitate widespread vaccine distribution and administration.

The Pandemic R&D and Response Ecosystem on the National Level

Even among wealthy nations, the United States stands out as having the actors and resources needed to sustain many of the elements of a domestic end-to-end vaccine R&D preparedness and response ecosystem. US government agencies— including the US National Institutes of Health (NIH), US Centers for Disease Control and Prevention (CDC), Biomedical Advanced Research and Development Authority (BARDA), US FDA, and Department of Defense—have the funding, expertise, logistics systems, and authorities to conduct basic and translational research, subsidize manufacturing and supply chains, oversee clinical trials, approve vaccines for use, monitor good manufacturing practices and postmarket safety, and perform or oversee distribution and administration functions before, during, and after a pandemic.² The United States also has robust academic and scientific institutions to conduct basic research and clinical trials. The strong US private pharmaceutical and biotechnology sector are similarly able, if not always willing, to engage in pandemic R&D, manufacturing, and distribution.

The United States also has the infrastructure—eg, laws, governance frameworks, and supply chains—to facilitate and expedite the development, production, approval, and delivery of vaccines for public health emergencies. For example, the 2006 US Pandemic and All-Hazards Preparedness Act⁷ authorizes federal appropriations to respond to presidentially declared public health emergencies, grants the secretary of the US Department of Health and Human Services the authority to hold meetings and execute specific agreements with potential vaccine developers that would otherwise violate antitrust laws and provides immunity from liability, except in the case of willful misconduct, for claims of loss resulting from administration or use of vaccines to diseases that the secretary determines to constitute a present, or credible risk of a future public health emergency. The US Defense Production Act of 1950,⁸ a Korean War-era law, allows the government to require US companies to prioritize federal contracts over others when doing so serves the national defense, including during a pandemic.⁹

Most countries, particularly poorer nations, lack the actors and infrastructure needed for a domestic end-to-end vaccine R&D preparedness and response ecosystem. Prior to the pandemic, the majority of the manufacturing of the drug product and drug substance for vaccines was located in India, Europe, and North America.¹⁰ Eighty percent of the manufacturing facilities pandemic influenza vaccines in particular were located in high-income countries, which have only 16% of the world's population.¹¹ Even the production of a majority of the capital equipment and single-use and consumable materials needed to make vaccines appears to be concentrated in the United States and Europe.¹²

Since relatively few novel vaccines have been developed for or manufactured in LMICs, regulatory agencies in these countries often have limited experience approving innovative vaccines or monitoring vaccine production facilities for compliance with core good manufacturing practice principles. Some countries do not have the funding, systems, or trained healthcare workers to ensure longer-term safety and effectiveness monitoring for vaccines once they are available to the public. Many countries lack the systems necessary to track inventory

and dose administration, especially for vaccines that require multiple doses or during large-scale emergencies that could necessitate vaccination operations over large geographic areas and for large populations. In the absence of global coordination, lower-resource governments may not be able to procure adequate vaccine supplies to address domestic needs, which can further exacerbate global health, economic, and social disparities during a large-scale emergency.

Pandemic R&D and Response Architecture on the Global Level

Much of the global pandemic R&D and response ecosystem initially emerged in response to the reemergence of H5N1 highly pathogenic avian influenza in 2004, the 2009 H1N1 influenza pandemic, and the 2014-2016 Ebola outbreak in West Africa.² The International Health Regulations (2005) (IHR),¹³ a binding international agreement revised in 2005 and signed by 196 countries, includes rules related to identifying and sharing critical information about epidemics and maintaining core capacities to prevent, detect, and respond to dangerous disease events. The IHR includes provisions relevant for vaccine R&D and response, including requirements that nations provide relevant public health information—which may include case definitions, laboratory results, incidence and mortality data, and information concerning the source and risk posed by the epidemic threat—to WHO following a potential public health emergency of international concern notification. The text of the IHR does not explicitly address genetic sequences or isolates, nor does WHO policy.

Launched in 2011, the Pandemic Influenza Preparedness (PIP) Framework¹⁴ is a formal but nonbinding agreement between WHO member states to improve preparedness and response for influenza strains of pandemic potential, with a focus on equity and benefit sharing. The negotiations of the PIP Framework were influenced by the 2009 influenza A (H1N1) pandemic, when wealthy nations bought virtually all vaccine supplies, supplies for LMICs were limited, and WHO was only able to provide 78 million donated doses to 77 countries.^{15,16} The PIP Framework has strengthened the Global Influenza Surveillance and Response System¹⁷—previously known Global Influenza Surveillance Network—a mechanism for monitoring global influenza viral activity, identifying strains for annual influenza vaccines, and forecasting potential pandemic threats. The PIP Framework provides that states that share influenza viruses with pandemic potential with the Global Influenza Surveillance and Response System are entitled to access specific benefits, including timely access to vaccines, in the event of a pandemic. The PIP Framework agreement only covers influenza strains of pandemic potential; its terms do not apply to other pandemic pathogens, such as SARS-CoV-2 or unknown threats. The PIP Framework and other access and benefit arrangements, such as the Nagoya Protocol on Access to Genetic Resources to the Fair and Equitable Sharing of Benefits Arising from their Utilization of the Convention on Biological Diversity,¹⁸ have yet to be tested in an influenza pandemic.

WHO developed its R&D Blueprint for Action to Prevent Epidemics,¹⁹ a global strategy and preparedness plan to accelerate R&D activities during epidemics; revamped its Health Emergencies Program to integrate research with outbreak response; and identified a set of priority, high-consequence pathogens to research. With support from Norway, the Wellcome Trust, and the Bill & Melinda Gates Foundation, the Coalition for Epidemic Preparedness Innovations (CEPI) was launched in 2017 as a global partnership among public, private, philanthropic, and civil society organizations to develop vaccines more rapidly and prevent and respond to future epidemics.

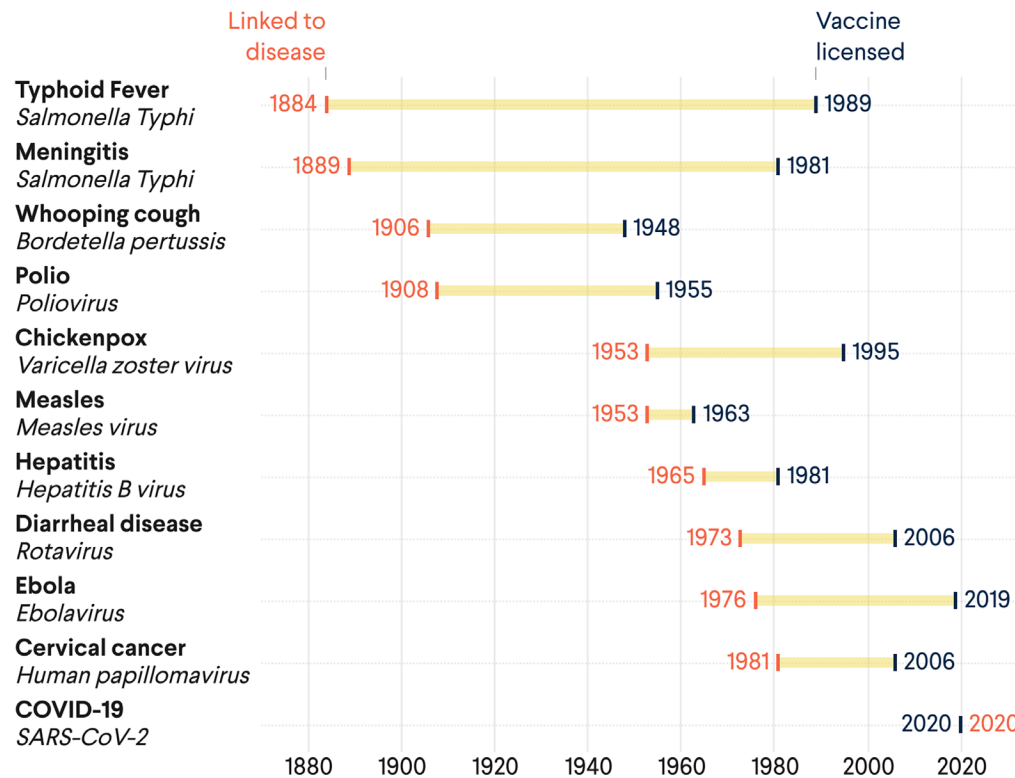
R&D and Response Ecosystem Performance During COVID-19

While the US response to the COVID-19 pandemic has had many shortcomings, it has highlighted the robustness of its R&D and response ecosystem. The Vaccine Research Center at US National Institute of Allergy and Infectious Diseases (NIAID) had previously entered into a public–private partnership with Moderna and invested in developing a candidate mRNA vaccine against the coronavirus that causes Middle East respiratory syndrome (MERS). These prior investments helped accelerate vaccine R&D for COVID-19 after the publication of the genetic sequence for the novel coronavirus. The US government announced the framework behind Operation Warp Speed (OWS) on May 15, 2020. It used the Department of Defense; the Department Health and Human Services, including BARDA; and other agencies to run OWS, coordinate and accelerate clinical trials, and scale up manufacturing in advance of regulatory authorization of candidate vaccines. This “at-risk” approach—spending money that would be lost if a vaccine were not ultimately authorized for use—was essential for making rapid progress. OWS helped expedite the development of viable vaccines able to obtain emergency use authorization from the FDA. It also coordinated and matched contract manufacturers with vaccine sponsors to ensure that those purchase orders would be fulfilled, invoking and leveraging the Defense Production Act⁸ when necessary. Through OWS, the US government also provided hundreds of millions of dollars in subsidies to expand the production of the inputs needed to manufacture vaccines (eg, bioreactors, mixer bags, cellular materials) and to deliver them into arms (eg, syringes, glass vials).⁴

The UK government also spent billions of pounds on advance purchase agreements for candidate COVID-19 vaccines, subsidies for clinical trials, and at-risk public investments in its domestic vaccine manufacturing and supply chains. Germany invested nearly €1 billion in 2020 in BioNTech and CureVac, 2 biotech companies developing mRNA vaccine candidates and devoted more than €600 million to expand local manufacturing capacity. The European Union also provided €175 million in debt financing and loans to BioNTech and CureVac and entered into advance purchase agreements with 6 vaccine sponsors. Australia and Japan provided small subsidies for local vaccine makers, and India did the same for Serum Institute of India and Bharat Biotech, but not until April 2021.

This heavy public investment in COVID-19 vaccine R&D and manufacturing succeeded beyond what anyone could have reasonably expected. Not one, but several highly effective vaccines against COVID-19 were developed, trialed, and brought to market in just 1 year from the availability of SARS-CoV-2 genomic data to emergency use authorization and administration in early COVID-19 patients (See [Annex A](#) for a detailed development timeline for leading vaccines). Prior to the COVID-19 vaccine, the mumps vaccine held the record for shortest time to market, at 4 years; many vaccines take more than a decade to reach that point.^{20,21} Since being authorized for expanded public use, more doses of COVID-19 vaccines have been manufactured in just 10 months (6.4 billion, as of October 10, 2021) than the world usually produces in an entire year for all other vaccines combined (3.5 to 5.5 billion doses) ([Figure 1](#)).^{22,23}

Figure 1. Development of a COVID-19 Vaccine Was Historically Fast



Notes: The speed of vaccine development is shown from the year the infectious agent was linked to the disease until when the vaccine was licensed in the United States, 1880–2020. Only infectious agents against which vaccines have been developed and licensed in the United States are included. Figure is adapted from Our World in Data.²⁴

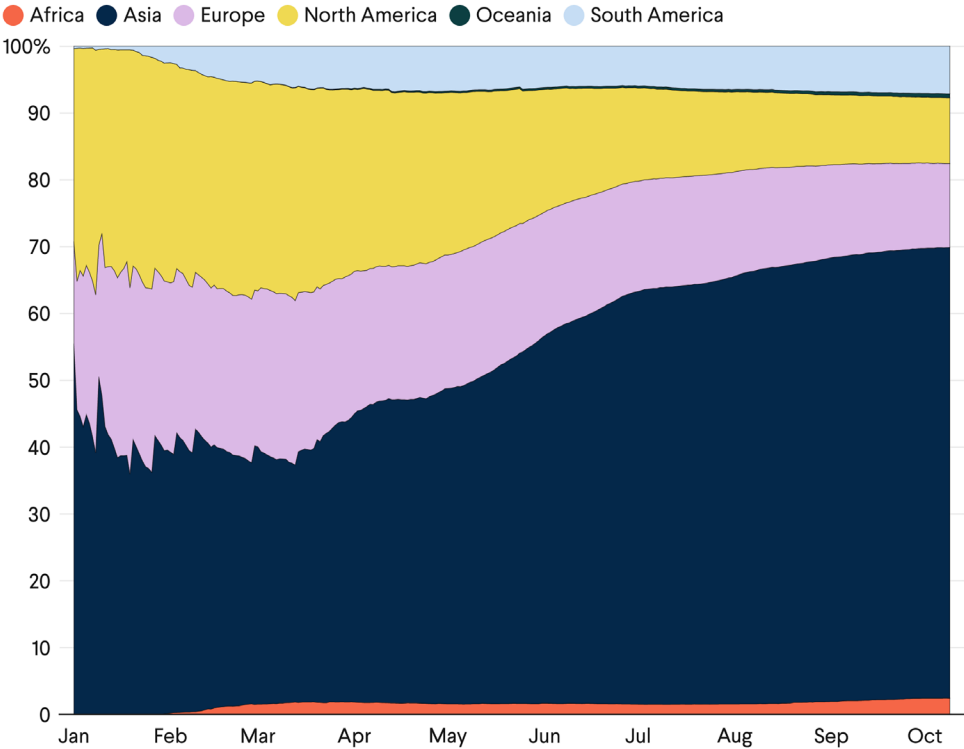
The COVID-19 pandemic, however, has also highlighted significant gaps and weaknesses in this global pandemic R&D and response ecosystem. There were no global entities with a mandate, financing, or capacity to initiate product development and to coordinate and incentivize multiple actors to test, approve, manufacture, scale up, or ensure equitable global access to new products. While experts around the world knew a severe, novel respiratory pandemic was inevitable and could emerge at any time, the pandemic R&D and response ecosystem was—in the words of Lurie et al—“fragmented” and a “conductor-less orchestra.”²² Accordingly, much of global infrastructure needed to respond to the COVID-19 pandemic has needed to be created through ad hoc partnerships and frameworks to fill governance gaps. In April 2020, WHO partnered with CEPI and Gavi to launch COVID-19 Vaccines Global Access (COVAX), a collaboration dedicated to procuring and providing equitable and timely global access to COVID-19 vaccines that meet international standards for safety and efficacy.²⁵ COVAX has had some notable successes, including attracting the engagement of 191 countries,²⁶ raising US\$9.8 billion in funding,²⁷ entering into contracts for the purchase of 4.3 billion doses of various COVID-19 vaccines for global distribution, and delivering 341 million doses to 144 countries through October 10, 2021.²⁸

Yet, COVAX has not been able to keep wealthy nations from purchasing and stockpiling most of the available COVID-19 vaccine supplies in bilateral arrangements (directly between national governments and vaccine manufacturers), reserving far more doses than they needed and

placing LMICs at the back of the line well before vaccines were on the market.²⁹ An additional hurdle has been securing committed doses from the Serum Institute of India, the world’s largest vaccine manufacturer. COVAX spent hundreds of millions of dollars to transfer the necessary technology to the Serum Institute of India and expand its vaccine manufacturing capacity to supply 1.1 billion doses for distribution to LMICs in 2021. When COVID-19 cases surged in India, however, the Indian government prohibited the company from exporting vaccine doses so that they could be directed toward the domestic response.³⁰ With Serum Institute of India and the Indian government slow to announce the expected duration of the ban, COVAX struggled to locate alternative sources of manufacturing. As a result, 40% of the doses that COVAX delivered by early October were donated, as opposed to purchased directly by COVAX, with some nations receiving less than half of what they were originally allocated.³¹

COVAX has not succeeded in keeping the global allocation and administration of COVID-19 vaccines from being deeply inequitable, as it has been in previous pandemics and epidemics (Figure 2). COVAX set the target of reaching 20% coverage for its participants’ populations, with the goal of protecting those at the highest risk of infection and severe disease—including frontline healthcare workers, individuals aged 65 years and older, and those with underlying risk factors—by the end of 2021. To meet that target, COVAX estimated needing to distribute 2 billion doses fairly in the places of greatest need. It is likely to fall well short of that goal, only having delivered approximately 24% of its 2021 end-of-year goal as of October 10.³²

Figure 2. Percent of Global Doses Administered by Continent



Notes: Data is from January 1, 2021 to October 9, 2021. Figure is adapted from Our World In Data.³³

As of May 2021, just 10 nations account for nearly 75% of all of the COVID-19 vaccine doses administered worldwide—a statistic that has barely improved since the first authorization. This global inequity has left many LMICs to battle increasing mortality, waning health system capacity, and hospitalizations. Since the global rollout of COVID-19 vaccinations began with the first authorization in the United Kingdom on December 2, 2020, COVID-19 mortality has increased faster in regions and income groups with the lowest levels of vaccination coverage than in nations with greater access (Table 1).³⁴⁻³⁶ Tragically, the cumulative global COVID-19 mortality so far in 2021 is already more than 50% greater than all of 2020, despite the availability of multiple highly effective vaccines.³⁷

Table 1. Deaths Have Increased Fastest in the Regional Groups with the Lowest Vaccination Rates

Region/Country Income Level	Doses Administered per 100 People	Percent Increase in Cumulative Deaths Since December 2, 2020
Central Asia	56.71	357.52%
Latin America and Caribbean	98.87	198.11%
Sub-Saharan Africa	6.74	345.89%
East Asia and Pacific	125.24	722.59%
South Asia	60.95	244.13%
Middle East and North Africa	54.06	172.43%
North America	124.86	159.45%
European Union	128.14	185.30%
Low income	3.94	338.80%
Lower middle income	49.94	277.93%
Upper middle income	126.25	234.80%
High income	130.97	166.74%
World	83.63	215.07%

Notes: Population vaccinated (doses administered per 100 people) compared to increase in cumulative deaths since December 2, 2020. Doses administered per 100 people may be higher than 100 due to 2-dose vaccination courses for most vaccines and use of booster shots. Data are from Our World In Data,³⁴ World Bank Data,³⁵ and Johns Hopkins Coronavirus Resource Center³⁶ and were current as of October 10, 2021.

For nearly 3 decades, countless epidemiologists, public health practitioners and researchers, intelligence community professionals, national security officials, and other experts have underscored the inevitability of a pandemic, especially due to the emergence of a novel pathogen. Governments and international agencies commissioned scenarios, reports, and functional and tabletop exercises that anticipated the toll and trajectory of a major epidemic and the glaring need for a robust vaccine R&D and response capacity.¹ Nevertheless, the COVID-19 pandemic has revealed that a true, end-to-end R&D and response ecosystem—meaning, one that both produces and delivers needed vaccine to global populations in a rapid and equitable fashion—remains an elusive goal. The subsequent sections of this report explore the consequences of the COVID-19 experience and lessons for future initiatives to improve the pandemic R&D and response ecosystem.

The World that COVID-19 Made

To prevent the devastation that has accompanied this pandemic from happening again, it is important not only to identify lessons from the global response to COVID-19 but also to anticipate how that response has changed country and industry perceptions and priorities for the R&D and response ecosystem for the future. The COVID-19 pandemic has also exposed and redefined the realities of the global vaccine R&D and response ecosystem in the following ways:

1. There Is Now Widespread Recognition that Safe and Effective Vaccines Provide Unparalleled Health, Social, and Economic Benefits During a Pandemic

The COVID-19 pandemic has demonstrated how investing at-risk in a portfolio of technologies to accelerate the development and delivery of vaccines during a pandemic can be a cost-effective strategy. Nobel Laureate Michael Kremer, referring to a then estimated expenditure of US\$13 billion, concluded that OWS paid for itself in just 12 hours in terms of the value provided by accelerating the pace of vaccination.³⁸ He estimated that the global benefits of the first 3 billion doses likely generated worldwide economic benefits of US\$17.4 trillion, or US\$5,800 in benefits per course. The International Monetary Fund estimated that vaccinating at least 40% of the population in all countries by the end of 2021 and at least 60% by the first half of 2022 would yield trillions of dollars in economic benefits globally, dwarfing the potential costs of doing so.³⁹

As of October 12, 2021, the COVID-19 pandemic has resulted in nearly 238 million cases and 5 million deaths reported worldwide.²³ In the first 2 months of the pandemic, higher-income countries spent more than US\$10 trillion on response operations and economic stimulus.⁴⁰ While COVID-19 has been bad, future pandemics may well be worse, depending on the pathogen's characteristics and transmission dynamics. For example, influenza generally has a shorter incubation period (2 days on average) than COVID-19 (5 to 6 days), which could lead to faster community and geographic spread on a local, national, and global scale and reduce the time in which a vaccine could be developed and deployed in time to ameliorate the health and economic toll of a pandemic influenza.⁴¹⁻⁴³

One consequence that has emerged from the widespread recognition of the potential benefits of accelerating vaccine development and production against pandemic threats is greater investment in updating pandemic R&D and response ecosystems. In February 2021, for example, the European Commission announced a proposal to establish the Health Emergency Preparedness and Response Authority Incubator—modelled on the US BARDA program—which will bring together researchers, biotechnology companies, pharmaceutical manufacturers, regulators, and government agencies to exchange data and cooperate on developing and adapting vaccines for emerging pathogens. The European Commission also established the Task Force for Industrial Scale-Up of COVID-19 Vaccines to increase vaccine production capacity in the European Union and alleviate supply chain bottlenecks. Both CEPI and the US NIH have launched separate initiatives to develop and expand the use of platform technologies more broadly for emerging pathogens in priority viral families. China, which hardly shipped any vaccines abroad prior to the pandemic, has now become the largest exporter of COVID-19 vaccines to date.⁴⁴ This increased investment in pandemic R&D and response ecosystems is a positive legacy, provided that these efforts are sustainable in the long term and remain collaborative and inclusive of global needs rather competitive and focused exclusively on domestic priorities.

2. In Times of Scarcity, National Governments Are Highly Unlikely to Share Their Early Supplies of Vaccines and Related Inputs Unless They Have Direct Incentives to Do So

Ending a pandemic as soon as possible is in everyone's interest, and yet, in global health crisis after global health crisis, appeals for a global altruistic approach to vaccine allocation and distribution have gone unheeded. For years, HIV/AIDS ravaged LMICs that were priced out of the market for lifesaving medications before donors launched global programs to address this inequity. During the 2009 H1N1(A) influenza pandemic, which killed 284,000 people globally, a vaccine was developed in just 7 months, but wealthy countries bought virtually all of the initial doses before LMICs could access them. Australia, Canada, the United States, and 6 other countries agreed to share 10% of their vaccines with LMICs, but only after determining that their remaining supplies would be sufficient to meet domestic needs.⁴⁵ During the first 4 months of the COVID-19 pandemic, more than 70 countries, plus the European Union, imposed export controls on supplies of personal protective equipment, ventilators, or medicines.⁴⁶

Based on historical experiences, it is clear that we should not have expected governments with early access to COVID-19 vaccines to forgo vaccinating their own populations to ensure access for other countries. For example, Israel, with a population of 9.2 million, has made additional booster doses available for all eligible individuals and required these extra doses for the individual to be considered fully vaccinated. As of October 2021, the country has shared vaccines in the amount equal to just 0.1% of the 15.6 million doses it has administered domestically.⁴⁷ Inequity in COVID-19 vaccination has exacerbated global mortality, fostered the emergence of variants of concern that exhibit increased transmissibility and disease severity, delayed economic recovery, and encouraged other nations to hoard their own resources, including critical input supplies, leading to supply chain disruptions.^{48,49}

The health and economic consequences of a prolonged pandemic have proven insufficient to motivate vaccine sharing with other nations. The time period for most political leaders' decisionmaking is short, especially those who are accountable to voters for reelection.⁵⁰ The potential for opposition for giving away needed vaccine supplies may seem like a bigger risk than international outrage abroad over hoarding supplies, especially if it is for a limited time and other countries are seen as likely to do the same. Many government leaders were apparently unconvinced that constituents would understand that the long-term health and economic consequences of SARS-CoV-2 spreading unabated abroad are greater than the immediate threat posed to their loved ones, even those who are low risk.

There are also other implications of the widespread recognition that countries are not willing to share scarce vaccines and related inputs in a crisis. First, many governments want to domesticate vaccine manufacturing after COVID-19 has wreaked havoc on the health of their populations and economies. The United Kingdom expanded its domestic vaccine manufacturing capacity for the Valneva and Novavax vaccines and is in negotiations to do the same with the GlaxoSmithKline product.^{51,52} The European Commission has committed economic recovery funds to expand pharmaceutical manufacturing capacity in the European Union.⁵³ In the United States, the White House has focused on purchasing domestically produced COVID-19 vaccines (eg, Pfizer-BioNTech and Moderna) for its donations and announced a plan to scale up US production capacity for vaccine inputs.^{54,55} The African Union plans to expand vaccine manufacturing to cover 60% of the continent's needs by 2040.⁵⁶

These efforts are not a surprise. There has been a near-complete overlap between the countries that are consuming the most COVID-19 vaccines and those producing them. Since COVID-19 vaccines first became publicly available in December 2020, more than 6.8 billion doses have been administered globally, but residents of just 10 nations have received nearly three-quarters of those shots.⁵⁷ According to a World Bank analysis, those same countries—China (2.2 billion doses administered), India (943 million), the United States (401.8 million), Brazil (248.2 million), Japan (172.1 million), Germany (109 million), France (95.9 million), Russia (94.3 million), United Kingdom (94.3 million), and Italy (86.2 million)—together with a few other countries, are also responsible for the overwhelming majority of the global production of COVID-19 vaccines and their key ingredients. Meanwhile, the entire African continent has been able to administer only 159.7 million doses for its more than 1.3 billion people.⁵⁸

The challenge of scaling out global vaccine manufacturing to reduce scarcity in pandemic times will be subsidizing and sustaining the excess capacity that is needed in emergencies during routine operations, meaning the period between pandemics. Prior to the COVID-19 pandemic, the total global vaccine market was approximately 3.5 to 5.5 billion doses per year, but current estimates suggest that approximately 10 to 14 billion doses of COVID-19 vaccines will be needed to achieve sufficient vaccination coverage (ie, full vaccination for 70% of the global population), on top of existing production needs against COVID-19 alone.^{3,22,59} Expanding and sustaining that volume of excess capacity to support pandemic demand will require significant public subsidies, potentially for years or decades, in order to be better prepared for the next pandemic.

Second, the experience of the COVID-19 pandemic could reduce countries' interest in participating in future global pooled procurement initiatives, such as COVAX for COVID-19, or access and benefit-sharing treaties or other international legal instruments or agreements, such as the PIP Framework for pandemic influenza, due to concerns that they might not be sufficient to provide timely, equitable quantities of vaccines for LMICs. With doses slow to emerge from COVAX, the Pan American Health Organization announced a plan in August 2021 to begin to purchasing vaccines itself for distribution among countries in the Americas in need.⁶⁰ Additionally, the African Union set up the Africa Vaccine Acquisition Task Team to reach 60% coverage on the continent.⁶¹ LMICs may be reluctant to commit fully to improving global disease surveillance and to sharing data, sequences, and isolates until there are greater guarantees of benefitting from expedited vaccine research and development that results.

3. COVID-19 Demonstrated that Pandemics Can Be Profitable for Vaccine Manufacturers

Vaccine R&D has often suffered from low profits, underinvestment, and concerns about the declining number of vaccine developers, but not in this pandemic.^{62,63} The motivation of vaccine manufacturers in developing products for recent regional epidemics, including the 2014-2016 Ebola epidemic in West Africa and the 2015-2016 Zika epidemic in the Americas, were primarily humanitarian and reputational. COVID-19 has been both a truly global health crisis and an enormous profit-making opportunity for vaccine developers and manufacturers.

On a May 4, 2021 earnings call, Pfizer projected its COVID-19 vaccine would generate US\$26 billion in revenues for 2021, sales that far surpassed those of any pharmaceutical product in history.^{64,65} The 2021 global market for COVID-19 vaccines could be as large as US\$190 billion, with the Pfizer-BioNTech and Moderna vaccines projected to generate revenues of tens of billions of dollars.^{66,67} Many of the manufacturers of COVID-19 vaccines have benefited from

direct public investments as well as billions of dollars in public advance purchase commitments, reducing risk to manufacturers.⁶⁸ Such large-scale public funding was necessary, especially for smaller biotechnology firms, to encourage companies to invest in R&D for COVID-19, since market returns are highly uncertain at the early stages of product development and expediting the development of potentially promising candidates was crucial from a public health perspective. Vaccine manufacturers also benefited from prepandemic investments to support international sharing of genomic sequencing data, which facilitated access to SARS-CoV-2 genomic data collected from early COVID-19 patients in China—via the publicly accessible GISAID platform—within approximately 1 month from the first reported cases. Access to such information enabled vaccine development to begin around the world without the need for access to any physical specimens.

A positive consequence of the pandemic is that new vaccine developers are entering the market. Only 14% of organizations involved in COVID-19 pandemic-related development had previously commercialized vaccines, although some, like Moderna, had prior experience in developing vaccines against pandemic threats (eg, MERS).⁶⁹ Some of the new manufacturers are located in LMICs, which provides the added benefit of expanding the global footprint of vaccine development capability to include countries that may be at elevated risk for the emergence of novel pathogens. The COVID-19 pandemic has also catalyzed a shift in vaccine industry toward messenger RNA (mRNA) vaccines, which can be manufactured at scale, are strongly immunogenic, and can be quickly altered should genetic variants arise.⁷⁰

Another consequence is that, in future crises, more vaccine makers may seek to avoid public sector and nongovernmental organization arrangements that could encumber potential profitmaking. Global health funders tend to provide earlier-stage investment to vaccine developers, before it is clear that a candidate is viable and at times when private sector funding may be more difficult to obtain.^{71,72} Early in product development, smaller investments (in the millions of dollars) can make a meaningful difference in product development. But the profitability of pandemic vaccines demonstrated in the COVID-19 pandemic could make vaccine developers more reluctant to take such funds if they are accompanied by extensive equitable access obligations. One reason is that such contracts could make it more difficult for biotechnology firms to be acquired by multinational pharmaceutical firms—which have the resources and experience to expand production capacity and shepherd products through regulatory review—that hope to commercialize these vaccines on a global scale. This could lead pharmaceutical companies to prioritize agreements with governments that are willing and able to pay more and accept fewer equitable access requirements, particularly in circumstances in which there may be multiple eager public sector buyers for scarce vaccine supplies.⁷³ During the COVID-19 pandemic, Pfizer entered into advance purchase agreements but did not enter other public funding arrangements. This approach may have enabled the company to escape some of the restrictions and criticisms directed toward other companies that accepted public funds in a variety of forms.⁷⁴

4. Geopolitics Constrained COVID-19 Response and Threaten Future Global Health Security

International health emergencies have historically been a cause for increased international cooperation, even among geopolitical rivals.⁷⁵ At the height of the Cold War, for example, the United States and Soviet Union cooperated on an intensified smallpox immunization campaign that ultimately contributed to eradicating the disease.⁷⁶ Even as Taliban fighters were launching

attacks against North Atlantic Treaty Organization forces in Afghanistan, they permitted healthcare providers funded by those same countries to administer polio vaccination efforts in areas under Taliban control.⁷⁷ The United States and China cooperated to help combat the 2014-2016 Ebola outbreak in West Africa, with technical staff from both nations working side by side in a Chinese lab in Sierra Leone.⁷⁸

Since 2000, the United States, other wealthy nations, and philanthropic organizations, such as the Bill & Melinda Gates Foundation, spent billions of dollars to research, develop, and distribute vaccines and therapeutics to vulnerable populations in LMICs around the world. Global health aid nearly tripled over the next decade, from US\$10.8 billion in 2001 to US\$28.2 billion in 2010.⁷⁹ New global health institutions emerged—such as Gavi and the Global Fund to Fight AIDS, Tuberculosis, and Malaria—to support the distribution of vaccines, therapeutics, and other lifesaving interventions worldwide, including, for a time, to China. In recent years, China has transitioned from a recipient to an influential global health donor.⁸⁰

The global response to the COVID-19 pandemic, however, has proven to be an exception, hopelessly constrained by geopolitical rivalries. In particular, it has been impossible, to date, to isolate broader United States–China competition from much-needed cooperation on COVID-19 response challenges. Geopolitical competition between China and the United States has hindered the Group of Seven (G7), Group of Twenty (G20), and United Nations Security Council from providing political direction to the international system, both in orchestrating a robust public health response and in coping with the economic fallout.¹ China, Europe, India, Russia, and the United States all raced to develop COVID-19 vaccines and donate excess doses, but their efforts have been driven not by public health need, but by competition with one another to woo strategic allies and cement spheres of influence via “vaccine diplomacy.”⁸¹

In the context of this geopolitical competition, not all nations may be willing to cooperate closely on national security matters such as pandemic vaccine R&D and response. Improved global disease surveillance and supply chain transparency, independent of state reporting channels, may not be welcome if countries are concerned those efforts could reveal secrets and wrongdoing that may be destabilizing to the government. The geopolitical environment has changed dramatically from the one that existed after previous epidemics (eg, H5N1, SARS, Ebola) and led to the adoption of the revised IHR in 2005 and the PIP Framework in 2011. These reforms, all produced in a more benign and collaborative international system, failed to prevent nations from hoarding early vaccine supplies and being slow to share genetic sequences, biological samples, and other vital information in the early days of the COVID-19 pandemic. These experiences caution against pandemic strategies that depend on charitable aid and the universal adoption of new rules and norms, particularly in an increasingly multipolar international environment.

Aid-driven institutions, nonbinding arrangements, and charitable partnerships that have characterized global health are well worth preserving, but they are not the answer to all the unsolved collective action problems that plague pandemic R&D and response. Only international cooperation based on shared, hard-nosed national interests can mobilize the global manufacturing, cross-border trade and investment, and delivery systems that will end the present public health crisis and help build a more resilient system for the future. This kind of cooperation may be more feasible in groupings of regional partners or like-minded states, with global cooperation instead focused on promoting supply chain transparency, common standards, and scientific collaboration.

Gaps and Opportunities in the COVID-19 Vaccine R&D and Response

The COVID-19 pandemic has revealed gaps in and future opportunities for each step in the value chain for vaccine production—from the sharing of genetic sequences and basic research through manufacturing, equitable allocation, and distribution, to postlicensure clinical and operational research. This section of the report identifies those gaps and opportunities, as well as our recommendations for addressing them. [Table 2](#) summarizes our priority recommended actions.

1. A Concerted Strategy for the Research and Development of Prototype Vaccine Candidates for Future Pandemics Is Needed

Expediting the development of future pandemic vaccines would benefit from a globally coordinated R&D strategy that supports the production of multiple vaccine candidates against pathogens with pandemic potential through early clinical trials, particularly in advance of the next crisis.⁸² Global health leaders and organizations, like CEPI, have put forth proposals that call for vaccines to be developed within 100 days of identification of the next pandemic. The Disease X Act,⁸³ introduced in the US Senate, also reflects this priority. Informal conversations with experts revealed different ideas regarding the desired endpoints of these 100-day proposals, with most focused on the potential to expedite the early stages of the value chain, including research and development and clinical evaluation of pandemic vaccine candidates.

Experts noted that achieving this vision will require changes to the way that vaccine candidates are typically developed and evaluated.⁸⁴ One of the key requirements for these proposals is that priority pathogens with pandemic potential are identified in order to focus vaccine development efforts on pathogens most likely to result in wide geographic spread and significant mortality and morbidity. If candidate vaccines could be developed and taken through early steps of the clinical evaluations, such as Phase 1 and 2 clinical trials, in advance of the next pandemic, that advanced preparation could potentially accelerate vaccine availability by months or even years. This is akin to a layered security approach in which development is idled at various stages reflective of the threat a particular pathogen poses. The advent of platforms such as mRNA make such an approach much more feasible than it was with traditional vaccine development techniques. From the onset of a pandemic, the 100 days of work could focus on modifying existing candidates to match the viral strain rather than developing new products or platforms from scratch. With an appropriate candidate in hand, researchers could proceed directly with larger Phase 3 trials, based on the success of the platform products' previous Phase 1 and 2 data. One of the key factors that contributed to the rapid development of COVID-19 vaccines was the decades of previous research on coronaviruses and mRNA vaccines. Even without any existing mRNA vaccines, the underlying foundation of research provided the framework for developing several of the earliest available products, including the Pfizer-BioNTech and Moderna vaccines.⁸⁵ Without this prior research, these vaccines would likely have been months or years behind products utilizing other platforms, such as viral vectors or live-attenuated viruses. Organizations, such as CEPI and NIAID have either expressed verbal support or have begun initiatives in support of viral family-based approach. But additional coordination and support for these efforts are needed.^{86,87}

Having multiple candidate vaccines proceed through Phase 2 clinical trials in advance of the next pandemic will require several steps and considerable up-front investment, including from

national governments and scientific funding bodies. Specifically, research must: (1) define a list of priority prototype pathogens, based on viral families, for which vaccine candidates are to be developed; (2) identify antigen targets and structural design of vaccine candidates; (3) identify immune correlates of protection to help assess the degree of protection; and (4) determine vaccine platforms that are best suited for various priority target pathogens. It is important to not exclude traditional vaccine approaches to which specific pathogens may be more amenable.

CEPI and WHO should continue to work with national scientific organizations to define a global R&D agenda and to support and coordinate research in each of the 4 areas outlined above. National governments and organizations (eg, the Bill & Melinda Gates Foundation, CEPI, the Wellcome Trust) that support scientific research should use this agenda to guide the funding of pre-pandemic research, including basic research and vaccine and vaccine platform development. This approach could cost an estimated US\$20 to \$30 million per vaccine candidate developed, but the extraordinary human and financial tolls of COVID-19 dwarf these costs by at least an order of magnitude.⁸⁴

Prepandemic Research on Priority Pathogens

Expediting the development of pandemic vaccines requires having some knowledge of the viral families most likely to cause the next pandemic and identifying a pathway to develop vaccines against those likely threats. Viral families have shared functional and structural properties making prototypic viral pathogens a promising strategy for informing the development of vaccines for novel pathogens.⁸⁸ Identifying representative pathogens within each family, based on an understanding of the structural biology and immune correlates, could allow for more rapid acceleration of vaccine development in the event of a pandemic. CEPI, along with NIAID, have contributed to building the framework for this type of technology.⁸⁹ The relatively rapid development of vaccines against SARS-CoV-2 was aided by previous research and development of vaccines for SARS-CoV-1 and MERS-CoV. Although COVID-19 presented a novel threat, knowledge of the structural features and pathogenicity of similar coronaviruses provided the basic information to move forward quickly with early development of new medical countermeasures. We may not be so fortunate with the next novel pathogen.

Candidate vaccines for a representative prototype pathogen within each viral family could be taken through Phase 1 clinical evaluation to collect early data on safety, dosage, and schedule of vaccine administration with that particular platform, antigenic target, or other design characteristics. Further, taking vaccines against prototype pathogens through Phase 2b clinical trials may help identify correlates of protection for different viral families. Larger trials, particularly Phase 3 trials, would have to be conducted on humans during a pandemic, as the trials require substantially more resources including thousands or tens of thousands of participants.⁹⁰ Prototypic viruses could also provide standards for early development of serological assays to measure functional activity for different viral types.⁹¹ This knowledge would help define mechanisms of neutralization and develop animal models for understanding pathogenesis. Similar activities were undertaken during the current COVID-19 pandemic.

Previous research on SARS and MERS coronavirus vaccine platforms provided basic information needed to support early development for COVID-19 vaccines. Prior to the emergence of SARS-CoV-2, vaccine platform development for yellow fever, Japanese encephalitis virus, dengue, and other members of the *Flaviviridae* family was applied to the emergency development of vaccine candidates for Zika virus.⁹⁰ Limited progress has been made for other viral families, and further investment and priority is needed to expand these efforts.

Success on a prototypic pathogen vaccine candidate approach depends heavily on our knowledge of circulating pathogens in animals across a variety of ecosystems.⁸⁴ Maintaining and expanding this knowledge requires continuous improvement in surveillance for zoonotic pathogens. With past pandemics, wild animal populations—including bats, pigs, and aquatic birds—have served as zoonotic reservoirs for pathogens. Despite ongoing international infectious disease surveillance efforts, there are substantial gaps in available data for geographic areas with frequent human–animal contact. During our informal discussions with experts, many noted the need for targeted strategies for monitoring forecasted hotspots of disease spillover, including the use of continuous disease surveillance programs for both human and animal populations and expanded use of genomic sequencing. They emphasized that developing a comprehensive atlas of zoonotic viruses will enable us to be better prepared to launch vaccine platform development efforts in response to future spillover events.⁹² The Global Virome Project has organized around this effort, gathering ecologists, epidemiological modelers, and field biologists to collect and characterize viruses.^{92,93} However, it is important to draw distinctions between viral cataloging and discovery, which may be highly useful to emerging infectious disease outbreak prevention and pandemic preparedness, as many zoonotic infections will not possess the ability to propagate extensively in humans.

In conjunction with systematic surveillance efforts for known zoonotic viruses,⁸⁸ screening for new viruses within families known to infect humans should be prioritized, especially when considering areas of high biodiversity. Within this group of viruses, those that have potential for human-to-human spread, especially through the respiratory route, should be the highest priority. While collecting genome sequence data on viruses circulating among livestock or wildlife and understanding geographic transmission do provide insight into potential pandemic threats, such viruses still need to be isolated and tested for pathogenicity markers in suitable animal models. Understanding pathogenicity markers will allow vaccine developers to prioritize research for viral strains that are more closely matched to emerging viruses with pandemic potential. There are more than 100 known viral families, of which only 25 are known to infect humans; however, within those 25 viral families, there are 120 known viruses that pose substantial risk for pandemic-level events.⁹¹ For most of these pathogens, no vaccines or countermeasures are currently available to mitigate the threat of infection, so it is critical to identify the most pressing threats and allocate limited research resources to those targets.

Antigen Selection and Structural Design

Creating vaccine candidates for each prototype pathogen requires knowledge of the specific antigens that candidate vaccines should target. For example, in the case of COVID-19 vaccines, the SARS-CoV-2 spike protein was quickly identified as a prime target for vaccines. Vaccines were designed to present the spike protein to the immune system to stimulate an immune response against it. Key antigens upon which candidate vaccines should be based need to be identified for each prototype pathogen on the pandemic potential list.

New technologies, such as structural biology, have been developed to understand atomic-level details of viral surface proteins, which can facilitate determining appropriate vaccine targets, associated enzymes, and replication mechanisms. In the last 2 decades, reverse vaccinology (ie, generating vaccines based on a pathogen’s genome) has taken a structural vaccinology approach in which antigen identification relies on bioinformatics to design optimal protein antigens that display protective epitopes to B cells, antibody-producing cells.^{94,95} In this approach, the atomic structure of the antigen and its epitopes are determined using microscopy, crystallography, or nuclear magnetic resonance.⁹⁶ Based on the structural determinants, the antigen or its

epitopes can be remodeled by reverse molecular engineering and incorporated into selected vaccine platforms. This approach led to the development of a successful vaccine candidate for the respiratory syncytial virus and is contributing to ongoing development of the first universal influenza vaccine.^{97,98}

Correlates of Protection for Prepandemic Vaccine Candidates

As efforts to develop vaccine candidates proceed, additional research should take place simultaneously to identify and characterize correlates of protection. Correlates of protection are biomarkers that provide objective evidence of the desired immune response that can then be quantified to project the associated degree of protection conferred to the individual. These data can supplement data from animal models and human clinical trials to improve our understanding of a vaccine's potential protective value before the wide circulation of the vaccine. The current lack of data related to correlates of immunity or correlates of protection for prototype pathogens may limit the pace by which vaccine candidates can advance through clinical trials prior to the occurrence of significant disease. In the absence of an outbreak or epidemic, very limited options are available to test vaccine efficacy in humans; correlates of protection could provide insight without exposing humans to the pathogen. Understanding correlates of immunity can help improve understanding of how much protection a vaccine is likely to offer prior to studying the impact of vaccines in populations where the pathogen is circulating.

Correlates of protection are also needed once pandemic vaccines are in use. The experts we consulted noted that the key elements of a protective immune correlate have not yet been determined for SARS-CoV-2.⁹⁹ Although it has been suggested that neutralizing antibodies may be a correlate of protection against the SARS-CoV-2 virus, some have argued that these may be too simplistic of a measure of immunity and may not adequately represent the degree of protection against COVID-19, as T-cell immunity is highly operative. The lack of an understanding of how biomarkers, such as neutralizing antibodies, might be used to assess protection against the virus has fueled debate over the duration and degree of protection and the need for additional booster doses for some COVID-19 vaccines.

Several experts noted that obtaining sufficient data to determine correlates of protection is challenging in the absence of a circulating pathogen. Therefore, detailing correlates of protection against similar viruses already circulating in human or animal populations in combination with protection data from animal models could potentially enable shorter and much smaller-scale Phase 3 trials when a new virus emerges within a particular viral family with well-characterized correlates of protection. With respect to COVID-19 vaccines, experts suggested that researchers could have looked at the type of immune response required for adequate protection from infection and reinfection for other known coronavirus circulating in human populations (eg, OC43, NL63, HKU1, 229E) to gain insights into possible correlates of protection for SARS-CoV-2. Additionally, successful animal vaccines against coronaviruses do exist and have been a potential source of relevant information. Had sufficient correlates of protection been identified for SARS-CoV-2, the need for large, costly trials may have been reduced, thereby condensing the development timeline.

Determining correlates of protection for different viral families could also inform platform and antigen selection, speed up production and clinical evaluation, and support vaccine formulation and delivery of vaccines for novel pathogens. Correlates of protection are often specifically defined by the clinical endpoint used (eg, infection, disease, severe disease, or mortality).⁸⁴ Predetermined correlates of protection based on these endpoints may help to circumvent delays

due to low enrollment in large Phase 3 trials required for licensure. These immune correlates could allow for licensure based on immune readouts, accelerating vaccine availability.

Platform Selection

Once a pandemic pathogen is identified, the availability of a candidate vaccine developed for a prototype pathogen in the same viral family could facilitate accelerated product development by adapting the existing vaccine to match the pandemic virus. The use of mRNA vaccine platforms greatly expedited the development and production of vaccines for the SARS-CoV-2 virus, but many experts emphasized the importance of maintaining broad approach to investments in platforms for future pandemic vaccines. mRNA vaccines provide flexibility in terms of antigen manipulation, which enable quick alteration of existing vaccines should genetic variants arise. Additionally, mRNA vaccines are strongly immunogenic and elicit both humoral (antibody-mediated) and cellular (T cell) immune responses. But while mRNA technologies showed promising results in COVID-19 vaccine, it is not a fail-proof platform across the broad scope of pathogens with pandemic potential.¹⁰⁰

Vaccine platform selection depends on the nature of the pathogen, and different platforms are more appropriate for specific pathogens. SARS-CoV-2, for example, had several features that made the virus amenable to mRNA vaccines. When the virus emerged, researchers had already been studying nucleic acid (DNA and RNA) vaccines for decades, including those developed for the related SARS and MERS coronaviruses, so when SARS-CoV-2 genomic data were published in January 2020, scientists had a strong foundation of underlying research to support early development.¹⁰¹ Prior research on coronaviruses determined that programing the mRNA sequence to stabilize the coronavirus spike protein in its prefusion state yielded positive results. Other vaccine platforms also benefitted from prior research on related coronaviruses, including specific viral vectors (eg, adenovirus), illustrating that multiple platforms can be effective against the same pathogen.

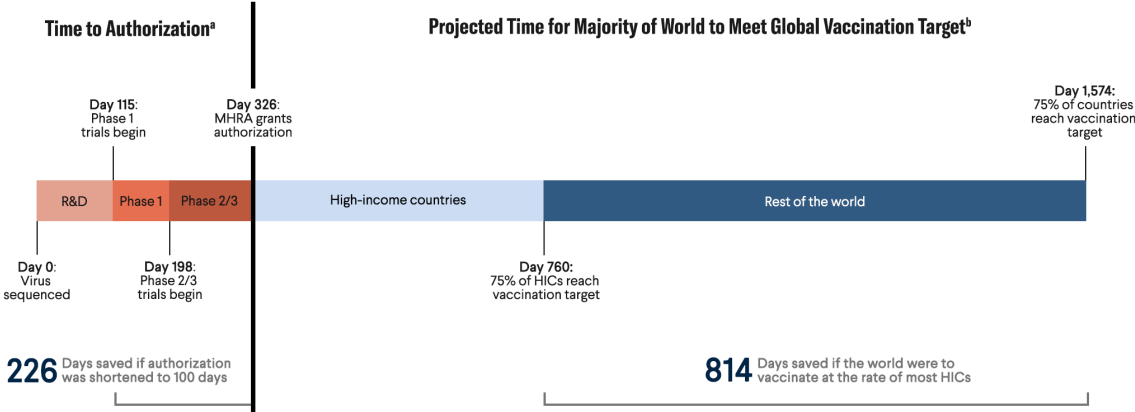
While COVID-19 created a use case for new vaccine platforms and paved the way for the first widespread use of mRNA vaccines, mRNA vaccines should not be assumed as the best hope for all future pandemic threats. Other vaccine platforms, including traditional approaches, may be better suited for other pathogens. For example, recombinant vectors and DNA vaccines have the flexibility of swapping antigens, which can make these platforms desirable for combatting highly mutable pathogens that may require more frequent updates to match circulating strains. Vaccine platform selection should be optimized for the specific biology of the pathogen and the disease it causes. In addition, operational concerns, including the required storage temperature, which can impact vaccine distribution and administration activities, need to be considered. For example, the mRNA vaccines against COVID-19 must be maintained at much colder temperature than vaccines that utilize other platforms, which adds logistical challenges for transporting and storing doses (cold chain). These factors could make some vaccines less appropriate for use in certain environments, such as areas without the infrastructure or equipment necessary to establish or reliably maintain ultra-cold storage conditions.¹⁰²

It should be noted that from a regulatory perspective, products are approved, not platforms.¹⁰³ With this in mind, the adoption of future vaccines based on a previously authorized product does not guarantee regulatory authorization. The new candidate would still need to demonstrate adequate safety and efficacy, but utilizing an existing platform could potentially accelerate the development process and provide initial confidence based on the historical performance of the underlying platform.

2. Scaling Up Global Vaccine Manufacturing in a Pandemic Requires Financing, Policy Support, and Governance

Producing a safe and effective vaccine within 100 days of a pandemic threat being detected would save significant time, but the benefits of that accelerated development timeline will be limited to those nations that can manufacture it at scale or secure adequate access to early supplies (Figure 3). The potential benefits of ensuring that every nation can administer vaccines at the same pace as the majority of high-income countries in the COVID-19 are even larger and would accrue worldwide.

Figure 3. 1,040 Days Could Be Saved in Vaccine Development and Global Vaccination



^a The authorization timeline shown is for Pfizer-BioNTech, the first vaccine to be approved by a stringent national regulatory authority. The United Kingdom’s Medicines and Healthcare Products Regulatory Agency approved the Pfizer-BioNTech COVID-19 vaccine on December 2, 2020.

^b The global vaccination target is for every country to vaccinate at least 70% of their population. These projections are determined as of October 21, 2021, using the average rate of vaccination over the past 30 days for each country. Notes: Timeline to authorization is for the Pfizer-BioNTech vaccine, which was the first vaccine to be approved by a stringent national regulatory authority. Vaccination data accessed from Our World in Data.¹⁰⁴ Abbreviations: HIC, high-income country; MHRA, Medicines and Healthcare Products Regulatory Agency.

Scaling up vaccine manufacturing quickly early in a pandemic requires substantial financing and government policy support, as the experiences of the United States and the United Kingdom have illustrated.

The US government announced the framework behind OWS on May 15, 2020. The efforts made by OWS, now known as the Countermeasure Acceleration Group, were not flawless, but they provide a useful example of the potential benefits of establishing an entity to scale and coordinate pandemic vaccine manufacturing. Through OWS, the United States began making large advance vaccine purchases in July 2020 and coordinated and matched suppliers with vaccine sponsors to ensure those purchase orders would be fulfilled. OWS also subsidized capacity expansion for production of the glass vials, syringes, and other ancillary supplies needed for making, packaging, and administering vaccines. The United States worked with manufacturers and suppliers, including invoking the Defense Production Act⁸ on multiple occasions, to identify and untangle potential input bottlenecks.⁴ The UK government and its Vaccine Task Force likewise helped build and coordinate supply chains for vaccine companies, including “effectively commandeering” a manufacturing facility.¹⁰⁵

A corresponding effort is needed to harness the potential capacity for global vaccine manufacturing. A global mechanism, however, does not currently exist to identify, track, subsidize, and coordinate the production of critical components necessary to manufacture pandemic vaccines in a short time. Nor is there a global mechanism for forecasting demand of critical components during surges of increased consumption, such as during a pandemic.

Some of the ad hoc approaches that emerged to fill these government gaps in the COVID-19 pandemic are worth preserving as examples or potential platforms for the future. Early in the crisis, for example, CEPI developed a list of critical supplies such as bioreactor bags, filters, and tubing as well as gaps in manufacturing capacity.

In May 2021, COVAX created a Supply Chain and Manufacturing Task Force to identify urgent shortages and facilitate the free flow of critical components for manufacturing COVID-19 vaccines.¹⁰⁶ CEPI and COVAX also launched the COVAX Marketplace to convene vaccine industry partners on an ongoing basis to improve the flow of critical inputs and eliminate short-term production and supply bottlenecks.¹⁰⁷ The Marketplace provides vaccine and nonvaccine company suppliers with a platform to contribute and reallocate needed and available materials.

Despite these relatively successful examples, additional resources and coordination are needed to better respond to future pandemic threats. COVAX and its leading agencies lack the financing and necessary clout with vaccine sponsors to prioritize and redirect needed supplies, adequately subsidize production, and provide the support and assurances required to convince vaccine sponsors to transfer technology and tap unused contract vaccine manufacturing in well-regulated markets. These activities would be better suited to a secretariat at a regional body (eg, the African Union) or at a development bank (eg, the Asian Development Bank) working to coordinate the actions of a coalition of like-minded governments to bolster pandemic vaccine manufacturing and to strengthen supply chains in the region.

Faster and More Widely Distributed Vaccine Manufacturing Is Needed Globally, but Is Unlikely to Be Cheaper in the Near and Medium Term

Ten months into a deeply inequitable global vaccine rollout, LMICs continue to struggle to access critical doses of COVID-19 vaccines and, understandably, they no longer want to depend on a small number of wealthy nations for access in this or future pandemics. The world would be safer with a more flexible, robust, and geographically distributed vaccine manufacturing network to produce at scale vaccines using platforms, such as mRNA, that can be adapted for the present crisis and for future pandemic threats. Yet, progress in achieving this objective has been slow to deliver public health benefits in the current crisis.

The firms behind some of the major coronavirus vaccines developed so far in Europe and the United States—AstraZeneca, Johnson & Johnson, and Novavax—have already licensed their patents to Indian manufacturers. Vaccine manufacturers in Russia and China have done the same with their vaccines.¹⁰⁸ The Bill & Melinda Gates Foundation provided US\$300 million to boost the capacity of Serum Institute of India, India's largest vaccine manufacturer, which was contracted to produce the AstraZeneca/University of Oxford vaccine.¹⁰⁹ The AstraZeneca/University of Oxford vaccine is also being produced through a network of facilities in Australia, Europe, Japan, South America, Thailand, the United Kingdom, and elsewhere. Yet, global shortages in ingredients, equipment, and components needed to make vaccines and insufficient local government investment, experienced personnel, and capable vaccine manufacturing facilities hindered vaccine production in India and elsewhere.⁴⁹

Johnson & Johnson was first to invest in vaccine manufacturing capacity in Africa, but it is currently limited to fill-finish operations conducted by Aspen Pharmacare in South Africa, which only started in July 2021.¹¹⁰ In October 2021, Moderna announced plans to build a 500 million-dose mRNA vaccine production facility in Africa, but the site has not yet been selected, and the company has not yet announced a timeline for when it could become operational.¹¹¹ Pfizer-BioNTech signed an agreement with Biovac in South Africa, also for fill-finish operations for its vaccine, but this facility is not expected to come online until 2022.¹¹² To date, no companies have agreed to join the WHO global technology transfer hub.¹¹³

International institutions and donors have already begun pursuing alternative avenues to promote more distributed manufacturing and the emergence of regional vaccine manufacturing hubs. In April 2021, the WHO issued a global call for “expression of interest” in establishing COVID-19 mRNA vaccine technology transfer hubs, which could scale up production and access to COVID-19 vaccines.¹¹³ In May, the 2021 Rome Declaration of G20 leaders called for voluntary licensing and technology transfer to increase global production of COVID-19 vaccines. At that summit, the European Commission announced that it would provide €1 billion to help “develop a number of regional manufacturing hubs across the continent.”¹¹⁴ A partnership between the Africa Centres for Disease Control and Prevention (Africa CDC), COVAX, a network of universities, and several vaccine manufacturers announced the first COVID-19 mRNA vaccine technology transfer hub in South Africa.¹¹⁵ In June 2021, Africa CDC and the African Union launched the Partnership for Africa Vaccine Manufacturing,¹¹⁶ which set the goal of ensuring that African countries can produce at least 60% of the vaccines used regionally by 2040. The US International Development Finance Corporation, a federal agency that funds and oversees private development projects in LMICs, offered at least US\$2 billion in incentives to companies in LMICS to help spur vaccine development.¹¹⁷

Establishing vaccine manufacturing capacity in LMICs is essential for future pandemic preparedness, but it should be viewed as a complement, not a near-term substitute, for investing in the economies of scale afforded by centralized production capacity. Expanding regional manufacturing will require time, sustained financing, and a multipronged, comprehensive effort to succeed. Such an effort should include:

1. *Mechanisms to facilitate technology transfer of potential pandemic vaccines and associated platforms.* Companies with proven vaccines and manufacturing technology have few requirements or incentives to transfer that technology to LMIC manufacturers, except in the rare instance that a funder, such as the Bill & Melinda Gates Foundation or CEPI, includes the obligation to do so in agreements with awardees. Developing and including standard terms in government, academic, and philanthropic R&D funding or licensing agreements and guidelines would facilitate the transfer of more technology to qualified LMIC manufacturers. In order to provide an acceptable arrangement for vaccine manufacturers, recipient countries would need to provide assurances that they will protect the licensed and transferred technology and maintain robust regulatory oversight of manufacturing to ensure that the final product meets stringent quality assurance and quality control standards. Donors seeking to facilitate technology transfer must be willing to invest in creating the enabling environment to support it, including through regulatory capacity building.
2. *Experienced personnel with necessary expertise.* Technology transfer is not, on its own, sufficient to establish vaccine manufacturing capacity; other resources are needed in order to develop sustainable systems and operations at manufacturing facilities. One of

the most difficult resources to develop is a cadre of personnel with the experience and expertise needed to operate vaccine manufacturing facilities and implement reliable quality control systems. Developing a sustainable training pipeline requires experienced individuals to provide the intermediate technical expertise and train the permanent staff on matters such as technology transfer, chemistry, manufacturing processes and controls, and quality control and assurance systems. BARDA and WHO Global Action Plan for Influenza Vaccines (GAP)'s Influenza Manufacturing Capacity Building Partnerships¹¹⁸ had some success providing training, technical assistance, and financial support to manufacturers and nations that submitted letters of intent and committed local funding to the project. It is worth noting, however, that the manufacturing capacity created from the GAP program represents less than 10% of total global influenza pandemic production capacity.¹¹⁹

3. *Flexible business models to make expanded manufacturing capacity viable during interpandemic periods.* It is prohibitively expensive to leave surge manufacturing capacity unused in the periods between pandemics, and it is not feasible to start production operations in a “cold” (ie, inactive) production line due to operational, logistical, and regulatory requirements that must be met and sustained before production can commence. Manufacturing facilities should be designed to make routine products, such as seasonal influenza vaccines, monoclonal antibodies, or new vaccines coming on to market for dengue, malaria, and tuberculosis to maintain the level of operational readiness for the facilities and relevant experience and expertise for facility personnel. It is easier to switch some of that capacity to making products or inputs during a pandemic than to start up an inactive production line. Local governments and international procurement entities need to commit to purchase from LMIC vaccine manufacturers and/or provide subsidies to offset the increased cost in order to keep these facilities financially viable, especially in the early years when facilities may not yet be at full capacity or efficiency.
4. *Manufacturing innovation.* Another option to reduce the time, expense, and expertise required for vaccine manufacturing is through innovation.¹²⁰ For example, modular vaccine manufacturing units—meaning, prefabricated, ready-to-assemble kits—could be sent inside shipping containers to geographic locations where capacity is needed in a crisis. This technology is generally more expensive and cannot yet produce pandemic-level production, but it could provide on-demand local production capacity in smaller-scale emergencies or to provide local supply for specific populations. Flexible manufacturing techniques, such as single-use components for all stages of production, may also enable more continuous vaccine production by reducing the frequency of equipment cleaning.
5. *Investments in regional supply chains.* Vaccine manufacturing requires timely access to hundreds of components, resources (equipment as well as human), and raw materials, much of which is in limited availability, particularly during a surge demand for vaccine such as in a pandemic. Like existing vaccine manufacturing capacity, these resources, as well as the upstream manufacturing of many components, are largely concentrated in a small number of mostly higher-income nations. Distributed vaccine manufacturing facilities will not provide the associated increase in the regional production capacity of inputs and supplies without access to the necessary resources. With this in mind, parallel efforts must be made to develop geographically distributed supply chain hubs, which can supply the necessary equipment, components, and well-trained personnel necessary to make full use of distributed manufacturing facilities in LMICs.

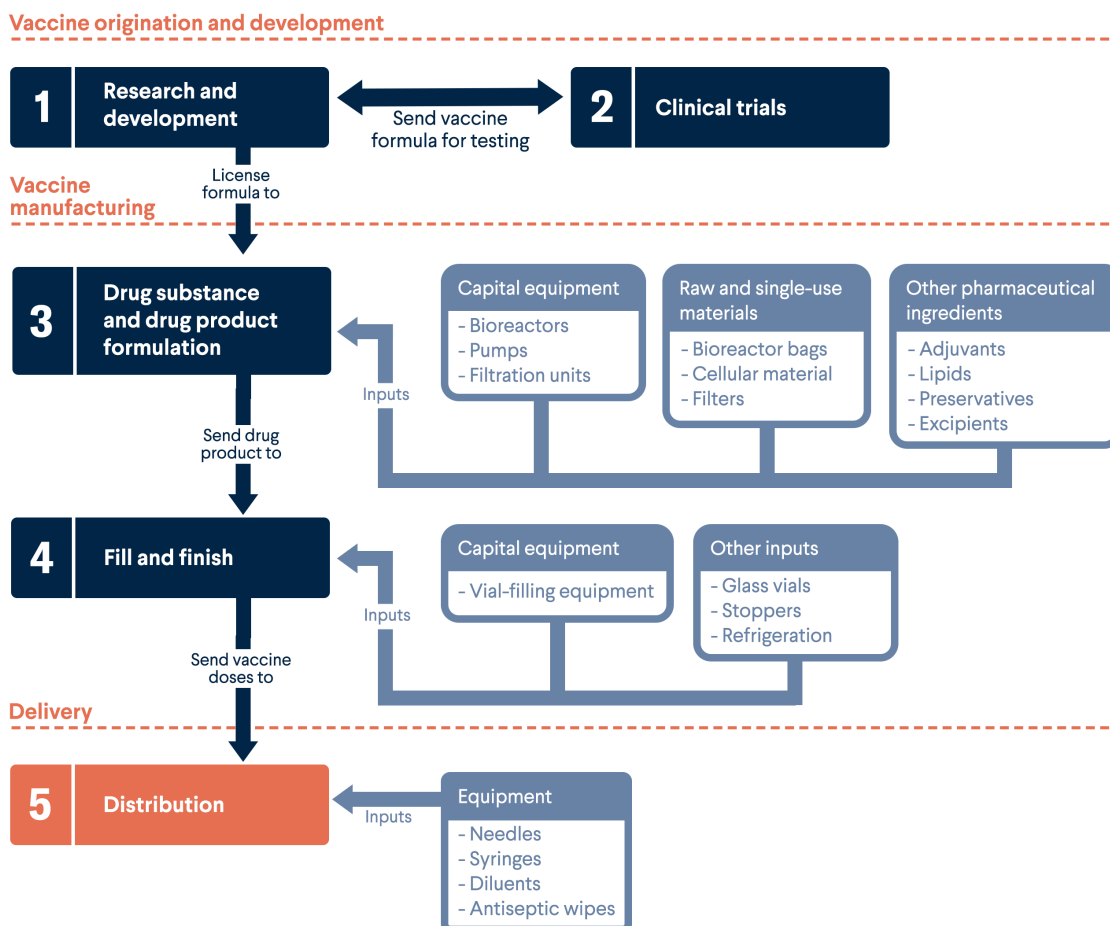
Expanding Vaccine Manufacturing Depends on Cross-Border Trade and Transparency

After a new vaccine is developed and approved or authorized for public use, manufacturers must scale its production to meet the demand. Beyond the active pharmaceutical ingredients, scaling up production capacity necessitates sourcing and securing supplies of hundreds of different specialized and often bespoke components—including disposable bioreactor bags, glass vials, sterilization filters, tubing, stabilizing agents, and syringes—that may be produced by suppliers distributed around the world.³ Few, if any, vaccines are produced start-to-finish in a single factory, or even in one country. The Pfizer-BioNTech COVID-19 vaccine, for example, is comprised of 280 ingredients originating from 19 different countries.¹²¹ If the supply of one of these inputs falters, then the entire production of a vaccine can grind to a halt ([Figure 4](#)).

Vaccine manufacturing depends on ensuring cross-border trade and investment. Yet, in the COVID-19 pandemic, many governments imposed export restrictions or bans and other policies that favor domestic needs over the international flow of critical inputs (eg, capital equipment, raw materials, single-use components) and outputs (eg, finished vaccines). The resulting supply chain disruptions have prolonged the COVID-19 pandemic and contributed to unnecessary infections, hospitalizations, and deaths.

Export restrictions also undermine efforts to prepare for future pandemic threats by discouraging international investments in vaccine and input manufacturing capacity. In a pandemic, countries may be reluctant to subsidize production of vaccines or inputs in other countries if they believe export restrictions could be imposed on those products. Likewise, countries with domestic manufacturing capacity for critical vaccine inputs have little incentive to subsidize scaling up production of those supplies for export without confidence that it will obtain timely access to the resulting finished vaccines made abroad.

Figure 4. Vaccine Manufacturing Is a Multistage Process that Requires Extensive Collaboration and Specialized Inputs



Note: Select stages and inputs depicted illustrate general vaccine production processes and are not comprehensive. Figure is adapted from a Peterson Institute for International Economic working paper.⁴

Few countries have vaccine markets large enough to maintain local production of the full range of input materials needed for production. With the exception of several large countries (eg, Brazil, China, India), most LMICs do not have populations large enough to sustain such a market, and government health spending tends to be low relative to higher-income countries. Even in large, wealthy vaccine markets such as the United States or Europe, sustaining the scale and range of vaccine input production that may be needed in a pandemic is only possible with subsidies, especially if more suppliers enter the global market as other regions seek to establish their own input production capacity. Historically, the willingness of even high-income countries to maintain such subsidies tends to wane in the years between major health emergencies.¹ Even proposals to establish pandemic vaccine production capacity in countries with smaller populations, such as Singapore, would only work if their manufacturers could secure timely, reliable access to adequate vaccine input supplies produced abroad in the crisis.¹²²

The success of efforts to reduce the scarcity of vaccine supplies and increase the geographic diversity of their production in this and future pandemics depends on reducing the threat of export restrictions, which could be addressed in 3 crucial ways: by entering into pandemic trade and investment agreements, promoting standardization, and increasing supply chain transparency.

Pandemic trade and investment agreement

Participants in vaccine-manufacturing hubs could enter into regional trade and investment agreements that would cover vaccines and vaccine-related inputs. These agreements could establish an investment fund to expand regional manufacturing capacity for both vaccines and related inputs, which participating governments would pay into on a subscription basis with escalating, nonrefundable payments to encourage participation. The agreement should include commitments on the part of participating countries to facilitate the cross-border flow of vaccines and related materials and to refrain from imposing export restrictions on supplies destined for other participating countries. In the African context, high-level political interest stemming from the COVID-19 pandemic provides a unique window of opportunity to pursue such an effort as a companion agreement to the recently concluded African Continental Free Trade Agreement.¹²³

In a pandemic, if all vaccine-manufacturing countries prioritize their own populations to the exclusion of global needs, there is no incentive for other countries to participate in multilateral cooperation, and, therefore, every country would be on its own. In this respect, vaccine allocation resembles the classic game theory problem known as “the prisoner’s dilemma.”¹²⁴ In a dynamic in which every nation perceives other nations to be uncooperative, game theory suggests that the only way to achieve cooperation is through reciprocity. In the case of vaccine production and allocation, countries would refrain from imposing export restrictions because doing so would result in exclusion from the benefits of the trade and investment agreement and empower other countries to impose export restrictions on them in response. Trade agreements are designed to address such problems by arresting the cycle of retaliation and imposition of unilateral and nontransparent destructive measures such as tariffs.¹²⁵

In the context of pandemic vaccines and related supplies, the arrangement only works if there is pooled procurement and sufficient subsidies to ensure that LMICs are not excluded from the benefits by other nations purchasing all the available vaccine doses and supplies. Donors and development banks seeking to support vaccine production in LMICs could contribute to these subsidies in the investment fund. Linking such agreements to existing networks of regulators, such as the International Coalition of Medicines Regulatory Authorities,¹²⁶ might help ease concerns about manufacturing oversight and help create a more transparent pathway to the licensing of novel vaccines and facilitate technology transfer.

Standardization

Globally standardizing specialized inputs required for vaccine production and administration would expand the sources for critical material and promote supply chain sustainability. Currently, many critical inputs (eg, reagents, equipment) are bespoke products made for specific manufacturers and vaccines. The bespoke nature of these products not only increases the cost, but it can also lead to supply chain disruption in a crisis when export restrictions are imposed. International standard-setting bodies, such as the International Organization for Standardization, can help develop these standards through a consultative process with manufacturers, procurement agencies, and national regulators. Pooled procurement entities, such as those created by the United Nations Children’s Fund or the Pan American Health Organization, or regional trade and investment agreements can promote adoption of such standards.

Supply chain transparency

In response to dozens of countries imposing export restrictions on food staples during a perceived food crisis in 2008-2011, the G20 created the Agricultural Market Information

System to improve transparency and coordinate policy in the event of sudden scarcity. That system generated information and built trust in supply chains that arguably reduced the use and duration of agricultural export bans in the early days of the COVID-19 pandemic.¹²⁷ A similar effort by the G20 could help reduce unnecessary restrictions on essential medical provisions and be piloted on COVID-19 vaccines and ancillary supplies such as syringes, tubing, and vials. Export controls have stemmed in part from the inability to determine whether vaccine sponsors have double-booked orders of vaccine doses. Without greater vaccine manufacturing and distribution transparency, there may be more export restrictions and supply chain disruptions.

3. Financing Is Needed to End COVID-19, but Will Not Solve the Procurement Problems this Pandemic Revealed

The devastating toll of COVID-19 worldwide, and in high-income nations in particular, has mobilized significant government and industry investment for the rapid research, development, and manufacturing of COVID-19 vaccines. As of June 2021, OWS alone had invested about US\$18 billion, much of which was channeled into late-stage clinical development and early manufacturing of COVID-19 vaccines. International global health institutions contributed as well, including CEPI, which invested US\$1.4 billion to support the development of COVID-19 vaccines. In the 20 months since SARS-CoV-2 was first identified, national regulatory authorities worldwide have authorized more than 20 vaccines, and more than 6.5 billion doses have been administered globally. Global production has been extraordinary, far surpassing what might have been expected at the start of the pandemic. In fact, the global demand for COVID-19 vaccines is expected to triple the ordinary annual vaccine market (approximately 3.5 to 5.5 billion doses per year), with approximately 10 to 14 billion doses of COVID-19 needed to achieve full vaccination for 70% of the global population, on top of other vaccine production.^{22,59}

Meeting global vaccination targets will require vaccine-producing nations to invest more, even while some of those governments seek to provide additional boosters to some or all members of their populations. At the US-led Global COVID-19 Summit during the September 2021 United Nations General Assembly, world leaders pledged to vaccinate at least 70% of every country by the United Nations General Assembly in September 2022.¹²⁸ Given current national vaccination rates, over 70 countries are not on track to meet that goal.¹²⁹ If vaccination campaigns in LMICs falter, booster doses are universally adopted in higher-income nations, and doses continue to be not allocated equitably, it may be even harder to reach that target on time. The additional investment in vaccine production and distribution needed to achieve this goal is well worth it. In May 2021, the International Monetary Fund estimated that vaccinating at least 60% of the population in every country by the first half of 2022 would yield trillions of dollars in economic benefits globally, dwarfing the potential costs required to achieve the necessary levels of vaccine manufacturing, purchase, distribution, and administration.³⁹

New funds have been proposed for future pandemic vaccine R&D, including for preclinical research into the top 25 pathogen families known to infect humans and the development of vaccine platform technologies. The White House's American Pandemic Preparedness proposal includes US\$24 billion for the development of technologies that can create vaccines against the next pandemic threat within 100 days of identification.¹³⁰ CEPI is seeking to raise US\$3.5 billion over the next 5 years to assist in that same goal, but with a focus on global and LMIC needs.¹³¹ It is critical to rapidly develop vaccines in future pandemics that are better-suited for low-resource healthcare settings, including thermostability and, if possible, oral administration. Increased funding for CEPI and similar research initiatives is also needed because epidemics that do not

affect higher-income nations as hard, such as Ebola and Zika, have not generated similar levels of government and industry investment for vaccine R&D and response.

In 2021, the G7 summit in June and the United Nations General Assembly in September advanced discussions about the possible creation of a Global Health Threats Fund,¹³² structured as financial intermediary fund and hosted at the World Bank. It would be financed with an initial investment of US\$10 billion and maintained through annual direct contributions by G20 and other governments, as well as philanthropic and corporate donations. The United States has expressed support for the concept of a financial intermediary fund, as has the European Commission. The G20 High Level Independent Panel on financing for global pandemic preparedness and response published a proposal for the fund to include R&D for innovations “that can achieve transformational change in efforts to prevent and contain future pandemics”¹³³ and “enable public-private partnerships for rapid development, manufacturing and delivery of medical countermeasures on a global scale.”¹³⁴ The proposal is expected to be discussed further at the G20 meeting in October 2021 and at the special session of the World Health Assembly in November.

The increased funding outlined in the G20 High Level Independent Panel proposal is important but should not be a substitute for solving the equitable procurement and allocation governance challenges that emerged in this pandemic. Lack of buy-in from countries with resources and vaccine manufacturing capacity undermined COVAX, not necessarily a lack of financing. Even if COVAX had more funding early in the pandemic, wealthy governments would still have been able to outbid a multilateral initiative or seize locally produced vaccine doses when early vaccine supplies were scarce and the pandemic might otherwise spread unabated locally. Higher-income and vaccine-producing nations have done both. More money may not have created much more early production capacity either. Manufacturers of COVID-19 vaccines and associated input supplies have been slow to scale their production to meet global demand in this pandemic. The African Union has repeatedly indicated that it has the funds and willingness to purchase doses, but none have been made available to buy. Higher-income countries have always been able to move back to the front of the line to purchase further vaccine doses, as they have continued to do with subsequent purchases of booster doses. Further study is needed to better understand and address the reasons for the failure of manufacturing capacity for vaccines and related inputs to scale with demand, the fears of creating future overcapacity, and the reluctance to transfer technology to produce vaccines in LMIC markets.

In these circumstances, the only chance for COVAX to achieve its goal of procuring and allocating doses equitably was if higher-income or vaccine-producing countries were also willing to rely on the multilateral initiative for their own doses. For wealthy nations severely affected by early waves of COVID-19, this would have meant entrusting the lives of their populations to an independent initiative created ad hoc in the midst of a global crisis that is operated by institutions on which they had not previously relied for vaccine procurement. It would have also required the COVAX model to provide more assurances against the threat of governments seizing locally produced vaccine supplies, which is what ultimately transpired in India. Export bans were widely deployed earlier in the pandemic on other critical supplies, including personal protective equipment and ventilators, so additional bans on vaccines were foreseeable.

Enabling a more equitable allocation of vaccines in the next pandemic requires establishing pooled procurement mechanisms in which vaccine-producing nations are willing to participate on the same level as LMICs. This must be done in advance of a crisis because it will be much

more difficult to generate confidence in and adherence to a new mechanism created amid a crisis. COVAX has achieved a lot but concerns about its underperformance makes it unlikely to be trusted in the next pandemic. Regional mechanisms may offer the most hope. In the present crisis, the African Vaccine Acquisition Trust (via the African Union), the Pan American Health Organization's Revolving Fund, and the Asia-Pacific Vaccine Access Facility (via the Asian Development Bank) have successfully begun securing doses for member states to augment COVAX distributions. These regional efforts should be supported at the global level with technical assistance for the development and adoption of common vaccine product standards as well as regulatory cooperation and capacity building. It is also worthwhile to preserve and improve upon COVAX's liability policies and vaccine injury program, rather than leave each nation to engage in time-consuming negotiations with manufacturers over indemnity and other legal complexities. Finally, regional and global procurement mechanisms should include the measures recommended in this report on reducing the unnecessary use of export restrictions and promoting expanded regional vaccine and input supplies manufacturing capacity.

4. Build the Systems Needed to Enable Vaccine Distribution, Allocation, and Uptake Now for the Next Pandemic

While inadequate supplies are still considered to be the single biggest factor limiting vaccine coverage globally, COVID-19 has illustrated the need to devoting adequate and timely attention to distributing and allocating vaccines and to communicating with the public regarding the associated risks and benefits. The historically rapid pace of COVID-19 vaccine development and authorization for public use has exposed public health and healthcare systems as largely ill-equipped for these tasks. This has been the largest global adult vaccination program in decades. The distribution of COVID-19 vaccines involved highly complex logistical challenges, including the ultra-cold storage required to maintain the appropriate cold chain for some vaccines as well as the need for multiple doses, which requires individuals to be adherent to vaccine-specific schedules. Delays in developing and finalizing plans for how COVID-19 vaccines would be distributed and allocated resulted in uptake delays. Similarly, inadequate plans for navigating communication challenges on vaccine use and safety in an information ecosystem rife with misinformation and disinformation about vaccines and COVID-19 have slowed uptake of vaccines—even where supplies are adequate.¹³⁵

To better respond to the COVID-19 pandemic and prepare for when the next pandemic inevitably strikes, governments, multilateral organizations, and private actors should build systems for distributing, allocating, and tracking vaccinations and promoting uptake of these lifesaving tools. Governments must take the lead in planning distribution of vaccines once they are developed, and these plans should consider how limited supplies may be allocated and what transportation, logistics, and other distribution plans will be needed to deliver and administer vaccines to identified priority groups. Dedicated plans are needed to ensure that highest priority groups—which in the case of COVID-19 include healthcare workers, immunocompromised individuals, and individuals with a range of preexisting health conditions—are able to be vaccinated. Similarly, should vaccines require multiple doses, centralized systems for tracking vaccinations and following up with patients will also be needed. As vaccines become more widely available, strategies for targeting hard-to-reach, vulnerable, or disenfranchised populations—such as lower-income, migrant, minority, or rural populations—that may experience access issues will be essential to ensuring that these subpopulations are not omitted from vaccination efforts.

Operationally feasible plans are also needed to support risk communication and community engagement. COVID-19 has exposed the damage that inadequate communication about the risks and benefits associated with vaccinations can cause to uptake. Part of this harm stemmed from the relatively late start in developing communication plans about vaccines and building partnerships with community leaders, media influencers, and others to disseminate relevant information about COVID-19 and vaccines. Focus groups and research studies are also needed to inform the development of evidence-based risk communication campaigns. Social and behavioral science inputs are needed to better understand factors influencing hesitancy about vaccines and what messages or incentives can overcome them.

Finally, governments and international organizations should anticipate that the spread of misinformation and disinformation about vaccines will be significant, and they should develop plans to track and respond to false narratives. Tools such as the WHO Joint External Evaluation (JEE) framework¹³⁶ ask countries about their capacities to monitor and respond to rumors, and efforts to build national capacities to engage in 2-way communication should be prioritized. At the 2020 World Health Assembly, WHO member states passed a resolution that calls on member states to provide evidence-based COVID-19 information and to act to counter misinformation and disinformation.¹³⁷ The resolution also calls on international organizations to address misinformation and disinformation in online spaces and to provide credible information to the public.

These efforts should recognize that the information ecosystem is global. Rumors and lies that originate in one part of the world can rapidly spread globally, and global capacity to monitor vaccine- and disease-related misinformation and disinformation and develop evidence-based counternarratives should also be developed. With its recent focus on tackling “infodemics,”¹³⁸ WHO may be in a position to monitor and respond to misinformation and disinformation that arise, but it will likely need additional resources to better serve in this role. In particular, such efforts would require additional financial and technical support to track the spread of misinformation and disinformation via the internet and social media platforms and the support of governments to disseminate evidence-based messaging to counter misinformation and disinformation.

5. Plan for Global Coordination of Postmarket Research Studies in a Pandemic

COVID-19 demonstrated that national and international coordination of clinical trials is possible and beneficial. In particular, the WHO Solidarity trial¹³⁹; the United Kingdom RECOVERY trial, coordinated by its National Health Service¹⁴⁰; and the US NIH ACTIV effort have been highlighted as positive examples of national-level coordination of clinical trial protocols.^{141,142} Notably, the RECOVERY and ACTIV trials largely focused on coordinating studies conducted domestically, or led by institutions in those countries, while the Solidarity trial was a global effort. These efforts provided common study protocols, promoted geographic and demographic diversity, and facilitated the evaluation of multiple candidate products simultaneously.¹⁴³

While some level of national or international coordination control of clinical trials facilitated a more streamlined and efficient regulatory process for vaccines, insufficient coordination of follow-on clinical studies has compromised abilities to track vaccine effectiveness, monitor vaccine escape, and assess the need for boosters. The impact of this issue is seen in ongoing debate about the optimal dosing of COVID-19 vaccines. The emergent nature of the COVID-19

pandemic drove vaccine developers and manufacturers to make initial decisions regarding dosage and dose timing in order to give themselves a chance to complete initial clinical trials quickly and with positive results. But concerns about emerging variants, improving the global supply of vaccines, waning long-term effectiveness of vaccines, and detecting rare side effects have raised questions about whether other dosing strategies would be beneficial. Though some data have been made available by countries with national health systems and health information systems that can be readily mined to provide relevant data, other nations, such as the United States, have been constrained by the inadequate amount of data they have available to address these questions. This data disparity has created questions about the generalizability of data from countries such as the United Kingdom and Israel that have been able to produce data at the national level. Ideally, these questions would be addressed through globally standardized coordinated clinical investigations rather than company- or investigator-led research studies that may provide mixed results based on the study design and population.

Additional research questions should be addressed that would similarly benefit from globally coordinated clinical investigations, including assessing vaccine efficacy in priority vulnerable populations (eg, immunocompromised individuals), measuring the safety and efficacy of mixing doses of different vaccines, monitoring efficacy against emerging variants, and identifying correlates of protection. Studies are ongoing on many or all of these topics, but they are largely independent efforts. In addition, operational research that demonstrates what vaccine distribution efforts lead to better vaccination coverage, particularly among vulnerable or hard to reach populations, would be useful.

Operational questions about the distribution and uptake of vaccines would also benefit from globally coordinated research. With debates about different countries' use of booster doses despite ongoing vaccine inequities, modeling that compares global pandemic impacts under different vaccination strategies would help demonstrate the consequences of individual countries' vaccine allocation decisions.

An independent but government-supported organization like CEPI could provide this level of international coordination of follow-on clinical investigations. Ideally, any entity that serves in this purpose should be able to readily communicate with national regulatory authorities (eg, US FDA, China National Medical Products Administration) and research institutes (eg, US NIH, BARDA, Health Emergency Preparedness and Response Authority Incubator) as well as national and international authorities for both public health and clinical care (eg, WHO, national or regional centers for disease control and prevention, ministries of health). In particular, coordination between national regulatory agencies and researchers could help standardize, to some degree, the requirements that clinical trials must meet for regulatory review, as these currently vary from country to country.¹⁴⁴ While the entity would not necessarily need to have the resources available to implement large-scale clinical trials, it must have access to the relevant technical expertise, both to advise on clinical trial protocol design and implementation and establish research priorities. Additionally, it needs to maintain some operational and logistical capacity in order to provide direct assistance to both national-level coordinators and local researchers, such as compiling trial data from disparate study sites and providing support for the researchers conducting the study analysis to ensure that the data and analysis are able to meet relevant regulatory standards.

Another possibility is for WHO to assume a greater coordinating role on postmarket research studies by adapting its R&D Blueprint for Action to Prevent Epidemics.¹⁹ WHO could provide

technical support and the global perspective on emerging events, but other stakeholders would likely be needed to establish and maintain the networks and frameworks necessary to provide this kind of high-level coordination for individual trials and research agendas across multiple countries. WHO played this role in some of the COVID-19 clinical trials, although some experts cautioned that WHO assuming the role of coordinating large, multicountry vaccine clinical trial research would distract it from its more pressing operational work. WHO has developed for its R&D Blueprint for Action to Prevent Epidemics target product profiles to inform the development of vaccines, diagnostics, and therapeutics for 15 pathogens and may serve as a model for future work to coordinate development efforts for other pandemic threats ([Table 2](#)).⁶

Table 2. Summary of Priority Recommended Actions

<i>Recommendation Area</i>	<i>Priorities for the Future</i>
Research and Development – Product Development	
<i>Prepandemic Research on Priority Pathogens</i>	<p>Donors should provide the resources that a global organization such as CEPI needs in order to work with national governments, philanthropies, and science research organizations to define a research agenda and strategy, develop candidate vaccines for prototype pathogens that can be taken through Phase 2 clinical trials, and identify correlates of protection. This strategy should define actors, roles and responsibilities, timelines, and funding. The international organization should not only be able to fund necessary research but also coordinate with national governments and science research organizations already engaged in related work, but on an ad hoc and uncoordinated basis.</p> <p>WHO and the World Organisation for Animal Health should work with national governments and to define a strategy to improve knowledge of circulating pathogens in animals and different ecosystems, including screening for new viruses within families known to infect humans.</p>
<i>Manufacturing Scale-Up</i>	<p>Public and philanthropic funders of vaccine R&D should facilitate technology transfer to qualified manufacturers in LMICs that provide assurances to protect the transferred technology and maintain robust regulatory oversight.</p> <p>LMICs should enter into regional trade and investment agreements to support manufacturing hubs, promote standardization of inputs, build supply chains, and reduce export restrictions and other barriers to cross-border flows of supplies, expertise, and ideas.</p> <p>Local governments and international procurement entities need to commit to purchase from LMIC vaccine manufacturers and/or provide subsidies to offset the increased cost in order to keep these facilities financially viable, especially in the early years. Flexible business models and donor support for technical assistance, training, and regulatory capacity building would help as well.</p>
Product Delivery	
<i>Procurement and Financing</i>	<p>In the short term, invest the necessary funds to achieve the global COVID-19 vaccination goal of 70% on time. In the longer term, pair increased financing via a potential financial intermediary fund with the development of a trusted regional procurement mechanisms that can attract the participation of vaccine-producing nations.</p>
<i>Distribution and Allocation</i>	<p>National governments and organizations involved in the development, procurement, and distribution of vaccines should work now to ensure that there are plans and adequate capacities to support the distribution, allocation, and uptake of pandemic vaccines. WHO and national governments should build capacities to track and address vaccine misinformation and disinformation and to disseminate evidence-based communications to promote vaccine uptakes.</p>
Postregulatory Research	
<i>Postregulatory Research</i>	<p>An independent organization (eg, WHO or CEPI) with strong relationships with national governments should be explicitly tasked and resourced to provide this level of international coordination of follow-on postregulatory studies to study effectiveness of vaccine dosing regimens and distribution and uptake strategies. Both CEPI and WHO are doing work that may position them to serve in this role; however, additional support for national governments would likely be needed for CEPI or any organization to serve in a true central, coordinating role.</p>

Abbreviations: CEPI, Coalition for Epidemic Preparedness Innovations; LMIC, low- and middle-income country; R&D, research and development; WHO, World Health Organization.

Conclusion

COVID-19, and the global response to it, has highlighted that a true, end-to-end global vaccine R&D and response ecosystem remains out of reach. The development, financing, production, allocation, and distribution of vaccines have been deeply inequitable, while multilateral initiatives and bilateral aid have been insufficient to close those gaps. As such, COVID-19 has had staggering tolls, taking the lives of millions, costing trillions of dollars, and destabilizing societies. Such devastation continues today, even with several, effective vaccines on the market.

Beyond its human and economic toll, the pandemic has also exposed and redefined the realities of the global R&D response ecosystem. COVID-19 has illustrated the value of early and efficacious vaccines, the potential profitability of pandemics, and the negative influences of self-interest and geopolitics. Any future pandemic pathogen that emerges does so in a world forever changed by and aware of these realities. To ensure that these lessons are heeded and to prevent the devastation of the present crisis from repeating in the next pandemic, governments, multilateral and international institutions, and private actors must act immediately to address gaps and explore opportunities at each step along the vaccine value chain.

Stakeholders should coordinate regional hubs to produce and procure vaccines against pandemic pathogens. Such efforts should not be limited to the duration of the current pandemic, but rather, should begin well in advance of the next large-scale health emergency to ensure early, widespread, and equitable access to efficacious vaccines in a future crisis. These regional hubs must also establish and maintain sufficient vaccine manufacturing capacity to support surge demand during a pandemic. This will require robust and sustainable financing, promotion of flexible business models, and mechanisms to facilitate reliable cross-border flows of supplies, expertise, and ideas. However, financing alone will not solve procurement problems. These efforts should also be accompanied by investment in the transportation, logistics, regulatory, and communication systems needed to enable rapid and global vaccine distribution, allocation, and uptake.

Although COVID-19 is often described as a once-in-a-century crisis, there is no guarantee that will be the case. Other pandemic pathogens could emerge at any time, threatening loss of life and spillover economic, social, and political effects of the same, if not greater, magnitude than that which the world has suffered over the past 2 years. No one can say for certain how governments will respond when the next crisis emerges, as it inevitably will. But what it is certain that national, regional, and international responses to COVID-19 today are already writing the opening chapters of the next pandemic. Only by translating these lessons into action can the world change the pandemic narrative in time for the coming future crisis.

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Annex. COVID-19 Vaccine Development Timeline

The COVID-19 vaccine development timeline shows key milestones in the development, clinical trials, and regulatory processes for several of the major COVID-19 vaccines currently in use globally. These vaccines have received both World Health Organization (WHO) Emergency Use Listing and regulatory authorization from a stringent regulatory authority, as designated by WHO. The timeline shows the amount of time each vaccine took to go through each development and regulatory step, relative to the 100 days pandemic vaccine development goal proposed by some governments and international organizations. This graphic illustrates the relative duration of key components in vaccine development and regulatory authorization in order to support identification of opportunities for improvement. Not shown, however, are vaccine distribution and uptake timelines, which are much longer.

The COVID-19 vaccine development timeline can be found at:

<https://www.centerforhealthsecurity.org/sites/default/files/2023-02/211029-annex-covid-19-vax-dev-timeline.pdf>

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