

Scaling Up the Global COVID-19 Vaccination Program: Production, Allocation, and Distribution with an Emphasis on Equity

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After just over 2 years, the COVID-19 pandemic continues to contribute to extensive morbidity and mortality worldwide. In addition to the burden and loss caused by the virus itself, collateral consequences of the pandemic wreak havoc on the global economy, disrupt essential health care services and childhood education, and weaken existing mechanisms of preventing other infectious diseases such as HIV and tuberculosis (TB). These impacts are unequally felt in low- and middle-income countries due to an insufficient supply of COVID-19 vaccines and an unfair allocation process of distributing vaccines worldwide. An emphasis on equity throughout the continued scaling up of the global COVID-19 vaccination program with production, allocation, and distribution of COVID-19 vaccines could begin to mitigate the disparities in vaccinations seen across the world. Current policy solutions including COVAX, intellectual property waivers, technology transfer in South Africa, and dose donations are examined to evaluate efficacy in increasing equitable access to COVID-19 vaccines.

INTRODUCTION

Causes and Consequences of a Global COVID-19 Vaccine Shortage

Perhaps the most impressive accomplishment since the start of the COVID-19 pandemic in early 2020 has been the rapid development, manufacturing, and distribution of COVID-19 vaccines [1]. In less than a year, several viable COVID-19 vaccine candidates were developed and tested, and went on to receive emergency use authorization in countries throughout the globe [1]. Despite the unprecedented speed in vaccine development, and

reassurance from world leaders that COVID-19 vaccines would become a global public good, the scarce supply of vaccines and unfair inequitable vaccine distribution across countries and regions limits the speed at which the world can obtain herd immunity and recover from the pandemic [2]. Winnie Byanyima, the Executive Director of UNAIDS, was one of the first world leaders to bring light to this inequity, calling it vaccine apartheid [3]. The gross inequities in vaccine access in low- and middle-income countries led to Byanyima forecasting in February of 2021 that nine of every 10 people living in the world's poorest countries were set to miss out on a COVID-19

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Abbreviations: GDP, gross domestic product; LMICs, low- and middle-income countries; WHO, World Health Organization; CEPI, Coalition for Epidemic Preparedness Innovations; C-TAP, the COVID-19 Technology Access Pool; TRIPS, Trade-Related Aspects of Intellectual Property Rights.

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vaccine this year. As of April 2021, over 1.3 billion doses of COVID-19 vaccines had been administered throughout the globe, but only 0.2% of those vaccines were administered in low-income countries [4]. Since then, this statistic has improved marginally, but many countries on the African continent continue to experience delays in their vaccination campaigns. To name a few, the Democratic Republic of Congo has only vaccinated 0.96% of their population, Cameroon sits at 4.08%, and Chad has delivered enough vaccines to cover just 2.58% of their people [5]. The stark inequities in access to lifesaving COVID-19 vaccines affect the entire global population: delays in COVID-19 vaccinations around the world have and will continue to exacerbate mortality and morbidity from the virus and limit economic recovery from the pandemic.

As the COVID-19 pandemic continues to stretch on to nearly 2 years, the virus continues to kill and hospitalize hundreds of thousands of people every month, reduce global gross domestic product (GDP) on the scale of billions of dollars, and generate a massive loss of human capital by impairing the education and health systems. The International Monetary Fund (IMF) estimates a global GDP loss from the COVID-19 pandemic to be nearly \$12 trillion during the years 2020-2021, with an average monthly GDP loss of \$500 billion [6]. Overall losses from the COVID-19 are, however, far more comprehensive than GDP is able to measure and are estimated conservatively to add an additional \$500 billion of global monthly harm (\$1 trillion total in monthly losses). It is estimated that the inoculation of 3 billion people with COVID-19 vaccines worldwide would reap a global benefit equivalent of \$17.4 trillion, which would equate to over \$5,800 in monetary benefit per vaccinated individual—an incredibly cost effective intervention [7]. An investment in an additional 1 billion courses of vaccines would not only speed up vaccination efforts, but would also provide additional global benefits ranging from \$576-\$989 per person vaccinated, which is far greater than the stated cost to purchase a COVID-19 vaccine, which is between \$6 and \$40 [7].

In addition to the aforementioned economic losses from the pandemic, low- and middle-income countries also stand to lose hard-won progress on the mitigation of other infectious diseases due to COVID-19. The African continent has seen a 41% decrease in HIV testing services, a 28-29% fall in TB screenings, and interruptions in the UNICEF childhood immunization campaign that could leave 80 million children under 1 unvaccinated or under-vaccinated [8]. These losses can be attributed to movement restrictions which cause people to miss out on essential health care services, COVID-19 infections among health care workers, and employee shortages within the health care system overall. Global equity in

access to COVID-19 vaccines will be essential going forward in order to mitigate any further disruption of essential health care services in poor-resourced countries.

COVID-19 vaccines are known to reduce both hospitalizations and deaths from the virus. A study from the Yale School of Public Health that modeled infections in the United States determined that without a vaccination program in the US, by the end of June 2021, there would have been nearly 279,000 additional deaths and up to 1.25 million additional hospitalizations, which were averted through the relatively successful country-wide vaccination campaign [9]. With no vaccines, daily deaths from COVID-19 would have likely jumped up to 4,500 per day during the summer surge in infections. The study also found that a vaccination program with half of the actual real-world pace of the vaccination program in the US would also have reduced deaths from the virus by approximately 121,000 and hospitalizations by around 450,000, which is not quite as effective, but still prevents a significant amount of morbidity and mortality from the virus [9]. Thus, there is an immense potential impact of the rapid deployment of vaccines in addressing the COVID-19 pandemic and these results could be seen in low- and middle-income countries as they gain much needed access to vaccines. Without much needed access to COVID-19 vaccines in resource poor countries, the burden of morbidity and mortality due to the COVID-19 virus could be seen for years to come.

Though scaling up vaccination efforts would likely be a cost effective pandemic mitigation intervention, vaccination alone is not a certain route to ending the COVID-19 pandemic and should be incorporated along with other mitigation techniques to stop the spread of the virus including social distancing, face coverings, reliable diagnostic testing, and contact tracing [10]. Additionally, having vaccines that have received emergency use authorization is not enough to put an immediate end to the pandemic. Careful consideration of vaccine production, pricing, allocation, and distribution must be taken into account to ensure equitable access to COVID-19 vaccines going forward as the global vaccination campaign continues to be scaled up [10]. This paper will explore the various stages of scale-up for mRNA vaccines, current policy approaches to the COVID-19 vaccination campaign, and future policy recommendations to ensure vaccine equity going forward.

SCALING UP: COVID-19 mRNA VACCINES

Vaccine Manufacturing

The rapid development, production, and scale-up of COVID-19 vaccines has been an immense technological feat. The story of vaccine production in Marburg, Ger-

many best represents this achievement. In September of 2020, BioNTech purchased a manufacturing plant with 300 employees who had never worked with the new mRNA technology that the company was using to produce its vaccine. In a matter of less than 6 months, the production team at this plant completely transitioned from manufacturing cancer medicines to producing COVID-19 vaccines and later scaled up their output to a weekly production of millions of mRNA vaccine doses [11]. Multiple facilities around the world were able to accomplish similar transitions and rapidly begin producing COVID-19 vaccines. A report from Public Citizen, Imperial College London, and the Centre for Process Innovation used computational process modelling to exhibit how the story from Marburg, Germany could be repeated to establish regional hubs of vaccine production throughout the globe to produce mRNA vaccines for the world. The authors found that an investment of \$23 billion could cover the costs of producing 8 billion doses of the NIH-Moderna vaccine by May 2022. With 4,620 employees working at 55 production lines in 14 facilities, it could be possible to initiate the process of retrofitting vaccine production facilities, purchasing raw materials, synthesizing mRNA vaccines, and completing fill and finish orders [11]. Fewer resources would be required to produce the Pfizer-BioNTech or the CureVac vaccine.

According to the Public Citizen report, mRNA vaccines are an ideal technology for a rapid scale-up campaign in comparison to traditional vaccine methods of production that use cells to express the molecules used in vaccines. The production of mRNA vaccines does not involve cells and, as a result, is far simpler than cell-based vaccine production and is far more consistent in yield since the process is not burdened by the biological variability of cells. Additionally, the production of mRNA molecules, which are the active ingredient in mRNA vaccines, only takes 2 to 6 hours and the entire production process happens in just days, which contrasts with cell-based vaccines that can take months to produce a batch due to the growth process of the cells. The bioreactors for the production of mRNA vaccines take place in 30- to 50-liter containers, whereas cell-based vaccine bioreactors are typically 2000 liters, which can translate to mRNA vaccine production facilities that are much smaller and that have lower capital costs than cell-based vaccine production facilities [11]. An mRNA vaccine production facility is also adaptable: if new variants arise, no changes need to be made during the production process except for the template DNA strand that is used to synthesize all of the mRNA molecules. This means that any mRNA vaccine production facility can quickly alter their outputs for variants or can transition into creating mRNA vaccines for other diseases once the pandemic is over.

The report divides the process of scaling up mRNA vaccine production into four phases, each with a duration of up to 2 months: 1) early planning, 2) advanced planning, facility improvement, and technology transfer initiation, 3) technology transfer and process set-up, and 4) facility process validation and start up [11]. The first phase would identify candidate location sites that could serve as vaccine production sites for regional neighboring countries and consult regulatory authorities in the respective countries. The second phase would adapt chosen location sites to meet regulatory standards and would begin to retrofit those sites for the production of mRNA vaccines. After the repurposed facilities are deemed ready for vaccine production, the third phase would involve the configuration of all of the new equipment and the production of test batches of mRNA vaccines. Finally, the fourth phase would examine the quality of vaccine batches produced, test the consistency of the batches, and seek regulatory authorities to start official production of mRNA vaccines.

In less than 8 months, mRNA vaccine production could be initiated in facilities across the world, and with proper resource mobilization to purchase single use equipment and raw materials, up to 8 billion doses of mRNA vaccine could be produced in the following 6 months, which accounts for vaccine production for up to 80% of the world's population [11]. The report from Public Citizen outlines a model of mRNA vaccine production that could have been used for a global response to the pandemic that includes low- and middle-income countries in the vaccine manufacturing process and builds regional capacity for the production of vaccines. Not only could this method create a more equitable and democratic approach for global vaccine manufacturing, but it could also serve as a solution for the limited production capabilities and current vaccine production bottlenecks of facilities in high-income countries like the United States and Germany. Throughout the process of vaccine development, the vaccines would also need to be authorized by regulatory bodies in individual countries and the World Health Organization (WHO) to ensure that a quick transition to vaccine distribution can be made [10].

Vaccine Distribution

In addition to the scale-up of mRNA vaccine manufacturing to produce enough doses to vaccinate the world, distribution of mRNA vaccines is another hurdle for world leaders to overcome in addressing the pandemic. For a complete global vaccine coverage of 15 billion vaccines (assumes two doses per person), up to 200,000 pallet shipments, 15 million deliveries, and 15,000 freighter flights would be required across various regional supply chains [12]. To ship the Pfizer-BioNTech vaccine, an estimated 20 daily cargo flights around the world are need-

ed, in addition to coordination with regional and local transportation authorities [12]. This presents a challenge for low- and middle-income countries. In reaching rural areas, the transportation links for vaccines can be much slower, and medical facilities may be less equipped, for example, with cold storage for vaccines. The Moderna vaccine is supposed to be stored at -20°C , but is stable for up to 1 month in a refrigerator, and the Pfizer vaccine must be stored at an ultracold temperature of -70°C . Thus, the shipping, distribution, and storage of these vaccines is likely to become a barrier, both in terms of supply chain logistics and of cost, in low- and middle-income countries where current medical supply chains typically distribute vaccines and other medicines at a temperature between 2°C and 8°C [12].

To address the issue of cold chain storage for mRNA vaccines would require a significant amount of capital. Specialized freezers that can reach the low temperatures needed for mRNA vaccines can take between 4 to 6 weeks to manufacture and can cost up to \$25,000 [12]. In addition to cost prohibitive barriers, there are logistical barriers to vaccine distribution and storage, especially in rural areas of low- and middle-income countries. In areas with unreliable electricity, it may be a challenge to run a regular freezer for storage of the Moderna vaccine, let alone running one of the specialized ultracold freezers needed to store the Pfizer vaccine. To address this barrier, Pfizer has created a reusable container that is approximately the size of a suitcase which can be used to transport and store small amounts of their vaccine (1,000 to 5,000 doses) [12]. The containers can hold the ultracold temperatures for up to 15 days with regular refrigeration, but can be maintained indefinitely with dry ice, which is likely to be scarce in rural areas of low- and middle-income countries. Breaks in the cold chain of the distribution of mRNA vaccines can mean the loss of thousands of vaccines and can hurt global vaccination efforts; the final mile of vaccine distribution will be a huge hurdle to overcome in scale-up efforts.

Vaccine Administration

After mRNA vaccines have arrived, refrigerated, in clinics or community health centers, additional challenges may arise. Once a vial of product is punctured to remove the first dose of vaccine, the countdown clock starts; all doses in a vial must be used within 6 hours or thrown away. In order to avoid wasting vaccine doses, it is recommended that clinics schedule patients in advance [12]. This works somewhat well in high-income countries like the US where patients can call a hotline or schedule themselves via an online portal; however, could be next to impossible in low- and middle-income countries where functioning cell phones, cellular networks, and internet can be limited, especially in rural areas. Staff in clinics

with limited resources will also have to administer second doses for many of the COVID-19 vaccines, including mRNA vaccines. This would require either a database to keep track of vaccine doses or a vaccination card, similar to the one issued by the Centers for Disease Control and Prevention in the US, in addition to reliance on patients to return to the clinic for a second dose of vaccine.

In countries with limited infrastructure for the administration of vaccines, mass vaccination drives may be needed to create new vaccination centers to deliver doses of COVID-19 mRNA vaccines in a timely nature. These centers would need to keep track, most likely, of the delivery of multiple different vaccines, each with varied storage and dosing requirements [12]. This scale-up process would rely heavily on cooperation between national and local health departments, immunization efforts such as Gavi (the Vaccine Alliance), and other health care organizations such as Médecins Sans Frontières. Collaboration between national and local health officials is likely to be contingent on the governmental structure of individual countries and may be limited in countries that practice federalism, which could present yet an additional barrier to scaling up the COVID-19 vaccination campaign [13].

Scaling up vaccine manufacturing, distribution, and administration in clinics requires strategic coordination and shared vision between global, regional, and local health officials. Though there are scale-up challenges and considerations for vaccine distribution and administration, the following four policy solutions serve largely to address the scarcity of vaccines globally and the scale-up of the manufacturing process. Once the vaccine supply bottleneck is remedied, then a more nuanced approach to vaccine supply chains and vaccine administration in clinics can begin to be implemented across the globe.

CURRENT POLICY APPROACHES TO COVID-19 VACCINE EQUITY

COVAX Facility

Given the likelihood of global inequity in access to COVID-19 vaccines, a large multilateral fund called COVAX was created by the WHO, Gavi, UNICEF, and the Coalition for Epidemic Preparedness Innovations (CEPI) [14]. COVAX is a global alliance of 189 countries that have pooled their financial resources together to invest, allocate, and distribute COVID-19 vaccines in an equitable fashion, with a particular emphasis on ensuring access to vaccines in low- and middle-income countries. COVAX has been primarily focused on accelerating the development and manufacturing of viable COVID-19 vaccine candidates and to then guarantee “fair and equitable access” to such vaccines around the world [15]. Its aim has been to provide at least 2 billion doses of vaccines by the end of 2021 to vaccinate 20% of the world’s

population, with a focus on vaccinating health care workers and other vulnerable groups [8].

The COVAX Facility permits any country to join, but countries are broken into two funding streams: 1) self-financing countries and 2) advance market commitment (AMC) countries. Self-financing countries are all high-income and upper-middle-income countries that can afford the full manufacturer's price of a COVID-19 vaccine. AMC countries include 92 low- and middle-income countries, some of which will pay small amounts to the Facility, but whose participation is mostly subsidized by donor funding from wealthy countries or from non-governmental organizations such as the Bill and Melinda Gates Foundation [15]. All participants pool together funding in order to invest in candidate COVID-19 vaccines. Additionally, COVAX accounts for difference in supply chains and cold storage requirements across countries by permitting the exchange of allocated vaccines. Countries are able to trade their doses of vaccine with any other member country. For example, a country that is not capable of handling vaccines that require ultracold storage (ie, the Pfizer-BioNTech vaccine) in its supply chain may be willing trade its Pfizer-BioNTech vaccines for Moderna or AstraZeneca vaccines. Though this trade may come with a modest drop in vaccine efficacy, the trade permits countries to make decisions about their vaccine allocations that maximize their individual societal benefits and minimize wasted doses [7].

CEPI is responsible for taking the joint pool of funding and investing in a balanced portfolio of COVID-19 vaccine candidates to help subsidize vaccine research and development minimize the investment risk for any individual country. CEPI contributed sizeable investments that ranged from \$0.62 million for a pre-clinical vaccine from University of Hong Kong up to \$384.1 million to Oxford-AstraZeneca's vaccine which was in Phase III of clinical trials at the time of the formation of COVAX. CEPI, on behalf of the COVAX Facility, has invested in potentially viable vaccine candidates from: Inovio, Moderna, University of Queensland, CureVac, Novavax, University of Hong Kong, Oxford-AstraZeneca, Merck, and Clover Biopharmaceuticals [15]. Recipients of funds from CEPI through COVAX are required to abide by an equitable access policy which states that "appropriate vaccines [should be] first available to populations when and where they are needed to end an outbreak or curtail an epidemic, regardless of ability to pay," [16]. There is mixed evidence in practice of vaccine manufacturers actually following through on CEPI's equitable access policy.

Though the aim of securing 2 billion doses by the end of 2021 was quite ambitious for a single multilateral fund, it is inadequate when considering the immense global demand for COVID-19 vaccines. From the time of

its inception, COVAX was limited in monetary resources and as of March 2021, had only been able to purchase vaccine doses for around 250 million people [12]. In addition to being underfunded, COVAX has also been limited in its ability to purchase vaccines due to bilateral vaccine purchases between wealthy countries and vaccine manufacturers. High-income countries have claimed more than half of the doses of COVID-19 vaccines that came to market in 2021, with some countries reserving such an excessive number of doses that they would be able to vaccinate their populations multiple times [12]. As a result of high-income countries jumping the line by making individual agreements with vaccine manufacturers, vaccine doses earmarked for COVAX have been deprioritized and delayed, which will lead to an immense loss of life in low- and middle-income countries. In spite of an equitable access policy put in place by CEPI to try and prevent this situation from occurring, pharmaceutical manufacturers seem to have taken advantage of it. In particular, Moderna has been guilty of violating CEPI's equitable access policy, though it's difficult to say if the equitable access policy represents an actual contractual obligation for the company. From the beginning of the COVID-19 pandemic, Moderna has expressed intent to prioritize the United States and other high-income countries in bilateral deals for the purchase of its vaccines. In July of 2020, Moderna announced advance purchasing agreements with Canada, Switzerland, Israel, Qatar, and the US, but did not publicly announce deals with any low- and middle-income countries. Additionally, Moderna's pricing per course of vaccine seemed to be set high enough to be price restrictive to poorer countries, between \$64 and \$74 for smaller purchasing deals [15].

Though COVAX has been quite successful at stimulating investment in the research and development of vaccines, which are traditionally underfunded by pharmaceutical manufacturers, and has helped to fund a number of successful vaccine candidates, it has a fair amount of limitations that impair its effectiveness. The COVAX Facility does not take concrete actions to promote technology transfer and scale-up of vaccine production in low- and middle-income countries. The Facility merely encourages voluntary agreements from manufacturers in high-income countries, which have been very limited to date [15]. This approach will inherently underutilize global production capacity of COVID-19 vaccines and has contributed to an artificial, inequitable scarcity of vaccines in low- and middle-income countries.

Donations from High-Income Countries

As of August 2021, the US had donated more than 110 million doses of COVID-19 vaccines abroad to more than 60 countries after President Biden's promise to make the US the world's "arsenal of vaccines" [17].

Collectively, the donations from the US amount to more doses than all other countries combined, but is still a drop in the bucket of the total number of vaccine doses needed to vaccinate the world. From the beginning of the COVID-19 vaccination campaign, the Biden Administration has emphasized the “generosity” of the US, in spite of the fact that bilateral vaccine purchasing agreements and patent protection of COVID-19 vaccines have collectively contributed to the lack of access to vaccines in low- and middle-income countries. The donation-centered policy approach that the US has used is ripe with allegories about how democracy has led to the production of the most effective mRNA vaccines and the most charitable giving of vaccines to low- and middle-income countries. Through donating vaccines to specific countries like Taiwan, South Korea, and Israel, the US continues to practice what has been dubbed “vaccine diplomacy,” which is the use of COVID-19 vaccines to further political ideologies [8]. This patronizing approach also assumes that low- and middle-income countries are incapable of producing vaccines for themselves, protects the profits of vaccine manufacturers, and limits agency in pandemic response in resource-poor countries.

Technology Transfer: A Case Study on South Africa

South Africa, like many countries in early 2021, both joined COVAX and made purchasing agreements with vaccine manufacturers to supply COVID-19 vaccines to its people. In comparison to the price paid by the European Union for the AstraZeneca vaccine, South Africa paid more than double for an order of vaccines that was far smaller than the number it needed to vaccinate its entire population [2]. Unfortunately, smaller orders of vaccines tend to cost more, which can become burdensome to countries with a limited fiscal space to make risky investments in vaccine candidates still in the research and development pipeline. This situation is representative of the experience that many other low- and middle-income countries have experienced in attempting to purchase COVID-19 vaccines. In spite of difficulties purchasing COVID-19 vaccines, South Africa, to date, has received a total of 29.7 million doses of COVID-19 vaccines, with 11 million of them coming from bilateral agreements, 9.1 million coming from COVAX, and 5.66 million coming from US donations, and the remaining amounts coming from other unknown sources. With these vaccines, South Africa has been able to vaccinate 27.37% of their population, which puts its vaccination rate higher than nearly all of the other countries on the African continent [5,17]. To improve the vaccination rate within its borders and throughout the African continent, South Africa presents a promising new avenue to increase the scale-up of COVID-19 vaccines through the technology, knowledge, and data transfer to expand mRNA vaccine

manufacturing capacity.

In an effort to facilitate the transfer of the technology, knowledge, and vaccine recipes used to produce COVID-19 vaccines from current manufacturers in high-income countries to potential vaccine production sites in low- and middle-income countries, the WHO launched an initiative that would create regional hubs to support local production of mRNA vaccines called the COVID-19 Technology Access Pool (C-TAP) [4,18]. After difficulties finding donor manufacturers who were willing to voluntarily license the production of their product to potential vaccine producers in low- and middle-income countries, South Africa was chosen as the first WHO technology transfer hub in hopes that it would scale up the production of vaccines throughout the African continent [18].

This technology transfer hub would serve as a learning site that would teach vaccine manufacturers from throughout the continent how to make mRNA vaccines. With the help of vaccine manufacturers from high-income countries, local experts in mRNA research and vaccines, and WHO staff would collaborate to educate new vaccine producers the process of vaccine production, quality control, and licensing so that they might replicate it in another site on the African continent [19]. As COVID-19 vaccines are currently limited in supply, a successful solution to the production bottleneck created by vaccine manufacturers in high-income countries should incorporate technology transfer in order to expand global manufacturing capacity. The South African hub involves multiple local and regional stakeholders including the Medicines Patent Pool, Afrigen Biologics, the Biologicals and Vaccines Institute of Southern Africa, the South African Medical Research Council, and the Africa Centers for Disease Control and Prevention. In addition to incorporating multiple local stakeholders from South Africa and across the continent, the hub contains a research and development arm to examine mRNA vaccine technology and identify future ways of using it to scale up vaccine production or to produce new mRNA vaccines. Though technology transfer is not a very rapid response to addressing the immediate needs of the COVID-19 pandemic, with transfer times ranging up to 30 months, the technology transfer hub in South Africa represents one of the first steps in a long-term goal of self-sufficiency in vaccine production on the African continent [18].

The Trade-Related Aspects of Intellectual Property Rights (TRIPS) Waiver

The pricing of COVID-19 vaccines has contributed to a lack of equitable vaccine access in low- and middle-income countries [10]. One notable means of solving the problem of expensive vaccines and, as a result, controlling the cost of COVID-19 vaccines could be

through negotiations with the vaccine manufacturers [20]. Negotiations, even through the COVAX AMC, have unfortunately resulted in few voluntary agreements to lower prices for vaccines or to license production of vaccines to facilities in low- and middle-income countries. As there have been challenges in both a timely sharing of vaccine doses with low- and middle-income countries and through sharing vaccine production knowledge with the WHO's technology transfer initiative, there has been a resulting push for a World Trade Organization (WTO) proposal called the TRIPS waiver that would temporarily waive intellectual property rights on COVID-19 vaccines and permit vaccine manufacturers in low- and middle-income countries to use technology and vaccine recipes from successful vaccine candidates to create a generic version to be distributed in their own respective regions. In May of 2021, the Biden Administration surprised the world with its announcement of an intent to support the TRIPS waiver proposal [4].

In an absence of effective voluntary action from wealthy countries and from pharmaceutical manufacturers, the TRIPS waiver would provide a legal framework of rules to follow and mandatory commitments to ensure a swift end to the COVID-19 pandemic. Given that many vaccine manufacturers have relied on public funding from their respective country governments or pooled funding through the COVAX Facility, there is a strong argument for COVID-19 vaccines to become global public goods. The Moderna-NIH vaccine was almost entirely funded by the US government and received support from the National Institutes of Health (NIH), which even holds patents for portions of the vaccine [1]. In spite of NIH backing at many steps throughout its development process, the company has prioritized bilateral dose agreements with wealthy countries over sending doses for global distribution through COVAX and has priced their vaccines at a price that is higher than most low- and middle-income countries could afford. The TRIPS waiver, if successful, would prevent pharmaceutical companies like Moderna from taking advantage of governmental financial support to gain a profit.

Monopoly protection of pharmaceutical products, if anything, provides a disincentive for companies to provide vaccines to low- and middle-income countries [1]. A TRIPS waiver would ensure that vaccine manufacturers cannot 1) prevent production or access to raw materials that are needed to produce COVID-19 vaccines, and 2) charge artificially inflated prices for their products, especially during a global pandemic [4]. Pharmaceutical monopolies on vaccines in the past 20 years have led to high prices and a lack of equitable access to the vaccines, as can be seen in the example of the HPV and pneumococcal vaccines. Both HPV and pneumonia are leading causes of morbidity and mortality in low- and middle-

come countries, yet are largely preventable with vaccines [4]. As to not repeat the history of what has happened with HPV and pneumococcal vaccines, the TRIPS waiver's primary motive would be to save as many lives as possible. Though the Biden Administration's stance has been that the waiver should only apply to vaccines, the original WTO proposal applies to all medical technologies related to COVID-19, which could include diagnostic tests to identify the COVID-19 virus, medicines and antiviral treatments, and medical equipment such as ventilators. The Biden Administration should reposition their stance to be in support of the original waiver proposal from India and South Africa, which covers a greater, more expansive list of tools to help address the pandemic [21]. A successful waiver would also provide clear, unambiguous language with a specific duration of how long the intellectual property rights would be suspended and would limit the ability of vaccine manufacturers to create legal challenges that would exacerbate the current state of inequitable access to vaccines.

In spite of a great deal of clamor when the TRIPS waiver for COVID-19 vaccines and medical technologies was first proposed in early 2021, government leaders in wealthy countries like the United States, the United Kingdom, and Germany have been hesitant to push it forward at the WTO and as a result the waiver has made very little progress since the summer of 2020. Those who oppose the waiver fear that it may stifle innovation or that low- and middle-income countries are not capable of producing vaccines at the same regulatory standard at which vaccines are produced in high-income countries [1]. This has been proven wrong time and time again with vaccine production in India, for example. Up until the late 1990s, Hepatitis B vaccines were produced almost entirely by Merck and GSK, but their domination of the Hepatitis B vaccine market was challenged when Shantha Biotechnics, an Indian vaccine manufacturer, were able to reduce the cost of a dose from \$23 to only \$1. Since then, vaccine coverage for Hepatitis B has increased wildly and vaccine producers in low- and middle-income countries have become absolutely essential for worldwide vaccination campaigns. In 2018, low- and middle-income countries produced more than half of the 2.4 billion vaccine doses that were purchased by UNICEF for their child vaccination initiatives [4]. An intellectual property waiver, if passed, would permit the scale-up of the production of low-cost vaccines throughout low- and middle-income countries that could be distributed regionally to help address the COVID-19 pandemic.

POLICY SOLUTIONS AND RECOMMENDATIONS

Table 1 briefly summarizes some of the strengths and

Table 1. Health Policy Strategies to Increase Vaccine Equity during COVID-19 Vaccination Scale-Up

Policy Option	Strengths	Limitations
COVAX Facility: Advance market commitments	Multilateral; ambitious; pools risky investments in candidate vaccines and minimizes risk.	Undermined easily by bilateral agreements; underfunded.
Dose Donations from Wealthy Countries to LMICs	Show charitable spirit and solidarity.	Patronizing; extremely inadequate in relation to current global need.
Technology Transfer to LMICs via WHO's regional hub program	Builds vaccine manufacturing infrastructure in LMICs; democratic.	Can take a long time to implement; need willing donor countries who want to share technology.
Intellectual Property Waivers (ie, TRIPS) suspending patents on COVID-19 vaccines and therapies	Can support the development of lower cost vaccines and therapies for LMICs.	Limited support from high-income countries; resistance from vaccine manufacturers.

limitations of each existing policy solution mentioned in the previous section of the paper. The COVAX Facility and its use of advance market commitments to fund the research and development of COVID-19 vaccines have been successful at bringing a diverse portfolio of viable vaccine candidates to the global market, but has been very limited in its ability to distribute vaccines on a mass scale due to bilateral agreements where vaccine manufacturers prioritized filling orders for high-income countries over distributing doses to COVAX which would have allocated the doses equitably. Dose donations from wealthy countries, though charitable, can be patronizing and should not be the only strategy used to promote global access to COVID-19 vaccines.

The two most viable strategies from Table 1 are technology transfers and intellectual property waivers. Both of these strategies emphasize democratization of vaccine manufacturing and work towards building vaccine manufacturing capacity in low- and middle-income countries while also working towards a swift response to the COVID-19 pandemic. A joint approach with intellectual property waivers to produce generic versions of COVID-19 vaccines would keep costs low and combined with technology transfer hubs would also assist in creating infrastructure for low- and middle-income countries to produce their own vaccines. This low-cost approach would create a sustainable means to equitably scale up the production, allocation, and distribution of COVID-19 vaccines while also building long-term and much needed vaccine production infrastructure throughout the Global South. Any successful effort to increase the supply of COVID-19 vaccines is likely to be cost effective and is likely to create a positive externality on the greater global economy.

CONCLUSION

Inequitable access to COVID-19 vaccines is largely

driven by limitations in supply and unethical allocation decisions made by vaccine manufacturers. Scaling up vaccine production worldwide requires policy solutions that limit the power of pharmaceutical monopolies and democratize the knowledge of vaccine production throughout the world. With intellectual property waivers combined with regional technology transfer hubs that teach vaccine producers in low- and middle-income countries the manufacturing process, successful scale-up of the production and a more equitable allocation of mRNA vaccines can be achieved to facilitate a global vaccination effort.

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