Policy Actions to Increase the Supply of COVID-19 Vaccines in the Short Term

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Vaccination rates in developing countries lag those in developed countries by a huge margin. This Research & Policy Brief identifies and quantifies the impact of six policy and regulatory actions that could increase vaccine supply to developing countries before the end of 2021. The actions focus on measures to accelerate regulatory approvals, optimize production capacity across firms, reconfigure prioritization of low-risk groups, and adjust generous dosage thresholds. Together these actions could help yield enough supply to reach the interim target to vaccinate at least 40 percent of the population of every country by the end of 2021, as a means to vaccinate 60 percent of global population by mid-2022, thereby helping to end the pandemic earlier, reducing uncertainty and raising growth.

The Worldwide Shortage of Vaccines

On May 31, 2021, the heads of the World Bank, International Monetary Fund (IMF), World Trade Organization (WTO), and World Health Organization (WHO) jointly endorsed a $50 billion proposal outlining actions to end the COVID-19 pandemic. Immediately, donors responded by almost entirely fulfilling the proposal’s request for additional vaccine financing, through two commitments to COVAX, the global vaccine cooperative: an additional cash grant of almost $4 billion, announced on June 2, 2021; and an in-kind grant of at least 800 million vaccine doses (valued at $8 billion or more), announced on June 13, 2021. Earlier analysis by Agarwal and Reed (2021) shows that these two commitments would be sufficient to finance vaccines for 60 percent of the population in 91 low- and lower-middle-income economies (a theoretical threshold for herd immunity to the alpha variant, a target of public health authorities, including the Africa Centers for Disease Control). Though additional line items included in the $50 billion related to COVID-19 diagnostics and treatment remain unfunded, donors have committed most of the financial resources requested to procure vaccines for the poorest countries. Nonetheless, the pace of vaccination remains unacceptably slow in these countries because of a lack of vaccines. For example, by August 10, 2021, COVAX was able to supply merely 191 million doses against a target of 2 billion doses in 2021.

Analytical Approach to Identifying Additional Supplies

To develop options to increase vaccine supply for low- and lower-middle-income countries, this Brief focuses on potential excess supply in a relevant group of the largest vaccine-producing and purchasing economies: China; the European Union (EU) members; the G-7 (Canada, France, Germany, Italy, Japan, the United Kingdom, the United States); and India, which we call collectively the G-10. These economies have contractual rights over much of supply through advance purchase agreements (Duke Global Health Innovation Center 2021), and according to company-reported production estimates, these economies will account for 88 percent of all COVID-19 vaccine production in 2021 (Casey 2021).

Estimating excess COVID-19 vaccine supply through the end of 2021 requires a forecast of (1) global production levels and (2) doses that vaccine-producing economies will use for their own populations. Our approach is as follows. First, we use population data to estimate the number of doses needed for domestic abundance, by which we mean there are enough vaccine doses to fully vaccinate everyone over the age of 12 and provide boosters. Second, we assume the production rate remains constant through the end of 2021, consistent with persistent shortages of inputs (for examples, see Chatham House 2021) and the time needed for new capacity to come online. Third, excess supply is calculated as the number of doses left once the major vaccine-producing economies achieve domestic abundance at the current rate of production. Our approach is described in further detail in Annex A.

Baseline Scenario

Under our approach, excess supply of COVID-19 vaccines from the G-10 is expected to be 271 million doses by the end of 2021 (figure 1). China is expected to produce 200 million such doses, with the G-7 and the EU supplying the remainder. India is unlikely to obtain domestic abundance in 2021. The United States, which has committed to provide 500 million doses of BNT162b2 (the vaccine developed by BioNTech/Pfizer) to COVAX, of which 200 million doses will be provided in 2021, will also run short unless further policy or regulatory changes are considered.

These baseline results suggest that at current rates of production excess supply in the G-10 is insufficient to vaccinate 40 percent of the population of every country by the end of 2021. Accounting for doses already administered and employing all available excess supply of single-dose vaccines, 1.625 billion doses are required to fully vaccinate 40 percent of the 2.5 billion people in 91 low- and lower-middle-income economies eligible for subsidized vaccines through the COVAX AMC facility. In these “AMC91" countries, two doses of any vaccine have been administered for just 2 percent of the population. In addition, 1.036 billion more doses are required to cover 40 percent the 1.4 billion people

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Erratum: A previous version of this Brief incorrectly stated the target to vaccinate 40 percent of the population in the AMC91 countries. The correct target is 1.625 billion doses, accounting for doses already administered and employing all available supply of single-dose vaccines.

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who live in economies outside the G-10 that are richer than the AMC91. Two doses have been administered for only 3 percent of this population, though 14 countries in this group have vaccine-manufacturing capabilities. Given the scale of the gap between excess supply and requirements, further actions are needed to meet the interim target for the end of 2021.

**Six Policy Actions to Expand Excess Supply**

Six policy and regulatory changes are considered to expand supply. For each policy action, the result from immediate action is quantified in terms of additional doses available from the G-10 economies, using available data and our assumptions about production and use. The responsible party to undertake each action is identified: either a government authority or a national regulatory authority (NRA).

1. **Stringent regulatory authorities (SRAs) support WHO emergency use listing (EUL) for effective vaccines (+582 million doses)**

   COVID-19 vaccine development efforts have resulted in highly effective vaccines that are not yet authorized for use. COVAX, multilateral development banks including the World Bank, and many NRAs rely on emergency use authorization (EUA) from a group of so-called stringent regulatory authorities (SRAs), which are the NRAs of Australia, Canada, the European Union, Switzerland, the United Kingdom, and the United States (WHO 2020). The WHO has its own process for providing emergency use authorization (called “emergency use listing,” or EUL), although in practice it relies on advice from these same SRAs to make that decision. SRAs decide to provide emergency use authorization if their own analysis of raw clinical trial data supports the drug’s safety and efficacy. In normal times, this process can increase efficiency since it means data are reviewed only once.

   An action to expand supply is for the SRAs to expedite review of all vaccines that developers have found to be more than 50 percent effective in Phase 3 trials, as required by SRAs for authorization. Additional doses would follow satisfactory EUA inspections of manufacturing facilities in economies with the capacity to export. Two candidates for expedited review based...
on clinical trial evidence are NVX-CoV2373 (the vaccine developed by Novavax), which has an efficacy of 89.7 percent (Heath et al. 2021) and which COVAX supply relies upon; and Gam-COVID-Vac (the vaccine developed by the Gamaleya Research Institute and the Health Ministry of the Russian Federation), which has efficacy of 91.6 percent (Jones and Roy 2021). Other vaccines have been authorized for emergency use, but not when they are produced in certain plants. The developers of BBIIBP-CorV (the vaccine developed by Sinopharm) and Coronavac (the vaccine developed by Sinovac) together report 4 billion doses in annual production capacity, though only around 10 percent of this has EUL. Facilities in Argentina, China, Brazil, Russia, and Thailand have licenses to produce ChAdOx1 nCoV-19 (the vaccine developed by Oxford/AstraZeneca), but have not satisfied site inspections.

Within the G-10, satisfactory inspections of manufacturing facilities in China would yield the most additional doses. In China, supporting EUL for 10 percentage points of the annual capacity of Sinovac and Sinopharm would yield 200 million doses (since the year is half over), for all facilities producing ChAdOx1 nCoV-19, 99 million doses, and all facilities producing Gam-COVID-Vac, 61 million doses. Canada, the United Kingdom, and the United States have advance purchased 222 million doses of NVX-CoV2373. Additional EUL inspections in India would not yield excess production in 2021, assuming prioritization of domestic needs. In total, satisfactory EUL inspections at facilities in the G10 economies would deliver a total 582 million doses.

2. The EU, German, and UK governments request that the capacity to produce ineffective CVnCoV be converted to produce BNT162b2 or mRNA-1273 (+275 million doses)

Not all COVID-19 vaccine development efforts have resulted in highly effective vaccines, but vaccine development efforts by firms have resulted in capacity to produce vaccines. This policy action creates additional production capacity through capacity conversion—whereby vaccine development efforts that are yet to be effective pivot to effective vaccines. One example is CVnCoV (the vaccine developed by CureVac N.V.), which has proven only 48 percent effective against disease across age groups after two doses (CureVac 2021), below the indicative threshold. This production capacity could be productively repurposed, following precedent. Merck abandoned development of its COVID-19 vaccine after unsuccessful trials and, through a partnership brokered by the White House, has committed two plants to produce the more effective JNJ-78436735. Similarly, Sanofi Pasteur has bottled and packaged doses of BNT162b2 and JNJ-78436735.

A new partnership could be executed by the European Union and the United Kingdom, which have purchased 225 million and 50 million doses of CVnCoV respectively—a total of 275 million doses, while Germany holds an option for additional purchases (Duke University Global Health Innovation Center 2021). These governments could assess whether CureVac would be willing to cede reserved production capacity and whether this capacity is suitable for BNT162b2 and mRNA-1273 (the vaccine developed by Moderna). They could also assess whether scientific collaboration between Pfizer, Moderna, and CureVac would accelerate progress toward a normal cold chain mRNA vaccine with high efficacy.

3. NRAs delay booster shots for those with healthy immune systems (the immunocompetent) aged 12–70 (+243 million doses)

This policy action entails a global effort to delay booster shots for low-risk populations. While developers have a private profit motive to promote the sale of boosters, evidence suggests that delaying boosters for the nonvulnerable will have limited consequence for mortality in the G-10 economies. For instance, in the presence of more contagious delta variant, a study in Scotland (Sheikh et al. 2021) found that vaccines remain highly effective after two doses. Rather than using available doses as booster shots now, using them as first and second shots in economies with scarce supply would significantly reduce mortality and morbidity in those economies and contain the spread of the pandemic more rapidly. The baseline scenario assumed that the G-7 and EU economies reserved supply for one-third of the immunocompetent population ages 12-70, reflecting a status quo in which individuals can get vaccines for free without documentation. A moratorium until the end of 2021 on vaccination of this nonvulnerable population—though not the immunosuppressed and elderly—would free up 243 million doses.

4. NRAs delay second doses for those with confirmed prior infection (+83 million doses)

There is strong evidence that immunity comparable to two doses of vaccine can be achieved with one dose and confirmed prior infection (Frieman et al. 2021). This policy action involves delaying the second dose for those with confirmed infections. The French health authority, for example, has recommended that immunocompetent people with a dated SARS-CoV-2 infection (symptomatic or not) proven by polymerase chain reaction (PCR) or antigen test could delay their second dose, given post-infection immunity to SARS-CoV-2 (HAS 2021). However, given relatively low case counts as a share of the population—for instance, in China (0.01 percent), India (2.3 percent), and the United States (10.5 percent), this measure yields few excess doses. Using these infection rates, a moratorium until the end of 2021 on vaccination of this nonvulnerable population would yield 83 million doses, though this number will grow over time if infections rise.

5. NRAs delay doses for the immunocompetent ages 12–17 (+71 million doses)

COVID-19 vaccines are increasingly authorized for younger populations. This policy action entails delaying vaccination for the youngest low-risk populations. As of August 10th, in the United States 349 people under age 18 have died of COVID-19, while 606,389 adults have died of the disease (CDC 2021). More deaths of children and adolescents are attributable to cancer, car accidents, heart disease, homicide, or suicide than to COVID-19 (Woolf, Chapman, and Lee 2021). While
susceptibility of children to newer variants bears monitoring, G-10 economies prioritized vaccination of the elderly when vaccines were scarce. Today, rather than vaccinating adolescents with extremely small chances of death or serious illness, shifting doses to economies with scarce supply to significantly reduce mortality and morbidity there would stop the spread of the pandemic globally. The baseline scenario assumed the G-10 reserved vaccines for all adolescents. A moratorium until the end of 2021 on vaccinations for the immunocompetent in this age group would yield 71 million doses, reflecting the relatively small adolescent population in most G-10 economies.

6. NRAs approve half doses of mRNA-1273 (+55 million doses)

The effectiveness of vaccines does not necessarily depend on the size of a dose in a linear fashion. This policy action is for NRAs outside of the G-10 to authorize administration of half doses, effectively doubling available excess supply while using the scientific method to ensure efficacy is not compromised. While initial doses chosen in clinical trials can be large given a reasonable desire to demonstrate effectiveness, developers can adjust dosing downward and regulators can authorize fractional doses, increasing the available supply without a loss in effectiveness (Cowling, Lim, and Cobey 2021). For instance, Phase 3 trials of JNJ-78436735 and NVX-CoV2373 proceeded with the smaller of two dose options tested in early trials, after those trials found no statistically significant difference in immune response between the two doses.

There is precedent for reducing dose sizes in emergencies (while holding the time between doses constant). In the case of yellow fever, WHO’s Strategic Advisory Group of Experts (SAGE) has recommended dose fractionation down to one-fifth of the standard dose to overcome scarcity during epidemics. An option is for NRAs to immediately authorize 50μg rather than a 100μg dose of mRNA-1273, based on evidence that the immunogenicity response was not significantly different with half doses. BNT162b2, which is on the same platform, is delivered in 30μg doses. Melissa Moore, Chief Scientific Officer for Moderna, has said that fractional dosing could have the effect of “reducing side effects without compromising protection.” This policy would yield 55 million doses, given mRNA-1273 is just one of many vaccines. Więcek et al. (2021) outline low-cost options to obtain more information about the impact of fractional dosing during the implementation of this policy, and to explore the feasibility of fractional dosing of other vaccines.

Conclusion

Despite financing and production commitments to provide sufficient COVID-19 vaccines to reach global herd immunity, at current production levels and given countries’ actions to prioritize their own populations, there is a significant shortage of vaccines, especially for low- and lower-middle-income countries. Without swift action, the pandemic will continue, and economic recovery will remain under threat as these developing countries remain unable to vaccinate a significant share of their populations—despite the financial resources and pledges from donors.

To address this global crisis, this Brief outlines six specific policy and regulatory actions that would address the vaccine shortages facing these countries. It provides quantitative estimates of the potential impact of each of these actions. There are several combinations of actions that, if implemented, lay out a path to vaccine availability to achieve interim targets of vaccinating 40 percent of the population of low- and lower-middle-income countries by the end of 2021. While the Brief is agnostic about which set of actions should be prioritized, the quantitative estimates provide relative “order of magnitude” ranking in terms of potential dose availability. Under the admittedly conservative but realistic assumptions made in this Brief, most if not all measures would need to be taken seriously to have an impact on the availability of doses for the poorest countries.

References


