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Not Enough: Six Reasons Why COVID-19 Vaccine Manufacturing Must Be Rapidly Scaled-Up

Massive vaccine shortages are prolonging the global pandemic. In January, COVAX, the global program to supply low-and-middle income countries, projected that it would have 235 million vaccine doses available to distribute by the end of April.¹ In March, COVAX lowered that estimate to 165 million doses.² By the end of April, COVAX reported that it had shipped less than 50 million doses.³ COVAX delivered only one-fifth of its projected target, but it is not alone in struggling to meet demand. Many countries are also behind where they expected to be.⁴

Despite the scale and gravity of vaccine shortages, a narrative is emerging that the supply problem will soon be resolved. This analysis, based on self-reported manufacturing estimates, has been weaponized against structural reforms aimed at expanding supply. In March, the Pharmaceutical Research and Manufacturers of America (PhRMA) wrote to President Biden opposing an intellectual property waiver by noting “current estimates are that COVID-19 vaccine manufacturers will supply approximately 10 billion doses by the end of 2021, enough to vaccinate the entire current global vaccine eligible population.”⁵ We provide six reasons why these estimates understate the precariousness of global supply.

1. Some vaccines may not be widely authorized by stringent regulatory authorities.

Several vaccine manufacturers expected to produce huge volumes have yet to receive regulatory authorization in any country. For example, Novavax initially promised to produce two billion doses in 2021, serving as one of two critical COVAX suppliers.⁶ Novavax has not received any regulatory authorization for its vaccine, and has never brought a vaccine to market in its 34-year history.⁷ Neither has CureVac, which expects to produce 300 million doses, in its 20-year history.⁸

Other manufacturers have received regulatory authorization in some countries, but not by stringent regulatory authorities or the World Health Organization, which may limit their uptake. For example, Sinovac is expected to produce billions of doses. The Sinovac candidate has so far been authorized by several middle-income countries, including Brazil, Chile, Mexico and Turkey.⁹ But Phase III clinical trial data has not been published in a peer-reviewed journal. In addition, Sputnik V was recently rejected by Brazilian regulators.¹⁰

¹ Covax Global Supply Forecast (January 20 2021) (on file).

² Covax Global Supply Forecast (March 2 2021) (on file).

³ <https://www.unicef.org/supply/covid-19-vaccine-market-dashboard> (accessed April 30 2021)

⁴ Operation Warp Speed aimed to produce and deliver 300M doses by January 2021. HHS, Fact Sheet: Explaining Operation Warp Speed, <https://tinyurl.com/6s978urp>

⁵ <https://phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/P-R/20210305-PhRMA-Letter-to-President-Biden.pdf> (pg. 2)

⁶ AstraZeneca and Novavax constitute the vast majority of COVAX supply in 2021.

⁷ <https://www.nytimes.com/2020/07/16/health/coronavirus-vaccine-novavax.html>

⁸ <https://curevac.gcs-web.com/node/6356/html> pg. 15.

⁹ <https://www.bmj.com/content/373/bmj.n912>

¹⁰ <https://www.washingtonpost.com/world/2021/04/27/sputnik-vaccine-brazil-russia-coronavirus/>

2. Existing manufacturers may not be able to rapidly scale-up.

Manufacturers often overstate their ability to scale-up. The original analysis underpinning the ~10 billion dose estimate noted that COVID vaccine manufacturers successfully produced just *four* percent of their 2020 dose projections.¹¹ While some candidates are being rapidly scaled up, others are lagging behind.

Table – Select Risk Disclosures Made by COVID-19 Vaccine Manufacturers

Manufacturer	Risk Disclosed to Investors (emphasis added)
Emergent BioSolutions (J&J, formerly AZ)	“Even if these product candidates are safe and/or effective and receive authorization or approval by a health regulatory authority, the manufacturing processes for our CDMO COVID-19 programs are under development and will be complex. As a result, there <u>can be no assurance that we will be able to produce any significant quantity of these products in a timely basis or at all...</u> ” ¹²
Novavax	“ <u>We cannot guarantee that we will be able to timely and effectively produce NVX- CoV2373 in adequate quantities to meet global demand...</u> We have limited experience manufacturing any of our vaccine candidates in the volumes that will be necessary to support large-scale clinical trials or commercial sales. While we have recently increased our projected global manufacturing capacity for NVX-CoV2373, our efforts to establish manufacturing capabilities may not meet expectations as to scheduling, scale-up, reproducibility, yield, purity, cost, potency or quality.” ¹³
CureVac	“Even if we obtain marketing approval for any of our product candidates, <u>there is no assurance that we or our manufacturers will be able to manufacture the approved product to specifications acceptable to the FDA or other comparable foreign regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential commercial launch of the product or to meet potential future demand.</u> ” ¹⁴

Most prominently, Emergent BioSolutions, one of four sites producing Johnson & Johnson viral vector drug substance, was ordered by U.S. regulators in April to temporarily stop all production.¹⁵ J&J has yet to confirm if it is still on track to produce 1 billion doses this year. Meanwhile, Novavax has delayed its clinical trials twice due to scale up challenges, and recently said it will not meet its peak production target until the fourth quarter of this year.¹⁶ Raw material shortages for some manufacturers are exacerbating the problem, even as other manufacturers accumulate “safety stocks.”¹⁷

3. Boosters may fuel additional demand.

There is still considerable uncertainty about the duration of immunity provided by different vaccines. If booster vaccinations are required, production projections may significantly underestimate global demand. Production capacity may be diverted towards boosters, opening up the possibility that some people receive booster doses before others get even their initial dose(s).

Regulators will need to assess the need for boosters. The head of Pfizer has predicted that “A likely scenario is that there will be likely a need for a third dose, somewhere between six and 12 months and then from there, there will be an annual revaccination, but all of that needs to be confirmed.”¹⁸ Several

¹¹ https://www.ifpma.org/wp-content/uploads/2021/03/Airfinity_global_summit_master_final-1.pdf pg. 4.

¹² <https://investors.emergentbiosolutions.com/node/20191/html> pg 28.

¹³ <https://www.sec.gov/Archives/edgar/data/1000694/000100069421000004/nvax-20201231.htm> pg. 26.

¹⁴ <https://curevac.gcs-web.com/node/6356/html> pg. 40.

¹⁵ <https://www.nytimes.com/2021/04/21/us/politics/emergent-johnson-covid-vaccine.html>

<https://docs.house.gov/meetings/IF/IF02/20210223/111226/HHRG-117-IF02-Wstate-NettlesR-20210223.PDF> pg 7. Merck partnership was announced later. <https://www.merck.com/news/merck-to-help-produce-johnson-barda-to-provide-merck-with-funding-to-expand-mercks-manufacturing-capacity-for-covid-19-vaccines-and-medicines/>

¹⁶ <https://www.reuters.com/article/us-health-coronavirus-novavax-vaccine/novavax-expects-delayed-u-s-covid-19-vaccine-trial-to-start-in-coming-weeks-idUSKBN28A1E1> <https://www.nytimes.com/2021/05/11/health/covid-vaccine-novavax-delays.html>

¹⁷ <https://seekingalpha.com/article/4409082-moderna-inc-mrna-ceo-stephane-bancel-on-q4-2020-results-earnings-call-transcript>

¹⁸ <https://www.cnbc.com/2021/04/15/pfizer-ceo-says-third-covid-vaccine-dose-likely-needed-within-12-months.html>

rich countries have already started placing orders for booster doses.¹⁹ The UAE has already started offering boosters for the Sinopharm vaccine.²⁰

4. Variants may render some current vaccines ineffective.

The virus is changing. Doses are currently being produced for the strain that emerged in Wuhan. The longer it takes to vaccinate the world, the greater the risk that new variants will emerge that render the current vaccines ineffective. One troubling possibility is that by the time production for some vaccines is sufficiently scaled-up, those doses will no longer be considered effective.

While mRNA vaccines can be quickly adapted to new variants, not all vaccine platforms can be rapidly modified.²¹ AstraZeneca, which aimed to provide 3 billion doses in 2021, has said “it is likely the process from start to finished product would take 8 to 9 months to complete.”²²

5. Countries may stockpile doses.

Given the uncertainty around the duration of immunity and the possibility that viral variants may escape the protective immune response provided by current vaccines, many countries may create significant vaccine stockpiles. While this raises legitimate concerns about global health equity, it also highlights the urgent need to overcome vaccine scarcity. A plan to vaccinate the world cannot assume efficient allocation of scarce doses.

Already, the U.S., European Union, and India have restricted exports. The head of the Serum Institute of India, which had been expected to produce 2 billion doses of the AstraZeneca and Novavax vaccines, told the Associated Press he was concerned about what might happen if India’s new cases continue to rise. “I am scared of what ... we will have to do, and what will happen,” he said. “We are going to have to keep supplying to India, and not anywhere else. Because we have to protect our nation.”²³

6. Even if 10 billion doses are produced and distributed equitably, it may not be enough.

Even if none of the risks identified above materialize, more than 10 billion doses likely will be needed. While the vaccines were only initially authorized for adults, the FDA has recently expanded the emergency use authorization for the Pfizer vaccine for adolescents and clinical trials are underway to test the vaccine in children.²⁴ If 80 percent of the global population needs to be vaccinated to reach herd immunity, then vaccinating the world will require 12 billion doses.

Vaccinating the World

The world urgently needs much more vaccine. More than 60 groups, led by Public Citizen, recently urged President Biden to launch a global vaccine manufacturing program.²⁵ A whole-of-government effort to share technology, source raw materials and provide technical assistance can help the world produce billions of additional doses. Public Citizen estimates that the U.S. government can help rapidly produce 8 billion doses of mRNA vaccine for \$25 billion. A waiver on intellectual property can further help remove obstacles to production. The unprecedented global crisis demands an all-hands-on-deck response.

¹⁹ <https://abcnews.go.com/Health/wireStory/canada-reaches-deal-pfizer-vaccines-future-years-77272115>

²⁰ <https://www.nytimes.com/2021/03/22/world/the-uae-offers-a-third-dose-of-chinese-vaccine-to-some-with-low-immune-response.html>

²¹ <https://www.ft.com/content/a67d1c2e-9963-4fd0-9ba6-dc677f68a216>

²² <https://tinyurl.com/m2nnepc7> pg 6.

²³ <https://apnews.com/article/world-news-india-global-trade-coronavirus-pandemic-dd58b5c596f261f8a5655e8d8b5d6984>

²⁴ <https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/pfizer-biontech-covid-19-vaccine>

²⁵ <https://www.citizen.org/article/letter-from-60-groups-urging-biden-to-launch-global-manufacturing-program/>