



Researchers at the Serum Institute of India in Pune are manufacturing a COVID-19 vaccine developed at the University of Oxford, UK.

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THE UNEQUAL SCRAMBLE FOR CORONAVIRUS VACCINES

Wealthy countries have already pre-ordered more than two billion doses.

By Ewen Callaway

Wealthy countries have struck deals to buy more than two billion doses of coronavirus vaccine in a scramble that could leave limited supplies in the coming year. Meanwhile, an international effort to acquire vaccines for low- and middle-income countries is struggling to gain traction.

Most experts say that late 2020 or early 2021 is the soonest vaccines could be approved and rolled out; they must first undergo large-scale phase III clinical trials to assess their effectiveness and safety. (Russia has approved a vaccine for limited use, but it hasn't completed phase III trials.)

Yet pre-orders are rolling in. By mid-August, the United States had secured 800 million

doses of at least 6 vaccines in development, with an option to purchase around one billion more. The United Kingdom was the world's highest per-capita buyer, with 340 million purchased: around 5 doses for each citizen. The European Union nations – which are buying vaccines as a group – and Japan have purchased hundreds of millions of doses of vaccines for themselves (see 'Vaccine capacity and pre-orders').

The rush is dispiriting for public-health experts who have urged that vaccines be equitably distributed across the world. "We're not going to get rid of the pandemic until we get rid of it everywhere," says Mark Feinberg, head of the International AIDS Vaccine Initiative in New York City, which is developing a COVID-19 vaccine with US drug company Merck. "We need to prevent vaccine nationalism," said

Tedros Adhanom Ghebreyesus, the director of the World Health Organization (WHO), at an 18 August briefing.

The situation is reminiscent of the 2009 H1N1 influenza outbreak, when a handful of wealthy countries secured most of the supplies of a vaccine, says Richard Hatchett, head of the Coalition for Epidemic Preparedness Innovations (CEPI), a fund based in Oslo that was created to finance and coordinate vaccines for outbreaks, and which has supported the development of nine vaccines for COVID-19.

The 2009 pandemic was much milder than the COVID-19 outbreak, but the hoarding meant that relatively few people who stood to benefit from the vaccine got it in time to make a difference. "If COVID-19 vaccines are misallocated in the way they were in 2009, the pandemic will last longer, more people will die and the disruption will be greater than it needs to be," Hatchett says.

International effort

The main international effort to secure vaccine supplies is a joint fund called the COVAX facility, spearheaded by Gavi, the Vaccine Alliance in Geneva, Switzerland, which funds vaccines for low-income countries, along with CEPI and the WHO. It aims to secure two billion vaccine doses. One billion are for 92 low- and middle-income countries and economies

(LMICS), which encompass half the world's population. The vaccines will cost these regions little or nothing. The other one billion are for up to 75 wealthier countries, who will pay for their own vaccines.

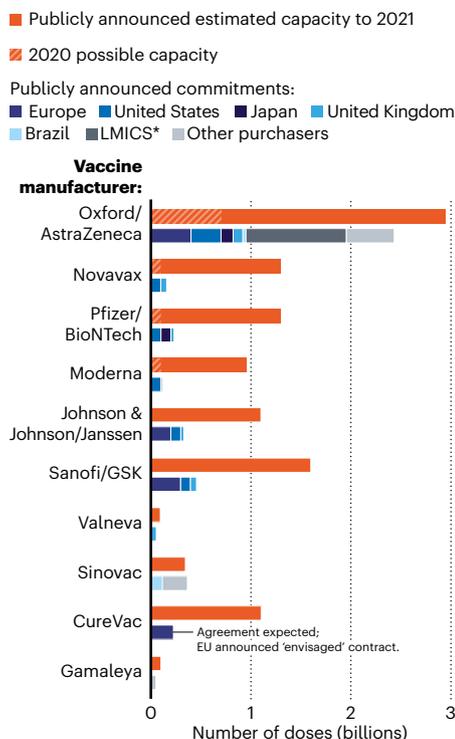
COVAX has made a few orders already – such as a deal to buy 300 million doses of a vaccine being developed by the University of Oxford, UK, and UK pharmaceutical company AstraZeneca. But it's far short of raising the roughly \$18 billion that it estimates will be needed from donors to help manufacturers to scale up production, and to procure and deliver the 2 billion doses. Some wealthier countries, such as the United Kingdom, have expressed interest in joining COVAX, but few have committed to it.

“Their experiment of trying to convince rich countries to join to hedge their bets has gotten very few takers,” says Brook Baker, who studies access to medicines at Northeastern University in Boston, Massachusetts.

Some LMICS have struck advance-purchase deals themselves. Brazil and Indonesia, for example, have agreements to buy millions of doses of vaccines that are undergoing phase III trials in their countries (see ‘Best and worst supplied’). The Serum Institute of India (SII), a leading vaccine manufacturer, signed a licence with the University of Oxford to produce one billion doses of its vaccine per year. The doses are intended for LMICS – including doses

VACCINE CAPACITY AND PRE-ORDERS

Manufacturers intend to ramp up their capacity to produce COVID-19 vaccines by the end of 2021. The wealthiest nations have already struck deals to buy more than two billion doses.



*92 low- and middle-income countries and economies eligible to receive doses through the COVAX international facility.

committed to COVAX – although the SII has stated that half of the doses will go to India. Some observers say there is little to prevent the country's government from demanding more.

Hatchett says COVAX is working out how to allocate vaccines, including to participant countries that have signed their own bilateral deals with manufacturers. He hopes countries will be transparent about the deals they have made. “We are not viewing countries that are engaging in bilateral agreements as bad guys,” he says. One proposal is to curtail a country's access, through COVAX, to a vaccine that they've already purchased for themselves.

Some scholars and activists have suggested that governments could force developers to license their vaccines to domestic manufacturers – allowing countries to make their own versions of successful vaccines. Under World Trade Organization rules, such ‘compulsory licensures’ are allowed; these have been used to make generic forms of antiretroviral drugs against HIV. But these rules cover only patents, not other proprietary information that goes into making a vaccine and getting it approved, says Baker, who argues that countries ought to look into other mechanisms to force vaccine makers to divulge this information.

But Feinberg says compulsory licensure is “meaningless” when it comes to vaccines, which are vastly more complicated to make than small-molecule drugs. “It's not realistic to think every country is going to be making their own version of a vaccine,” he says.

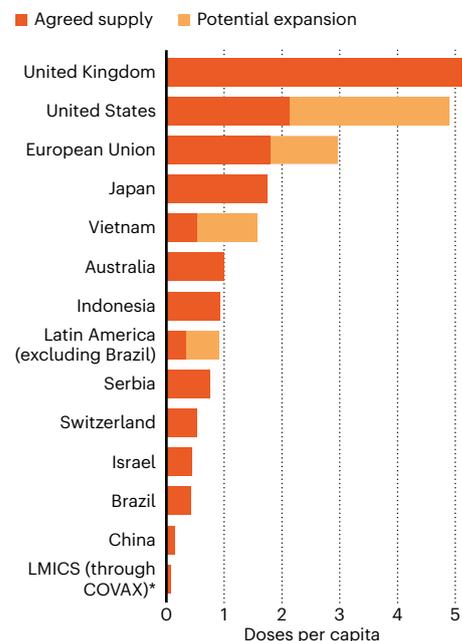
Capacity estimates

If all of the frontrunner candidate vaccines are approved, more than ten billion doses could be available by the end of 2021, according to companies' estimates of their manufacturing capacity. Most vaccines will be made in the United States or Europe. But those figures should be taken with a pinch of salt, says Jeffrey Almond, a vaccinologist and visiting scholar at the University of Oxford, who previously led French pharmaceutical company Sanofi Pasteur's vaccine-development efforts. “They're a guesstimate,” he says, based on assumptions about how production capacity can be scaled up – some of which, he notes, are “overly optimistic”. Many of the vaccines are based on technology that has never been scaled up to the manufacturing levels that companies are hoping for.

Airfinity, a life-sciences market analytics firm in London, currently projects that just one billion doses will be available by the fourth quarter of 2021. The firm adjusted each developer's capacity on the basis of its candidate's status and the developer's track record for manufacturing the technology on which the vaccine is based. From May to June, CEPI anonymously surveyed 113 manufacturers that produce components of the vaccines,

BEST AND WORST SUPPLIED

The United Kingdom has pre-ordered enough vaccines for five doses per person.



*92 low- and middle-income countries and economies eligible to receive doses through the COVAX international facility; some, such as India and Indonesia, have also ordered doses separately.

and estimated that production capacity will be 2 billion to 4 billion doses by the end of 2021, presuming trials go well. (Both estimates will change if companies ramp up manufacturing capacity.)

The number of people who can be vaccinated will also depend on the number of doses that need to be administered. Many of the frontrunner vaccines, including those of Moderna, Pfizer and Novavax, are set to be administered in two doses. Johnson & Johnson intends to trial a one-dose vaccine, and the AstraZeneca–Oxford team is looking at one- and two-dose regimens.

Financial details for many of the purchase deals are shrouded in secrecy. CEPI, the United Kingdom and the United States have paid for vaccines and funded the research to develop them; often, little is known about the terms attached to this funding, says Duncan Matthews, who studies patents and access to medicines at Queen Mary University of London.

It's clear that vaccine costs will vary: the United States, according to its purchase agreements, is paying less than \$4 per dose for the AstraZeneca vaccine but \$25 for each dose of the Moderna vaccine, for instance. But few costs have been published for many of the deals, and little is known about whether countries can pull out of purchases if vaccines don't reach a certain level of efficacy – or when some purchasers might be able to buy additional doses ahead of others.

“What's in the deals that they're signing and who will get access to the vaccine and at what price – it's a complete lack of transparency,” Matthews says.