

## ***COVAX plan boosts Covid-19 vaccine hopes for developing countries***

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ON THE heels of extraordinarily successful results announced by four Covid-19 vaccine developers within three weeks of one another, the question of whether developing countries will be “left behind” continues to be asked. COVAX, a massively funded global collaboration involving 187 countries, aims to ensure that they are not, helping 92 of the least advanced countries to buy and roll out a vaccine for the most vulnerable 20 percent of their populations - although only about 3 percent of all countries’ populations will receive vaccines through COVAX early in 2021. The past few weeks have seen astonishingly uplifting news about Covid-19 vaccines: Global pharmaceutical giants Pfizer/BioNTech, Moderna, and AstraZeneca all announced better-than-expected effectiveness of three vaccines from large-scale clinical trials (two above 90 percent, one at 70 percent), making the longstanding promise of vanquishing coronavirus a reality. But these are still early days: The best estimates of large-scale vaccine availability - for any country - point to the end of the first quarter in 2021. Newly announced limitations of the AstraZeneca vaccine - that the clinical trial did not include anyone over 55, a surprising omission given the well-known higher risk borne by older people - have dimmed some of the excitement, and none of the vaccines has yet achieved regulatory approval (Pfizer and Moderna have applied for “emergency use authorisation” from the US Food and Drug Administration).

Though news headlines have touted the prospect of Pfizer’s vaccine becoming available in the US as early as December 11, that is simply a date on which approval might be granted in an office in Washington, DC, not the date on which millions will receive their vaccinations. In the absence of a large magic wand, no country will immediately be able to vaccinate very large numbers of people. For developing countries, including South Africa, the hurdles between a vaccine approval in the northern hemisphere and a needle going into someone’s arm in the “global south” are infinitely more complex and challenging. All countries are working hard on three main elements - cost, logistical feasibility and regulatory approval. For low- and middle-income countries, “vaccine readiness”, especially regarding logistics, is critical. To help African countries, the World Health Organisation, UNICEF and other partners have provided all 47 countries in WHO’s Africa region with a “vaccine readiness assessment tool”, intended as a “road map” for use by countries’ health ministries to plan their vaccine distribution, and build on routine-immunisation infrastructure they already have. At a WHO media briefing late last week, Dr Matshidiso Moeti, the organisation’s regional director for Africa, reported that 40 of those countries so far had shared data with WHO based on their self-assessments of 10 “key areas”, including planning and coordination, resources and funding, regulatory processes, delivery, training and supervision, monitoring and evaluation, vaccine logistics, risk communication, community engagement and safety monitoring. It is unclear where South Africa is on the vaccine readiness spectrum (a national Department of Health spokesperson did not respond to a request for comment). It is expected that “priority populations” will be frontline health workers, possibly in areas where infection

rates are still escalating such as the Eastern Cape, and where personal protective equipment is in short supply - but this is yet to be confirmed. As part of COVAX's assistance to countries, following the vaccine readiness assessments, Gavi, the Vaccine Alliance, UNICEF and WHO are providing technical support - including for cold-chain infrastructure - to receive and deliver Covid-19 vaccines. As for the vaccines themselves, the AstraZeneca vaccine seems much better suited to African and other developing countries with less money, fewer clinical resources and weaker supply and cold chains. It is much cheaper than the others, at about \$3 (about R45) to \$4 per dose (Pfizer's is \$20, Moderna's is \$33), and it is much easier to store, in a regular refrigerator at 2-4 degrees Celsius (Pfizer's needs -70 degrees Celsius and can be kept in a fridge for up to five days once on the road; Moderna's needs -20 degrees Celsius and can be kept refrigerated for up to 30 days). This is partly because AstraZeneca's vaccine vehicle is a "viral vector", which is less complicated and more stable than the mRNA vehicle being used for the first time in the other two vaccines. Pfizer is reported to be looking at ways to modify its vaccine so that it doesn't need ultra-cold storage. After last Friday's sharp intake of breath at the news that AstraZeneca's clinical trials did not involve elderly volunteers, the company has announced that it will undertake a smaller follow-up trial to test the vaccine's effectiveness in older people.

Also, its results did not include data from the South African arm of the clinical trial, though it is known that very few people among the 2 000 trial volunteers in South Africa developed Covid-19 across both the "real" and placebo arms of the study. Dr Pontiano Kaleebu, director of the Uganda Virus Research Unit, said "it would be desirable to have studies in Africa to know how these vaccines fare in the African population, but it's not a condition for use" because safety and effectiveness had already been proven, and because monitoring and surveillance of the vaccine would continue over time.

Data from the South Africa trial cohort will ultimately form part of AstraZeneca's final safety and immune-response results, according to Professor Helen Rees, executive director of the Wits Reproductive Health and HIV Institute, chairperson of the South African Health Products Regulatory Authority (SAHPRA) and chairperson of the African Regional Immunisation Technical Advisory Group. "Equitable distribution" is the term on the lips of most sensibly-minded politicians, and the global mechanism for this is the vaccines "arm" of the WHO-led ACT Accelerator, which was established to ensure equitable access and fair allocation of vaccines, treatments and tests for Covid-19. COVAX is coconvened by WHO, the Coalition for Epidemic Preparedness (CEPI) and Gavi, the Vaccine Alliance, and 187 countries have signed up for it. It aims to provide the first 20 percent of all countries' vaccine needs by sharing investments from 90 wealthier economies ("advance market commitments" or AMCs) with 97 "AMC-eligible" poorer countries. This upends the "vaccine nationalism" that has compelled many wealthy countries to pre-buy vaccines just for their own populations, in some cases in parallel with their participation in COVAX. And vaccine nationalism has not gone away: rich countries including Canada, Australia, the US, the UK and Japan, as well as a European "bloc" of countries, have each advancebought between two and 10 vaccine doses per person, hedging their bets by placing orders with a few [Type here] different manufacturers. But the COVAX facility means poorer countries will at least get their "starter" vaccines for priority high-risk populations. Initial COVAX funding and supply will support equitable access covering only 3 percent of the targeted 20 percent population coverage by the end of 2021, but "the end game is to incrementally go up", Rees said.

AstraZeneca has made a “no-profit pledge” on its vaccine price, so that “it will be affordable and globally available, supplying hundreds of millions of doses on approval,” AstraZeneca CEO Pascal Soriot said. This is aimed at low- and middle-income countries. And, because more vaccines than anticipated have already proved to be effective, countries that have already bought multiple doses per person from several different manufacturers may ultimately have a surplus. There is a suggestion in global health circles that rich countries may be willing to put their excess doses back into the global system, making even more vaccines available for countries that have not had the funding to secure supplies in advance. Eventually, with more vaccines still in clinical trials, many of which are expected to work too, there may be enough to go around. We could see South Africa and all of Africa starting to deploy vaccines at the same time as the advanced economies, even if in smaller numbers. In South Africa, regulatory authority SAHPRA normally would need to license any vaccine (as with any other medical product) for use in this country. SAHPRA already has a vaccines working group ready to leap into action once pharmaceutical companies lodge their applications for approval, and they may need additional clinical evidence to register vaccines that have not held clinical trials in South Africa (such as Moderna’s). In such a case a “bridging” study - a small-scale assessment of safety and efficacy within the population that will be vaccinated - can be done first.

There is also a quicker path to domestic registration of a new medicine: In 2019, SAHPRA agreed to use a “reliance” mechanism provided by WHO, for countries that may not have regulatory authorities or when their decisions may take too long. The authorities on which countries can formally “rely” include the US’s FDA and the European Medicines Agency (EMA), the ones most likely to soon be licensing successful Covid-19 vaccines. In addition, SAHPRA has the power to bypass all of that and authorise emergency use of an unregistered medical product through Section 21. In any case, we can anticipate a rapid local approval process once it becomes clear which vaccines South Africa can feasibly procure. The three vaccine frontrunners so far could together produce more than four billion doses by the end of 2021 - still far short of what is needed to immunise the global population of 7.8 billion, especially as some of the effective regimens so far already require two doses per person. But if recent history is anything to go by, several more vaccines will prove successful in the near future. Though donor countries have so far invested more than \$2-billion in COVAX’s AMC financing, surpassing its 2020 target, another \$5-billion is needed for COVAX to deliver its targeted two billion doses for developing countries by the end of 2021. To supplement this, the World Bank has announced a \$12-billion financing facility that poorer countries will be able to access to increase their 20 percent vaccine “coverage” to about 60 percent. Moeti said COVAX is highly subsidised as a solidarity mechanism and platform to enable African countries to have the vaccine like every other country, but they are also expected to make some effort.