The Russian vaccine for COVID-19

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For **Putin's announcement** see https://www.youtube.com/watch?v=jFmiK52gFNM&feature=youtu.be

For the **Russian vaccine study** see **Articles** *Lancet* 2020; published online Sept 4. https://doi.org/10.1016/S0140-6736(20)31866-3

For the **Sputnik vaccine website** see https://sputnikvaccine.com/

On Aug 11, 2020, Russia became the first country in the world to approve a vaccine against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The vaccine, which is based on two adenovirus vectors, was developed by the Gamaleya National Center of Epidemiology and Microbiology (Moscow, Russia). Its approval was announced by President Vladimir Putin. "I know [the vaccine] works quite effectively, helps to develop strong immunity, and has gone through all the necessary tests", declared Putin at a cabinet meeting. Nonetheless, there are widespread concerns that the approval is premature. At the time of approval, the vaccine had not even started phase 3 trials, nor had any results on the earlier stage trials been published.

Since then, the phase 1/2 results have been published in *The Lancet*. The vaccine induced a strong immune response in all 76 participants. Presumably these results were available to the Russian Ministry of Health. For regulators such as the US Food and Drug Administration (FDA) and the European Medicines Agency, however, data on immune response alone would not generally be an adequate basis for approving a vaccine. "Immune response might not be directly proportional to the degree of protection—you can only find this out in large-scale trials", explains Peter Openshaw, professor of experimental medicine at Imperial College London (London, UK).

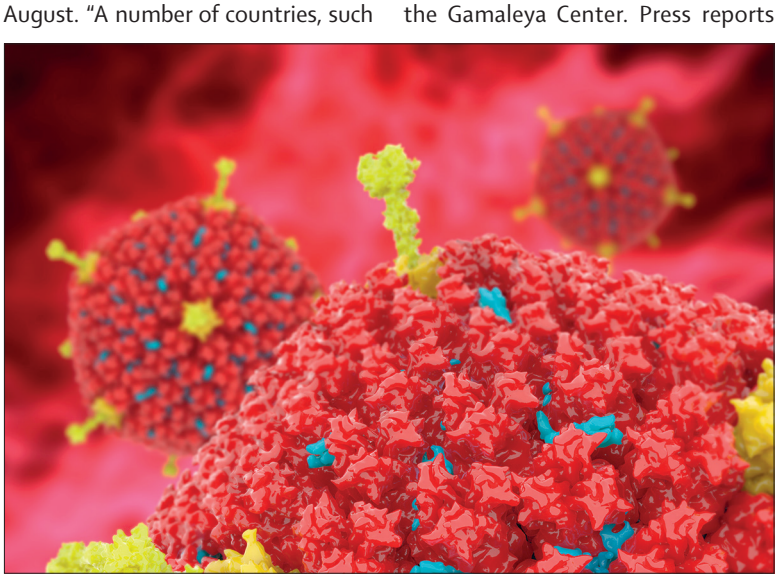
The Russian vaccine is named Sputnik V, after the Soviet-era space programme. One person to have received it is the president's daughter. "She feels well, and the concentration of antibodies is high", said Putin. "The main thing is to ensure unconditional safety and effectiveness of this vaccine in the future." Mass production is expected to begin in September, 2020. Russia, which has seen almost 1 million cases of COVID-19, said that it would be able to provide 500 million doses of Sputnik V per year.

"We have no idea whether this vaccine is safe or whether it works", cautions Ashish Jha, Dean of the Brown University School of Public Health (Providence, RI, USA). "It is really worrying when people start to bypass the standard process we have for vaccine development." Those behind the Russian vaccine have offered a combative response to such criticism. The official website was established with the stated aim to "provide accurate and up-to-date information about Sputnik V and to combat the misinformation campaign launched against it in the international media".

The vaccine is financed by the Russian Direct Investment Fund (RDIF), the country's sovereign wealth fund. Kirill Dmitriev, chief executive officer of RDIF, has complained that "instead of looking into the science behind the proven adenoviral vector-based vaccine platform Russia has developed, some international politicians and media chose to focus on politics and attempts to undermine the credibility of the Russian vaccine". Large-scale clinical trials of the vaccine, involving over 40 000 people, were scheduled to begin in Russia in the last week of August. "A number of countries, such as United Arab Emirates, Saudi Arabia, the Philippines, and possibly India or Brazil, will join the clinical trials of Sputnik V locally", noted the official website.

Dmitriev has confirmed that Russia has received international requests for 1 billion doses of its vaccine. On Aug 26, 2020, Russian news agency TASS reported that the country would supply more than 2 million doses of Sputnik V to Kazakhstan. Openshaw points out that the places that have expressed interest in the vaccine are unlikely to start mass administration until they are assured that it is safe and effective. "There is a huge difference between Russia registering a vaccine within its own borders, which it is entitled to do, and international approval or WHO prequalification", he said.

Countries all over the world have preordered millions of doses of other prospective COVID-19 vaccines, with the rollout contingent on the results of the phase 3 studies. For example, the USA has purchased 100 million doses of Moderna's mRNA vaccine candidate and 300 million doses of Astrazeneca's adenovirus vector vaccine. Other countries might choose to make similar arrangements with the Gamaleya Center. Press reports



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have quoted the Azerbaijani Foreign Minister saying that the country was "ready to consider the possibility of purchasing a Russian vaccine against coronavirus after the completion of procedures for its recognition by the WHO".

According to WHO, as of Aug 28, 2020, nine vaccine candidates were in late-stage trials. These included separate adenovirus vector vaccines, a couple of mRNA vaccines, and several inactivated virus vaccines. There are plenty of vaccine candidates in earlier stages of evaluation. Experts are confident that at least one of the candidates will be successful. COVAX, a joint initiative between Gavi, the Coalition for Epidemic Preparedness Innovations, and WHO, aims to ensure any eventual vaccine is distributed fairly and equitably. 92 low-income and middle-income countries are eligible for support. The initiative is backing a range of vaccine candidates, including seven in clinical trials.

Given the pace at which the candidates are moving through the stages of development, Jha wonders why Russia felt it was necessary to skip straight to approval. "I do not think it makes sense; the difference between doing things correctly and not doing things correctly is a matter of a few months", he said. "It seems like a very small gain, and the middle of a pandemic is not the time to be cutting corners." There has been speculation that the approval has been motivated by nationalism. Most countries would welcome the positive publicity generated by being the first to bring a vaccine against SARS-CoV-2 to market. The USA has also invoked the space age in its fight against COVID-19; it named its drive to secure 300 million doses of vaccine by January, 2021, Operation Warp Speed.

If Sputnik V does not work or results in some kind of unforeseen adverse event in the phase 3 trial, that could affect the public perception of the vaccine process. Moreover, an ineffective product could actually worsen the pandemic—those who received the vaccine might stop taking precautions against contracting SARS-CoV-2. "There is a huge risk that confidence in vaccines would be damaged by a vaccine that received approval and was then shown to be harmful", said Openshaw. A sizeable group of vaccine-hesitant people are already laying the groundwork on social media to discredit any potential COVID-19 vaccine. "We really do not want to make life any easier for those who are trying to undermine science", said Jha.

On the other hand, it is entirely possible that Russia will hold off vaccinating its general population until it has received favourable results from the phase 3 trial. In which case, the announcement of the approval of Sputnik V might amount to a political gesture, rather than a serious attempt to circumvent the standard process of vaccine development. The FDA has stipulated that a vaccine against COVID-19 should be at least 50% effective. Sputnik V might well meet this criterion. But until the phase 3 trial is completed and the results are made available, it will not be possible to make any judgement. "It is certainly not advisable for any vaccine to be used in an uncontrolled way before it has been through proper testing to determine whether the immune response it produces is actually protective, and there are no unexpected adverse events", stressed Openshaw.

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