In March, Russian Prime Minister Mikhail Mishustin (center) visited the institute that developed EpiVacCorona.
SPUTNIK/DMITRY ASTAKHOV/POOL VIA REUTERS

Russia's COVID-19 defense may depend on mystery vaccine from former bioweapons lab—but does it work?

By **Olga Dobrovidova** | Apr. 6, 2021 , 11:05 AM

***Science*'s COVID-19 reporting is supported by the Heising-Simons Foundation.**

When the Kremlin last month said Russian President Vladimir Putin had received the first dose of a homegrown COVID-19 vaccine, a guessing game began. Had he gotten Sputnik V, which Russia had given emergency use authorization—a world first—in August 2020 after testing in just 79 patients? Or had Putin been given another COVID-19 vaccine that Russia had sanctioned with much less fanfare—and with equally sparse evidence that it works?

Putin and state officials wouldn't say, but Russia's second COVID-19 vaccine, known as EpiVacCorona and first authorized in October 2020, has begun to emerge from the shadow of Sputnik V, bringing controversy of its own. Developed by VECTOR, the famed State Research Center of Virology and Biotechnology that once studied bioweapons and now

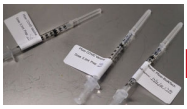
is one of two global repositories of the eradicated smallpox virus, the vaccine is key to the country's plans to combat the pandemic. Russia began to offer it to small numbers of people last year, plans to administer 1.5 million doses per month by this summer, and aims for a bigger national campaign.

Related

'Compromise' WHO report resolves little on pandemic's origins, but details probe's next steps

A rare clotting disorder may cloud the world's hopes for AstraZeneca's COVID-19 vaccine

Syringe size and supply issues continue to waste COVID-19 vaccine doses in United States



See all of our coverage of the coronavirus outbreak

But only in late March did VECTOR publish any clinical data on EpiVacCorona, which consists mainly of multiple protein bits, or peptides, from the pandemic coronavirus. The paper, in an obscure Russian journal, described safety tests in 14 people, and a phase 2, placebo-controlled trial in 86 people. The authors reported no safety issues and said volunteers who received vaccine produced antibodies that block SARS-CoV-2's infectivity. But VECTOR has not reported evidence that the vaccine actually protects people from COVID-19.

Two unusual letters from some of the trial participants to the Russian health minister, the first in January calling for the phase 2 trial to be publicly unblinded and the second in March asking for a review of the vaccine, have added to the doubts. The volunteers use commercial assays to look for virus-neutralizing antibodies and say they found none. They note that VECTOR used a special test system for the antibodies that is not public. "The very fact of the publication of this paper is a convincing argument for an

independent review" of the vaccine, says Russian entrepreneur Andrey Krynicki, a trial participant who organized the open letters.

Officials at VECTOR, which is under the authority of the Russian government agency in charge of pandemic response, defend the initial clinical studies and note a phase 3 efficacy trial in more than 3000 people is underway in Russia. Venezuela, which had already approved and received Sputnik V, also got a vaccine batch for its own trial.

Many COVID-19 vaccines generate an immune response to SARS-CoV-2's spike, the protein the virus uses to latch onto and fuse with cells. EpiVacCorona consists of three synthetic fragments of spike, attached to a carrier protein, which itself is composed of synthetic fragments of the virus nucleocapsid protein, known as N. One peptide is designed to create antibodies to the spike's receptor-binding domain, the part that hooks onto a human cell protein. The other spike peptides are meant to elicit antibodies that prevent the virus from getting into the cell. The N peptides may generate still other protective responses. VECTOR officials say the vaccine ultimately provides "three lines of defense."

The innovative peptide approach, which VECTOR also uses for an Ebola vaccine, intrigues some outside scientists. But no peptide-based vaccines have been licensed to date by the United States, Europe, or the World Health Organization (WHO). "There are several in clinical trials. This means we don't have definitive evidence they are effective, but they do look promising," says Sarah Caddy of the Cambridge Institute for Therapeutic Immunology and Infectious Disease.

Caddy adds that peptide selection is "crucial" for this type of vaccine. But Olga Matveeva, a Russian biologist who now works at a U.S. biotech and has tracked the development of EpiVacCorona, is not convinced VECTOR has chosen the best ones. "Unfortunately, last spring, when the vaccine developers at VECTOR were selecting their peptides,

4. Ancient Native Americans were among the world's first coppersmiths

5. The legendary dire wolf may not have been a wolf at all

Sifter

Climate change is triggering more lightning strikes in the Arctic
By Sofia Moutinho | Apr. 7, 2021

Tropical forest destruction increases, despite the pandemic
By Sofia Moutinho | Mar. 31, 2021

Pesticide-blocking gene transferred from plants to animals
By Sofia Moutinho | Mar. 26, 2021

Your spit could reveal whether you've had a concussion
By Adrian Cho | Mar. 24, 2021

Scientists have been underestimating the power of tornadoes
By Sofia Moutinho | Mar. 23, 2021

More Sifter

there was little information available on the virus and the most appropriate spike protein fragments that should be recognized by the immune system and launch an effective antiviral attack," she says.

VECTOR has said the chosen peptides vary little between strains, ensuring the vaccine will work against new variants of SARS-CoV-2, and that they were extensively tested in animals. Preclinical study results in animals are under review at a scientific journal, the center says.

Russians could use another COVID-19 vaccine to supplement Sputnik V, which despite initial uncertainties appears to be highly effective and has been authorized for use in nearly 60 countries. Although cases are not obviously surging in Russia, unlike in Europe, it has had nearly 100,000 COVID-19 deaths, by some estimates. Vaccine manufacturing is not Russia's strong suit, however; most of the 500 million doses of Sputnik V planned for this year will reportedly be made in India.

EpiVacCorona is easier to produce than Sputnik V, which consists of adenoviruses genetically engineered to make spike protein. It could boost a national vaccination campaign, if it clearly protects against COVID-19 and is embraced by Russians. There is significant vaccine hesitancy in the country, which stems in part from an overall distrust of the government and medical research it promotes. Participants in Sputnik V's early trials, for example, used the popular Telegram messaging app to trade information about side effects and results from commercial antibody tests widely available in Russia.

EpiVacCorona trial participants were also wary, banding together on Telegram and recruiting Alexander Chepurnov, a former head of infectious diseases at VECTOR who now works at another medical institute in Novosibirsk, to run their ministudy that looked in vain for neutralizing antibodies. Chepurnov declined to talk to *Science*, citing "too much politics in science today."

In a written statement, VECTOR Deputy Director Tatyana Nepomnyashchikh said the center is satisfied with the phase 1 and 2 trials, although the results are preliminary, with final data due in May. "We have also tested the sera of people vaccinated with EpiVacCorona for neutralizing activity, and it has been shown to work against both the reference strain and the British variant. We are confident in this result," Nepomnyashchikh said. She said the antibody validation test, developed by VECTOR specifically for this vaccine, is available in every Russian region where EpiVacCorona is distributed.

Svetlana Zavidova, who heads the Association of Clinical Trials Organizations in Moscow, praised the groundbreaking "citizen science" effort of volunteers, but cautioned against overinterpreting their limited results. And she doubts the protest letters will prompt an independent review.

VECTOR has not applied for an emergency use listing for EpiVacCorona from WHO or other stringent regulatory agencies, but says it will. "More than 60 private and government entities" have expressed interest in the vaccine, Nepomnyashchikh's statement notes. For now, VECTOR says, its priority is supplying Russian domestic demand.

Russia also has a third authorized COVID-19 vaccine, made by yet another research center and consisting of inactivated coronavirus, and even less is known about it. Zavidova laments that the practice of COVID-19 vaccine authorization and rollout before phase 3 trial results has largely gone mainstream in Russia, a concern she and her organization raised last year before the Sputnik V endorsement. "We've essentially crossed and burned that bridge," Zavidova concludes.

Posted in: **Health**, **Coronavirus**
doi:10.1126/science.abi8604

Olga Dobrovidova

Olga Dobrovidova, a science journalist in Moscow, currently works at Skoltech, a private university not involved in the development of COVID-19 vaccines.

Twitter

More from News

Food supplements that alter gut bacteria could 'cure' malnutrition

Special diets might boost the power of drugs to vanquish cancers

Breast milk ingredient may help power a healthy infant gut