

## Russian vaccines: a production bottleneck

Jadwiga Rogoża, Iwona Wiśniewska

Despite the high-profile propaganda campaign accompanying the registration in Russia of the Sputnik V coronavirus vaccine, the testing process is taking longer and longer, and the initial forecasts for large-scale production have proved to be unrealistic. The state has run up against numerous technological barriers resulting from its lack of experience in creating new, technologically advanced preparations: a shortage of spare production capacity demanding costly and time-consuming investments, as well as a lack of the equipment and components necessary to produce the vaccine. Other challenges include the problem of stabilising the vaccine (duplicating the preparation's composition identically) when producing it in bulk, as well as a lack of infrastructure to store it during the distribution process. As a result, at the beginning of November the state was producing only around 70,000 doses of the vaccine per week. At present Russia has a problem not only with implementing its ambitious export plans for Sputnik V (around 1 billion doses by the end of next year), but also with even beginning the mass-scale action for vaccinating its own citizens; this has been postponed once again, to the beginning of next year.

### Unwanted records

Recent weeks have seen a steady increase in the numbers of COVID-19 cases and deaths in Russia. Almost every subsequent day generates new records: the highest number of cases was recorded on 26 November (25,487), as was a new high in the death count (524 people). It should be noted that the rise in cases detected may to some extent result from the constant increase in the number of tests carried out: currently about 520,000–540,000 are being performed each day, which on average is around twice the figure which was reached during the pandemic's spring wave.

However, many commentators consider the data collected by *Rospotrebnadzor* (the Federal Service for the Supervision of Consumer Rights, the main governmental structure monitoring the spread of the pandemic) to have been underestimated, in comparison with the data from *Rosstat*, the main statistical office. The latter will apparently only publish its aggregate mortality statistics at the end of the year; however, on the basis of partial data from it and the local registry offices over the last six months (April–September 2020), independent media have calculated the number of deaths caused directly by COVID-19 at 55,000, while the figure from *Rospotrebnadzor* for the same period is less than half the size (20,700). According to the same calculations based on data from *Rosstat*, the total number of deaths in 2020 exceeded the average level from the previous five years by around 120,000, i.e. by 18% (the so-called excess mortality figure).

### Vaccines in clinical trials

Meanwhile, the final and most time-consuming phase of the clinical trials of the two Russian vaccines that have received provisional registration is underway. On 11 August Sputnik V received its initial approval for distribution until January 2021; it is currently in phase 3 of clinical trials, and is being tested on 40,000 volunteers. On 24 November, the partial results of this phase were announced; according to the vaccine's makers at the Gamaleya Institute, it showed an efficacy of over 95% within 42 days of the first dose. The institute emphasised that Sputnik's effectiveness exceeds the corresponding indicators of the competing preparation being developed by BioNTech and Pfizer, despite the fact that there are more and more media reports of cases of coronavirus infection among the volunteers who had received the Russian vaccine during the testing, as well as among doctors who had already been vaccinated.

The process of testing the EpiVacCorona vaccine, which has been created by the Vector laboratory in Novosibirsk, is even less advanced. It was registered last October for the period until the beginning of 2021. It is still waiting for phase 3 of its clinical trials; the start was originally planned for this November, but there have been no reports of this happening. The third Russian vaccine, being developed by the Chumakov Centre of the Russian Academy of Sciences, is in phase 2 of testing; if the results show promise, it may reach phase 3 in early 2021.

### **Problems with mass production**

The Russian government's initial optimistic forecasts regarding the possibility of producing large quantities of Sputnik V (over 10 million doses per month) have already proved unrealistic by the end of 2020. Previous experience in the field of preparing vaccines for mass production shows that this process will take significantly longer. As mentioned above, at the beginning of November, the country was only producing around 70,000 doses of the vaccine per week. For now, the challenge for Russia is to produce enough of the preparation to vaccinate its own citizens (the plan is to immunise 50% of the population, for which around 150 million doses will be needed, as Sputnik V is administered in two doses), while the ambitious export plans (to produce c. 1 billion doses) have been pushed into the background. At present, there have been only scarce reports on how production is progressing, and the government has also been reluctant to discuss the future availability of the vaccine.

Preparations for the mass production of Sputnik V actually began at the end of August, while Western companies had begun to do so before the summer holidays, together with phase 3 of their research. This process, carried out under the pressure of time, encountered numerous problems from the very beginning due to Russia's lack of experience in producing modern, high-tech preparations. So far, Russian companies have mostly been involved in producing generic drugs whose patents have already expired.

Above all, Russia has had to deal with a lack of spare production capacity for such modern preparations; it proved necessary to make costly and time-consuming investments in new production lines. As a result, only three bodies are involved in the production of Sputnik V: the Gamaleya Institute, which developed the vaccine, and two pharmaceutical companies – Binnofarm (controlled by AFK Sistema, owned by the billionaire Vladimir Yevtushenkov) and Generium (owned by the oligarch Viktor Kharitonin; it only received the Ministry of Health's authorisation for production at the end of October). Preparations to include more

companies in this process are underway.

The pharmaceutical companies also came up against another problem: there was not enough of the equipment which needed to be installed in the factories, something Vladimir Putin himself admitted at the end of October as he declared his readiness to cooperate with foreign partners (French media have reported that Putin asked President Emmanuel Macron for help in this matter). Moreover, due to the rising global demand, difficulties with importing components for the vaccine have arisen (Russia mainly imports these from China). The stabilisation of production, i.e. the identical duplication of the preparation's composition when preparing it in bulk, has also turned out to be a serious challenge. Further problems may arise at the stage of distributing the vaccine related to the shortage of freezers – although Sputnik V only needs to be maintained at a temperature of -18°C, which is a standard for most equipment of this type, and not below -70°C, as some of the competing preparations need.

These problems with producing Sputnik V have forced the plans for the mass-scale vaccination of Russian citizens to be postponed. The immunisation campaign, which was initially scheduled for October this year, but then postponed to November and December, is now – according to Aleksandr Gintsburg, Gamaleya's director – supposed to start in January or February 2021. However, the rollout in individual regions of Russia will depend on the state of each region's preparation: how effectively the vaccine supply chain has been organised (including maintaining the right temperature), the preparation and supply of equipment at the vaccination points, etc. At present, people in the so-called high-risk professions (mainly health care) are first in line for vaccination, but the scale of the process is limited due to the low availability of the preparation. So far, just over 2% of doctors have been vaccinated with Sputnik V, and reports are coming in from the regions that doctors and teachers are only being issued a few dozens of doses.

### **Seeking foreign recipients**

Despite the problems with implementing mass production, Russia is actively seeking foreign recipients for Sputnik V. One possible solution to the lack of the vaccine for export involves preparations to produce it abroad. In mid-November, the Russian Direct Investment Fund signed an agreement with the South Korean company GL Rapha to produce 150 million units of the preparation for foreign recipients. Production is scheduled to start in December 2020. The Fund's president has also announced that Russia has asked the European Medicines Agency to register Sputnik V; this would allow it to be produced in Europe, primarily in Hungary.

The Russian government is trying to attract potential recipients of the preparation by offering it at a low price. Sputnik V (two doses) is expected to cost around \$26, compared to \$39 for the Pfizer vaccine and \$50-74 for Moderna's product. Several countries have started testing it already: in October, phase-3 clinical trials of Sputnik V began in Belarus (100 participants), Venezuela and the United Arab Emirates. Preparations for this phase are also underway in India (where the vaccines have already arrived), Mexico and the Brazilian state of Paraná (pre-registration is underway in these two countries). These countries are interested in purchasing the preparation if its effectiveness is confirmed. In addition, Israel has already declared that it is ready to purchase 1.5 million doses of Sputnik V, as the Moscow branch of its Hadassah Medical Center is involved in phase 3 of research in Russia,

and intends to apply to register the vaccine in Israel. Samples of the vaccine (10 units) were also delivered to Hungary at the beginning of November; these will be used in laboratory tests that will decide on whether it is admitted to clinical trials.

Many other countries have also expressed interest in testing and then purchasing Sputnik V. However, problems with delivering samples mean that Russia may be outpaced by its competitors. For example, in early November Uzbekistan, impatient at having to wait for deliveries of the Russian preparation, began testing its Chinese counterpart. For its part, Kazakhstan is working on its own vaccine (in September it began phases 1 and 2 of clinical trials on this preparation), and so its interest in the Russian product has decreased.

### **Forecast**

The Kremlin will prioritise efforts to bring about herd immunity in Russian society, and so the production of Sputnik V, as the vaccine currently at the most advanced stage of research, will initially be targeted primarily at the domestic market. Cautious government estimates predict that the state will only be producing about 6 million doses of the preparation per month by April 2021, and so meeting domestic demand may take up most of next year. Russia's wide-ranging declarations about its leadership in the global vaccine race and its ambitious export plans are being submitted to harsh scrutiny by numerous technical and technological barriers; these are also causing a decline in interest in Sputnik V on the part of those countries to which Russia was most hoping to sell its vaccine.