News in focus

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Some 18,000 people globally have received the Oxford AstraZeneca vaccine so far.

RELIEF AS CORONAVIRUS VACCINE TRIALS RESTART — BUT TRANSPARENCY CONCERNS REMAIN

UK trials of the Oxford and AstraZeneca vaccine have resumed after a brief pause, yet key details of the events involved have not been released.

By David Cyranoski & Smriti Mallapaty

The UK trials of a leading coronavirus vaccine that were abruptly halted because of safety concerns have restarted.

The University of Oxford and pharmaceutical company AstraZeneca paused enrolment in the global trials of the vaccine on 6 September, after a person participating in the UK trials experienced an adverse reaction. But on 12 September, the university said an independent committee had found that it was safe to restart.

Scientists say that a pause is not uncommon in large trials, and that a speedy resumption of testing was to be expected. The episode shows that care is being taken with the trials, they say.

"Like anybody else who knows the importance of vaccines, I am very happy that the trial will continue," says Klaus Stöhr, a retired influenza researcher who previously headed the World Health Organization's research and epidemiology division for severe acute respiratory syndrome. But some scientists have criticized the trial sponsors for not releasing more information about the reason for the pause and about their decision-making.

The University of Oxford and AstraZeneca have not yet released details of the adverse reaction that led to the trials' pause and how the decision to resume the UK study was made. Regulators in Brazil announced on 12 September that trials of the vaccine have restarted there, but it is unclear when similar trials in South Africa and the United States might also resume.

Marie-Paule Kieny, a vaccine researcher at INSERM, the French national health-research institute in Paris, says she hopes that research groups working on this or other coronavirus vaccines will share more information about

clinical-trial holds in future. The transparency bar should be set much higher than this latest example, says Kieny. "When, ultimately, a vaccine will be made available, public trust will be paramount to ensure public-health impact. And trust needs transparency."

Leading vaccine

The vaccine, AZD1222, is one of the leading candidates being developed to protect against the virus that causes COVID-19, and one of a handful of immunizations in the final stages of clinical testing. The pause in global trials sent a shudder around the world.

Such a quick resumption of the trials was the most likely outcome, says Paul Griffin, an infectious-diseases researcher at the University of Queensland in Brisbane, Australia. In large trials, adverse medical events in volunteers are common, and trial holds are designed to ensure that such events are investigated and volunteers are protected, he says. But, most often, it is later decided that the event was probably not related to participation in the trial and does not pose a safety concern to the rest of the volunteers, says Griffin. That seems to be what has occurred in this case, he says.

It can be difficult to pin down the cause of adverse events, says Jonathan Kimmelman, a bioethicist who studies clinical trials at McGill University in Montreal, Canada. "Often, the best you can do is say that there is a possible link, and then proceed with collecting more data and monitoring outcomes," he says.

The University of Oxford said in a press release on 12 September that the pause, which applied to all trials of the vaccine, was necessary "to allow the review of safety data by an independent safety review committee, and the national regulators".

"The independent review process has concluded and following the recommendations of both the independent safety review committee and the UK regulator, the MHRA [Medicines and Healthcare products Regulatory Agency], the trials will recommence in the UK," the statement reads. The university also said that it cannot disclose medical information about the participant's illness for reasons of confidentiality.

It's appropriate not to disclose information, for patient confidentiality and to ensure valid interpretation of the trial results, says Kristine Macartney, the director of Australia's National Centre for Immunisation Research and Surveillance in Sydney.

Lack of details

But Paul Komesaroff, a physician and bioethicist at Monash University in Melbourne, Australia, questions the university's claim that it could not release information about the adverse event on the basis of confidentiality. It is possible to provide information in a manner that avoids identifying a particular individual, but still provides a summary of the clinical issues that arose, and the conclusions the committee reached about the implications for the study, he says. "It is of concern that they sought to avoid doing so," says Komesaroff.

The University of Oxford and AstraZeneca have not yet responded to requests for comment on this criticism.

Although the university and AstraZeneca have not released information about the adverse event to the public, Pascal Soriot, AstraZeneca's chief executive, reportedly told investors on a telephone call last week that a person in the UK trials had developed symptoms of transverse myelitis, according to health-news website STAT. This condition involves inflammation of the spinal cord, which can be triggered by viruses.

But other scientists say there is a good reason why the company hasn't released more details. If information about the trials is released prematurely, it could present a bias to the clinicians involved in them, says Griffin. The integrity of the trials is on the line, he adds. Griffin expects the pause to have little impact on the UK trials' overall timeline.

But it has not been reported when trials of the vaccine in the United States and South Africa will restart. A spokesperson for AstraZeneca told *Nature* that the company "will be guided by health authorities across the globe as to when other clinical trials of the vaccine can resume".

So far, some 18,000 people globally have received the vaccine. Phase III efficacy trials in the United Kingdom, which began in June, aim to recruit 10,000 people, and a phase III trial in Brazil hopes to recruit 5,000 participants. The US trial, which started in August, is aiming to recruit 30,000 participants. A phase I/II safety and efficacy trial in South Africa wants to recruit 2,000 volunteers.

THE UNDERDOG COVID-19 VACCINES THAT THE WORLD MIGHT NEED

Small developers struggle to get their candidates noticed, but they'll be crucial if front runners stumble.

By Ewen Callaway

When it comes to developing vaccines, Peter Palese is no slouch. A virologist at Icahn School of Medicine at Mount Sinai in New York City, he pioneered genetics techniques that are used to make some of the billions of influenza vaccine doses produced annually, and his team has won millions of dollars to develop a universal flu jab.

Palese is developing a COVID-19 vaccine, too. It consists of a bird virus that has been genetically modified to make a protein found on the surface of SARS-CoV-2. The vaccine fully protects mice from an experimental model of COVID-19, according to a preprint[1] (the research has not yet been peer reviewed). It also grows in chicken eggs, like most flu vaccines, so manufacturing could be ramped up using tried-and-tested technology.

Despite its potential, Palese's vaccine has struggled to gain the attention and funding needed to progress to human trials. "We thought this would be the best thing after sliced bread, and people would break down our doors to get it. That's not the case. We are very disappointed," he says.

As leading drug and biotechnology companies rush their COVID-19 vaccines through clinical trials and eye up fast-track regulatory authorization, dozens of underdog vaccines such as Palese's have stalled, or are advancing along a slower, more conventional path.

Scientists acknowledge that it would be a waste of resources to take every candidate to clinical trials. But they argue that it's essential to have a diverse selection of COVID-19 vaccines in development. Early favourites could fail, confer only partial protection or work poorly in certain age groups; high costs and other barriers might make some of the front runners unsuitable for wide-scale deployment in lower-income countries.

"Everyone is rooting for them to succeed beyond anyone's expectation, but it's prudent to think about what happens if they don't," says Dave O'Connor, a virologist at the University of Wisconsin–Madison. "We need to make sure we have back-up plans — and back-up plans to those back-up plans."

Dozens of candidates

There are more than 320 COVID-19 vaccines in development, according to a tally by the Coalition for Epidemic Preparedness Innovation (CEPI) in Oslo, a fund created to finance