December 2020

WHAT YOU NEED TO KNOW ABOUT

Covid-19 Vaccine Trials

PRO POINTS

- **Governments and scientists have walked a** tricky tightrope with the coronavirus: trying to compress the normal vaccine development timeline from years to months without sacrificing safety.

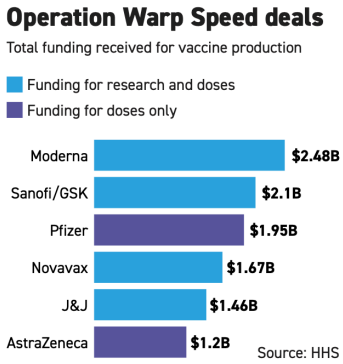
- **An independent data and safety monitoring board** oversees each human trial. These panels can pause a study to investigate safety issues, or end a trial if continuing would be dangerous or if preliminary data suggest that a vaccine isn't effective.

- **Most late-stage trials enroll healthy adults. More** studies are usually needed to find out whether a vaccine also works well in children, pregnant women and people with compromised immune systems, such as those with HIV.

- **Scientists won't know how long Covid-19 vaccines** protect against infection until more time has passed. It's only been about a year since the first known coronavirus cases emerged.

HOW WE GOT HERE

Reports of a new kind of viral pneumonia in China emerged in late December 2019. Within weeks, the deadly virus now known as SARS-CoV-2 had begun spreading around the globe. By mid-January, scientists in China had sequenced and published the virus' genome — allowing vaccine makers worldwide to start designing shots.



As U.S. cases passed the 1 million mark in late April — with over 50,000 deaths — President Donald Trump's administration began planning a program called Operation Warp Speed to accelerate the development of coronavirus vaccines. Led by a former GlaxoSmithKline executive, Moncef Slaoui, and Gen. Gustave Perna, the program spent billions of dollars over the next several months to support companies' research and testing and to pre-order doses.

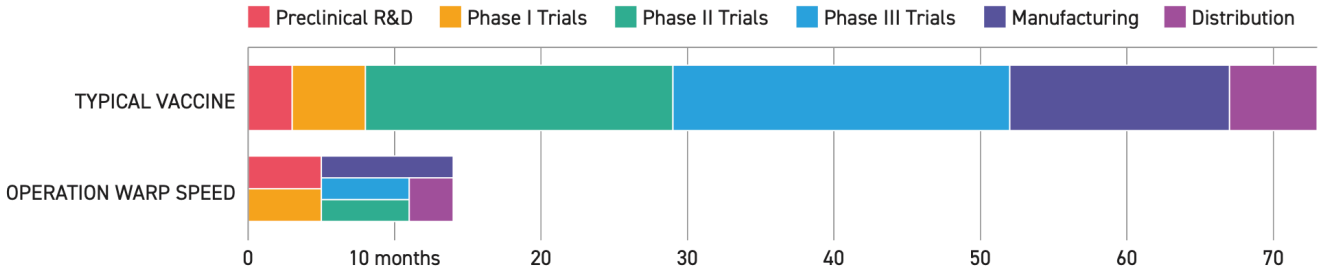
The fastest vaccine ever developed to that point — for mumps — took four years, but Warp Speed aimed to have a viable Covid-19 vaccine in one. Working with scientists at the National Institutes of Health and the FDA, the program helped vaccine developers cut years off the normal testing process without sacrificing safety.

The FDA has told vaccine developers that their late-stage, or Phase III, trials to determine efficacy and safety should enroll at least 30,000 people.

To determine whether a vaccine is effective, the data and safety monitoring board overseeing a study dips into the data at pre- determined points — comparing the number of Covid-19 infections among those who got the vaccine and those who got a placebo. The more infections in the placebo group, the more effective the vaccine. The FDA has said that coronavirus vaccines should be at least 50 percent effective to receive emergency authorization.

How Operation Warp Speed sped up the vaccine process, from 73 months to 14 months

Comparison of timelines for typical vaccine production and Operation Warp Speed's accelerated process



INITIAL RESEARCH

It usually takes months to design a potential vaccine, which is then tested in animals like mice, ferrets or monkeys as a first safety and efficacy check.

Several companies accelerated the design of their Covid-19 vaccines by repurposing work done for other diseases. Phase I safety trials in people began almost immediately, sometimes alongside animal studies.

CLINICAL TRIALS

Operation Warp Speed saved time by compressing the normal sequence of human studies, sometimes by combining phases.

The final stage, Phase III, is designed to prove whether a vaccine is effective and to uncover any safety issues. FDA has required vaccine makers to enroll at least 30,000 people in their Phase III studies, and to strive for age, gender and racial diversity.

MANUFACTURING

Operation Warp Speed funded risky early manufacturing for promising candidates at the same time clinical trials were run, to obtain a head start on production.

Once FDA approves a vaccine based on clinical trial data, distribution begins immediately while manufacturing continues.

WHAT'S NEXT

Results from the first late-stage clinical trials are rolling in — and a handful of vaccines appears to be safe and effective. Their developers are now applying for emergency authorization from the FDA and overseas regulators. That will allow vaccination to start while pharmaceutical companies compile the more detailed information needed to seek full approval, a process that normally takes years.

The FDA has told vaccine developers to monitor trial participants for two years, to see how long the protection from the vaccine lasts. Some companies argue that, given the deadly nature of the virus, trial participants who got a placebo should be given the option of getting vaccinated before those two years are up. The agency hasn't yet indicated how it will balance such ethical concerns with the need for gathering as much efficacy data as possible.

Because most vaccines are first tested in healthy adults, more studies will be needed to make sure they work — and are safe — for kids, pregnant women and people with weakened immune systems.

An overarching question is whether coronavirus vaccines will be able to stop the spread of the virus. The first successful vaccines have been shown to prevent people from getting sick, but scientists don't yet know whether they create the "sterilizing immunity" that prevents the virus from hopping from person to person. That should become clearer over time, with additional studies and real-world data.

POWER PLAYERS

FDA Commissioner Stephen Hahn
Hahn joined the FDA shortly after the coronavirus emerged in China, and the pandemic has dominated his tenure. He's battled the White House for stricter vaccine safety standards and has pushed for transparency in FDA's decision on Covid-19 vaccines.

Operation Warp Speed
The government's Covid-19 vaccine program focused at first on identifying promising shots and speeding their testing and development. Now, with some vaccines nearing the finish line, Warp Speed is getting ready to oversee their distribution.

The FDA's Vaccines and Related Biological Products Advisory Committee
The academic scientists, doctors and federal health officials on this panel will review data on each vaccine to determine whether it is safe and effective. FDA does not have to take the panel's findings into account, but it usually does.

Pfizer and Moderna
Each of these frontrunners in the global vaccine race announced in November that their shot was more than 90 percent effective. Both have applied to FDA for emergency-use authorization.

The CDC's Advisory Committee on Immunization Practices
The independent panel is issuing non-binding recommendations about who should be first in line for Covid-19 vaccines early on, when supplies are scarce.

Johnson & Johnson and AstraZeneca
Both companies have a vaccine in late-stage trials that could be ready for use early next year — which would accelerate the effort to vaccinate Americans.