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The Keys to Speed in Race for Vaccine, and Its Perils: QuickTake

By James Paton | August 26, 2020 9:40AM ET

When Merck & Co. won regulatory approval for its mumps vaccine in 1967, it set the record for speed. The process had begun four years earlier when scientist Maurice Hilleman was awakened one night by his sick 5-year-old daughter, swabbed her throat and took the specimen to his lab. This year, thousands of researchers in more than 30 countries have been racing to not just beat Hilleman's time but to bury it, collaborating and competing on more than 600 projects to develop a vaccine against the novel coronavirus. Authorities in China and Russia claim to be at the finish line, but researchers elsewhere are skeptical. With the best hopes for ending the pandemic resting on an effective vaccine, the stakes are immense. So are the challenges and the risks.

1. What are the Chinese and Russian vaccines?

Both countries have said they are using special regulatory provisions to deploy vaccines before they have undergone full testing. In June, a vaccine developed by the company CanSino Biologics was approved for use by China's military. In July, China authorized a shot made by developer Sinopharm for people such as medical workers who are at high risk of exposure to the coronavirus, according to a National Health Commission official. Russian authorities said in August that they would start mass inoculation with a vaccine, dubbed Sputnik V, as soon as October. The shot is being developed by Moscow's Gamaleya Institute, the Defense Ministry and the sovereign Russian Direct Investment Fund. The use of these vaccines outside of clinical trials raised concerns among researchers and regulators elsewhere.

2. What are the worries?

The use of vaccines that aren't fully tested puts people who get the jabs at an elevated risk of side effects that might have been discovered in clinical trials. The moves by Russia and China could place pressure on other governments to rush ahead of regulators and skip key safety steps as well.

3. What safety issues can arise with new vaccines?

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European regulators in 2011 recommended restricting the use of a swine-flu vaccine from GlaxoSmithKline Plc after it was linked to rare cases of narcolepsy. A vaccine against Lyme disease developed by the same company, then called SmithKline Beecham, was pulled in 2002 amid concerns about links to arthritis. Some vaccines have been shown to do the opposite of what they're designed to do by inducing unwanted immune responses. In the 1960s, an experimental vaccine for RSV, a common respiratory virus, not only failed to protect children, but made them more susceptible. Two toddlers died. In recent years, Sanofi's dengue vaccine was found to exacerbate symptoms in some who received it. Documented reports of unexpected side effects from new vaccines are different from the persistent and incorrect belief that well-established vaccines against childhood diseases carry significant risks. A fumbled Covid-19 shot could further damage perceptions of vaccines.

4. What's the process for minimizing safety risks?

An inoculation must clear a higher bar than a treatment because it's injected into healthy individuals. After testing a vaccine in animals, developers must show it's safe and effective in humans. That usually happens in three phases, starting with tests in a small number of people aimed at achieving the strongest immune response without significant side effects. Larger-scale studies follow. The final leg, which often requires thousands of patients and lasts years, evaluates how safely and effectively a vaccine prevents infection or disease in the population it's intended for. If a vaccine passes these tests, it must then satisfy regulators and be produced in large quantities. The process of bringing a conventional vaccine from inception to the finish line takes on average nearly 11 years. And just 6% of experimental vaccines make it all the way.

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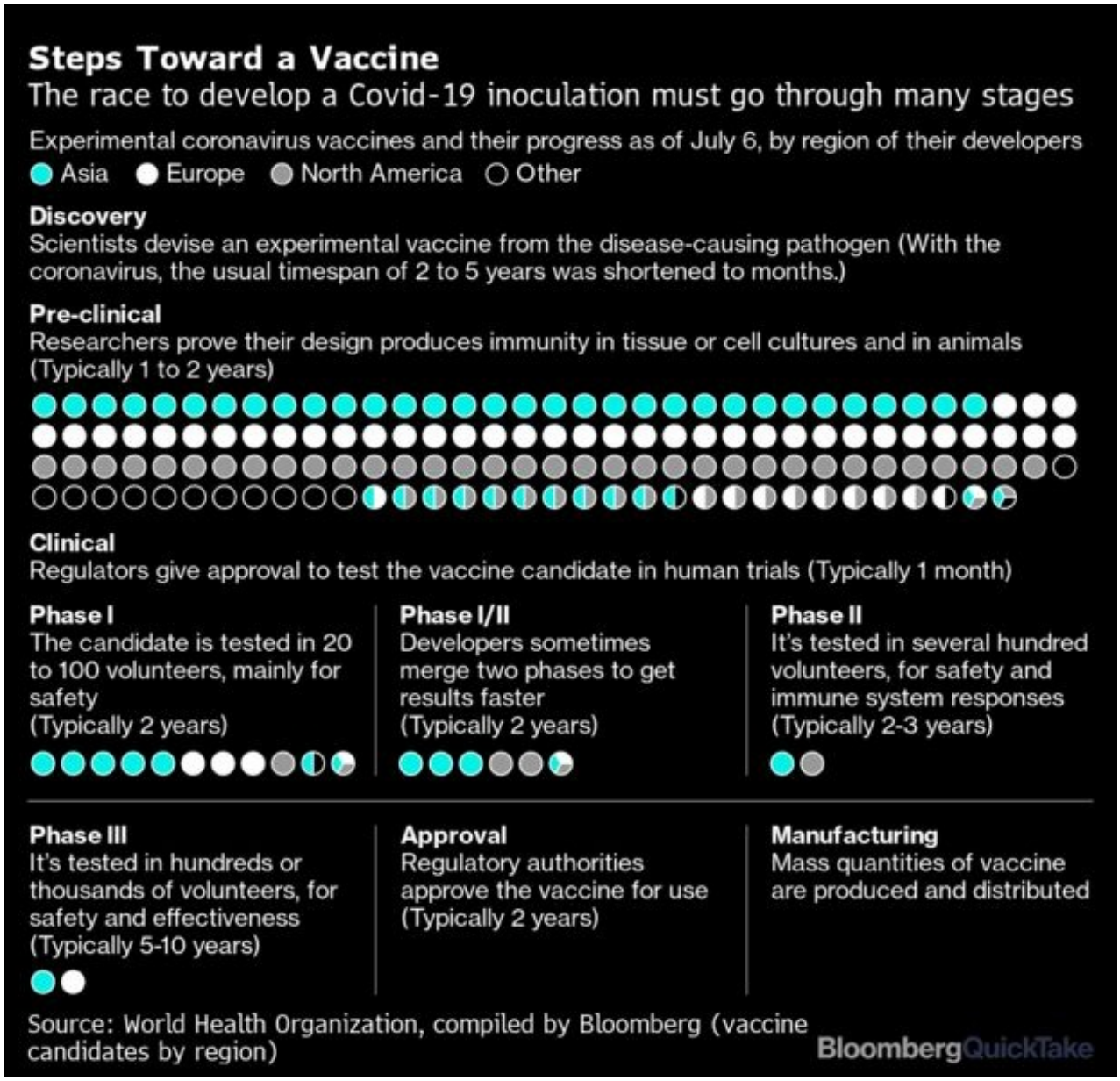

5. How has the development of Covid-19 vaccines been sped up?

- Using innovative vaccine designs. About a fifth of the Covid-19 vaccine projects rely on so-called gene-based technology. It uses the body's own cells to produce proteins that trick the immune system to react as if it's been invaded by a pathogen, training it for the real thing. These experimental vaccines can be made more quickly than conventional ones, which contain an inactivated or weakened version of a pathogen, or a piece of it. Using a gene-based platform, Moderna Inc. and the U.S. National Institute of Allergy and Infectious Diseases began the first human test of an experimental Covid-19 vaccine a record-short 66 days after Chinese researchers made public the coronavirus's genetic sequence. An important caveat: No gene-based vaccine has yet been licensed for humans, although a few are in use in veterinary medicine.
- Compressing steps. Another reason Moderna was able to move so quickly was that rather than testing its vaccine in animals before moving on to humans, it did both simultaneously. For Covid-19 vaccines, U.S. and European regulators in March waived the requirement for proving efficacy in animals first.
- Building on past work. Researchers at the University of Oxford got a jump by betting on a method they've used in their ongoing work on a vaccine against Middle East respiratory syndrome (MERS), which is

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caused by a related coronavirus. That vaccine appeared to be safe in animal and early human testing. The technique uses a modified cold virus as a harmless carrier to expose the immune system to the spiked protein that projects from the surface of a coronavirus rather like a crown, hence the name.

6. Would anything else quicken things?

Some researchers propose adopting so-called challenge trials. In the final stage of testing, researchers typically give a vaccine to one group of volunteers and a placebo to another, then wait to see whether significantly fewer in the first group develop the targeted infection. That takes time. A quicker but riskier alternative is to inject volunteers with the vaccine, then deliberately expose them to the pathogen. Such challenge trials are the basis for animal studies of vaccines, and they've been used in human tests of cholera, malaria and typhoid shots as well. Some prominent scientists have argued that the urgency of a Covid-19 vaccine justifies their use now, and the website 1daysooner.org has collected the names of tens of thousands of people who say they'd participate. Skeptics say it's unethical to use this trial design until there are better, proven therapies to treat those who would become sick.

7. Is a vaccine just a matter of time?

Despite the unprecedented mobilization, there's no guarantee developers will deliver an effective shot. A vaccine against HIV has eluded scientists for decades, as has a single shot that would prevent all strains of flu, though researchers think the coronavirus is an easier target because it doesn't appear to mutate as rapidly as those viruses do. The 2003 outbreak of severe acute respiratory syndrome (SARS), also caused by a coronavirus, was contained before researchers could come up with a vaccine. How effective a Covid-19 vaccine might be and how long its protection would last are other crucial questions. Still, a number of experts are hopeful. The head of French vaccine maker Sanofi said the key question is not whether successful vaccines can be devised, but how many doses can be produced rapidly.

8. If a vaccine pans out, how does it get mass produced?

Given the high failure rate for experimental vaccines, developers usually don't invest in the capacity to manufacture lots of doses before a new one looks like a winner. In this case, some of the most prominent players in the race, such as Johnson & Johnson, Sanofi and Moderna, are scaling up production facilities already. Philanthropist Bill Gates, is committing funds to the worldwide manufacturing effort. Glaxo is collaborating with Sanofi, two Chinese companies and others on projects that use its adjuvants, vaccine ingredients that boost the immune response, in the hope of making it easier to produce shots in larger quantities.

9. How would a vaccine get delivered to every corner of the globe?

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Some populations are bound to get vaccine supplies before others. One risk is that wealthier nations will monopolize Covid-19 vaccines, a scenario that played out in the 2009 swine flu pandemic. To prevent that, a collaboration called COVAX -- led by the Oslo-based Coalition for Epidemic Preparedness Innovations, the World Health Organization and Gavi, a global non-profit group focused on vaccine delivery -- aims to raise $18 billion from high- and middle-income countries. The fund would invest in developing and manufacturing the five to ten most promising vaccine candidates, with all contributors and poor countries ensured access to a proven vaccine for those who are at greatest risk, for example health-care workers and the elderly. Health advocates say that distributing vaccines evenly all over the globe isn't just the ethical thing to do. It's also critical to ending the crisis.

The Reference Shelf

- Bloomberg Businessweek examined vaccine nationalism as well as the challenges to develop an inoculation that works.
- Related QuickTakes on vaccine nationalism, myths and facts about vaccines, the search for Covid-19 therapies, coronavirus testing, and the virus and kids.
- A podcast on the rise of vaccine nationalism.
- The World Health Organization keeps track of Covid-19 vaccine candidates and trials.
- A Bloomberg tracker on the coronavirus vaccines and drugs under development.

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