Science You Can Use

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Dear Science: The hepatitis C, measles, polio, flu, and tetanus vaccines took about 10 years of research and clinical trials. So how can anyone trust the COVID-19 vaccines, which were muscled through in less than a year? -- Buck R.

Dear Buck: It's a good question. As of 18 December 2020, two vaccines had received "emergency"-use approval the FDA and CDC. On the surface, they appear to have been developed and approved in less than a year. One of these (which I will call the "P" vaccine), was developed by Pfizer (US) BioNTech (Germany). The other, (which I will call the "M" vaccine) was developed by Moderna. The short answer to your question has two parts.

First, the P and M vaccines have been given "emergency"-use approval only, whereas the other vaccine examples (for hepatitis C, measles, polio, flu, etc.) you mention have "full" approval. "Emergency"-use approval can be given on a short timeline when the FDA and CDC judge the benefits of a drug, vaccine, or procedure to outweigh the large risk (such as a pandemic with a relatively high death rate) of not using them. "Full" FDA/CDC approval, in contrast, typically requires many years of testing.

Second, the amount of research required to discover the P & M vaccines was based on about 10 years of research (mainly by Chinese scientists) on viruses closely related to the virus (SARS-CoV-2) that causes COVID-19.

The "emergency"-use approval, together with the research that had already been done on similar viruses, made it possible to develop promising vaccines for SARS-CoV-2 in a matter of months.

This short answer may seem less than convincing. For example, it doesn't answer two important questions: are the P & M vaccines *effective* and *safe* for, say, five years? The only way to answer questions like these with the kind of confidence we have in vaccines that have received full FDA/CDC approval (such as the measles or tetanus vaccines) is to administer the candidate vaccines to tens of thousands of people and monitor the health of those recipients for five years, comparing those results with the health of people who did not receive the vaccines.

Here is a longer answer.

Are the P & M vaccines safe? In testing to date about 20,000 people have been injected with the P vaccine; a similar number, with the M vaccine. The recipients of these vaccines have been monitored for less than a year. During that time neither vaccine has produced an adverse reaction that is any more severe than those experienced by recipients of flu vaccines. Most recipients have experienced a little soreness at the injection site, but nothing more.

Do the P & M vaccines prevent COVID-19? In testing to date the P & M vaccines have prevented COVID infection in about 95% of the test group, compared to the group that did not

receive the vaccine. (That success rate, by the way, is significantly higher than the success rate any flu vaccine developed to date.)

How were the P & M vaccines designed "overnight", seemingly bypassing years of research? The answer is that much of the research had already been done. Chinese scientists had already spent years characterizing the genetic encoding of a distinctive "spike" on the surface of several naturally occurring SARS viruses that are closely related to SARS-CoV-2. This spike plays a major role in how the virus infects a cell. Because of this research, the Chinese researchers were able to characterize, in a matter of days after isolating SARS-CoV-2, the genetic encoding of the spike on the virus's coat. Pfizer and Moderna were able to use this encoding to design, with computer assistance, a promising vaccine candidate within 24 hours. A few weeks after that, Pfizer had produced a small sample of the vaccine it now has in distribution.

The P & M vaccines represent a relatively recent breakthrough in vaccine technology. They are dilute suspensions of computer-designed ("messenger RNA" (mRNA)) molecules that are encapsulated in lipid ("fatty") nanoparticles (LNPs). When the LNPs are injected, various cells incorporate the LNPs (containing the mRNA). As an LNP enters a cell, the lipid coat falls away, and the mRNA "tells" the receiving cell to generate a protein that looks very much like a part of the spike protein on the coat of the SARS-CoV-2 virus. In response, the cell generates many copies of this part of the spike protein. The spike protein fragments produced by the cells is then sensed by the immune system, which mounts a defense against anything (including the SARS-CoV-2 virus) that "looks like" the spike protein. The mRNA design rubric holds high promise for the rapid development of a wide range of future vaccines for almost all diseases known to be caused by viruses.

For further information, see Florian Krammer, "SARS-CoV-2 vaccines in development", *Nature* 586 (22 October 2020), pp. 516-527. The FDA approval document for the P vaccine can be accessed at Pfizer-BioNTech COVID-19 Vaccine | FDA.

Jack Horner is a systems engineer. Thanks to Larry Platt for suggesting this topic.