

# COVID-19 shots might be tweaked if variants get worse

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In this Jan. 22, 2021, file photo, empty vials of the Pfizer-BioNTech COVID-19 vaccine are seen at a vaccination center at the University of Nevada, Las Vegas, in Las Vegas. The makers of COVID-19 vaccines are figuring out how to tweak their recipes against worrisome virus mutations—if and when the shots need an update. (AP Photo/John Locher, File)

The makers of COVID-19 vaccines are figuring out how to tweak their recipes against worrisome virus mutations—and regulators are looking to flu as a blueprint if and when the shots need an update.

"It's not really something you can sort of flip a switch, do overnight," cautioned Richard Webby, who directs a World Health Organization flu center from St. Jude Children's Research Hospital.

Viruses mutate constantly and it takes just the right combination of particular mutations to escape vaccination. But studies are raising concern that first-generation COVID-19 vaccines don't work as well against a mutant that first emerged in South Africa as they do against other versions circulating around the world.

The good news: Many of the new COVID-19 vaccines are made with new, flexible technology that's easy to upgrade. What's harder: Deciding if the [virus](#) has mutated enough that it's time to modify vaccines—and what changes to make.

"When do you pull the trigger?" asked Norman Baylor, a former Food and Drug Administration [vaccine](#) chief. "This is a [moving target](#) right now."

## FLU OFFERS A MODEL

The WHO and FDA are looking to the global flu vaccine system in deciding how to handle similar decisions about COVID-19 shots.

Influenza mutates much faster than the coronavirus, and flu shots have to be adjusted just about every year. National centers around the globe collect circulating flu viruses and track how they're evolving. They send samples to WHO-designated labs for more sophisticated "antigenic" testing to determine vaccine strength. The WHO and regulators then

agree on the year's vaccine recipe and manufacturers get to work.

For COVID-19 vaccines, Webby said a critical step is establishing a similar surveillance and testing network to flag the mutations that matter. Today, there's wide geographic variability in tracking and testing mutated versions. For example, Britain does more testing of the changing viral genome than the U.S.

Three variants first discovered in Britain, South Africa and Brazil are worrisome because of combinations of mutations that make them more contagious.

On Sunday, U.S. researchers reported a still different mutation found in seven variants that have cropped up in several states. No one yet knows if this mutation makes the virus easier to spread but the report, not yet vetted by other scientists, urges further research to find out.



In this Jan. 22, 2021, file photo, Tina Killebrew, a certified medical assistant, prepares a dose of the Pfizer-BioNTech COVID-19 vaccine at a vaccination center at the University of Nevada, Las Vegas. The makers of COVID-19 vaccines are figuring out how to tweak their recipes against worrisome virus mutations—and regulators are looking to flu as a blueprint if and when the shots need an update. (AP Photo/John Locher, File)

## HOW COVID-19 SHOTS ARE HOLDING UP

Just because a variant is more contagious doesn't mean it also will be impervious to vaccination. But the variant first identified in South Africa is raising concerns. Columbia University's David Ho put blood samples from people given the Pfizer or Moderna vaccines into lab dishes with the mutated virus. Vaccine-produced antibodies still protected, but they

were much less potent.

Preliminary test results of two other vaccine candidates—from Novavax and Johnson & Johnson—soon backed up those findings. Both still protected but were weaker when tested in South Africa, where that variant dominates, than when tested elsewhere. A far smaller test of the AstraZeneca vaccine in South Africa has raised questions about its effect.

"If the virus were able to make an additional mutation or two, it could escape even more," Ho warned.

## THE REAL RED FLAG

If fully immunized people start getting hospitalized with mutated virus, "that's when the line gets crossed," said Dr. Paul Offit, a Children's Hospital of Philadelphia vaccine expert who advises the FDA.

That hasn't happened yet, but "we should get ready," he added.

Moderna is about to explore one option: Could a third dose of the original vaccine boost immunity enough to fend off some variants even if it's not an exact match?

Columbia's Ho said it's a good idea to test because people may "still have plenty of cushion" if their overall antibody levels are very high.

## ADJUSTING THE RECIPES

Major manufacturers also are developing experimental variant vaccines, just in case.





David Williams receives a COVID-19 vaccine at the Martin Luther King Senior Center, Wednesday, Feb. 10, 2021, in North Las Vegas. The makers of COVID-19 vaccines are figuring out how to tweak their recipes against worrisome virus mutations—if and when the shots need an update. (AP Photo/John Locher, File)

COVID-19 vaccines produce antibodies that recognize the spike protein that coats the [coronavirus](#). When the virus mutates, sometimes the spike protein is changed in key areas so the vaccine-produced antibodies have a harder time recognizing it.

The Pfizer and Moderna vaccines are made with a piece of genetic code called messenger RNA that tells the body how to make some harmless copies of the spike protein that train immune cells. To update the

vaccine, they can simply change the payload: swap out the original genetic code with mRNA for the mutated spike protein.

The AstraZeneca vaccine and the Johnson & Johnson shot expected to roll out soon are made with cold viruses engineered to sneak a spike protein gene into the body. Adjusting their vaccines requires growing cold viruses with the mutated gene, a little more complex than the mRNA approach but not nearly as laborious as reformulating old-fashioned flu shots.

The Novavax vaccine also in final-stage testing is made with a lab-grown copy of the spike protein that also could be tweaked to match mutations.

## TESTING VACCINES 2.0

First-generation COVID-19 vaccines were tested in tens of thousands of people to be sure they work and are safe—research that took many months.

Simply changing the recipe to better target virus mutations won't require repeating those studies in thousands of people, Dr. Peter Marks, the FDA's vaccine chief, recently told the American Medical Association.

FDA still is finalizing requirements, but Marks said the agency intends to "be pretty nimble." If an updated vaccine is needed, tests in a few hundred people likely would be enough to tell if it triggers a good immune response, he said.

But an even bigger question: If only some places face vaccine-resistant virus mutants, would authorities want variant-only shots or vaccines that protect against two kinds in one jab? After all, flu vaccines protect against three or four different types in one shot.

Companies would first have to perform some basic research to be sure a variant-only version properly revs up the immune system, said the Immunization Action Coalition's John Grabenstein, a former Merck vaccine executive. Then a combination shot would need more testing to be sure there's an equal response to both types.

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