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HEALTH

Coronavirus vaccine could come from California, with no shot needed

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Bay Area researchers' proximity to leading health care centers and Silicon Valley has given them a leading role in developing drugs to treat COVID-19.

It could also give local companies and institutions a leg up in the global race to create a vaccine. Several have set out to create a highly effective product that can be distributed widely.

The stakes could not be higher. Even as doctors learn more about drugs to help patients who have contracted the virus, a vaccine remains potentially the most effective — and elusive — tool to fight the pandemic. Answers are likely still months away at the earliest, but government officials and health companies are trying to accelerate the process.

The odds are long: More than 130 vaccines are in development worldwide, according to the Milken Institute, a Santa Monica think tank. Only a small subset of those will likely be put to use. And successful companies must not only build a product that stops the virus, but also manufacture it on a truly enormous scale as fast as possible.

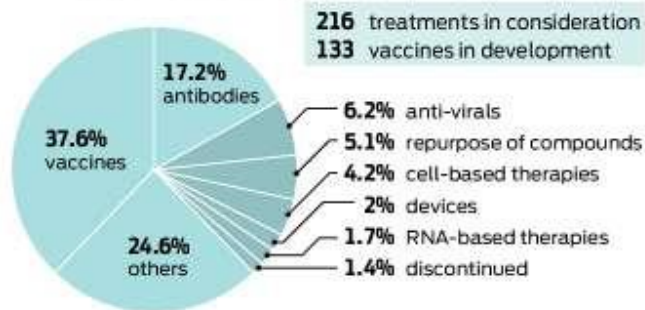
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Making a new vaccine

Vaccine development typically takes a long time to complete, starting with basic lab research before progressing into preclinical work that involves testing a vaccine candidate on animals. All of that can take years, but experts are trying to speed up the process to fight COVID-19. Even the clinical stages can take considerable time, though.

Here's how it usually works:

Coronavirus vaccines and treatments in research or development

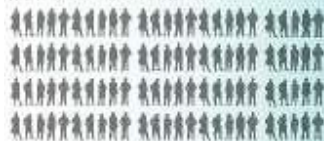


216 treatments in consideration
133 vaccines in development

CLINICAL DEVELOPMENT

Phase 1 Weeks

Scientists test the vaccine on a small group of people. The goal is to ensure the vaccine is safe and see the response it provokes in the immune system.



20-100 volunteers

Phase 2 Months

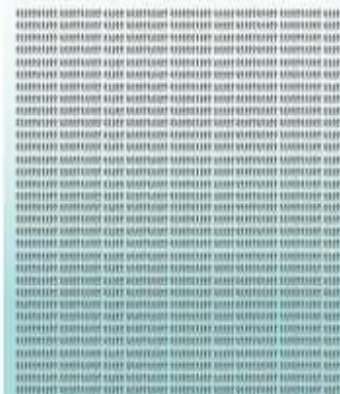
A few hundred people will receive the vaccine as scientists refine their approach and continue monitoring for safety and the immune response. A placebo group is included. Longer-term follow-up work may occur while Phase 3 is under way.



Several hundred volunteers

Phase 3 At least 1 year

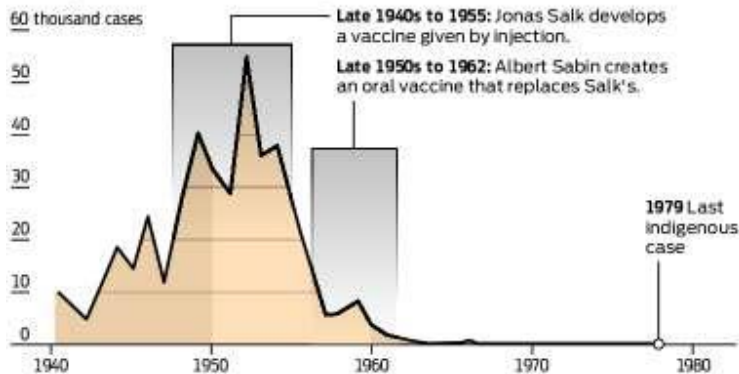
At least several thousand people, or even tens of thousands, get the vaccine in randomized, double-blind trials. Researchers seek to find out if the vaccine is safe in large groups and whether it effectively prevents disease from spreading.



Thousands of volunteers

EXAMPLE

U.S. polio vaccine development



Sources: Centers for Disease Control and Prevention, historyofvaccines.org, Chronicle research

After clinical development, vaccines typically need to undergo regulatory review and approval, manufacturing and quality control, which adds more time.

John Blanchard / The Chronicle

Some of the vaccines being studied locally would not be administered through a shot.

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Verndari, of Napa, is working on a potential coronavirus vaccine to administer through an adhesive patch. The idea is to take away the pain component, thereby circumventing anyone's aversion to shots, and to make something that can be kept

at room temperature. That could make the vaccine easier to distribute, especially in developing countries.

Dr. Daniel Henderson, Verndari's CEO, said the patches could even be sent through the mail and use temporary dye to leave a mark on a patient's arm. The patient could then take a photo of the dye and send that to their health care provider as proof they were vaccinated.

"We really do want to change the way vaccines are perceived," Henderson said. "And of course this goes far beyond COVID-19. It goes to the global distribution of vaccines everywhere. You could make them cheaper and have better efficacy and do away with the fear of vaccines."

Verndari's potential vaccine, which the company is developing at the UC Davis Medical Center in Sacramento, uses the virus' "spike" protein, which the virus uses to attach itself to human cells. By introducing that protein into a person's body, Verndari hopes it can train their immune system to recognize the virus when exposed to it and thereby prevent the person from becoming ill.

Henderson said he hopes to be able to start clinical trials that would test the vaccine on humans this summer. Forecasting when the vaccine might be rolled out, if it works and is safe, is more complicated given that the company is also proposing a new delivery method.

But Henderson said Verndari has already demonstrated that its patch is effective in humans when it was studying a potential flu vaccine. The company has also established a relationship with a California manufacturer.

South San Francisco's Vaxart is another one of the local companies that is working on a potential coronavirus vaccine. Like Verndari, Vaxart also wants to protect people from COVID-19 without giving them shots. But instead of using a patch, the company is exploring a vaccine that could be taken in pill form.

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Vaxart CEO Wouter Latour said the company has already shown efficacy through a clinical trial of a flu vaccine pill. Now, it's trying to develop a similarly effective tool for the coronavirus.

Latour said the company wants to use an inactivated common cold virus as a vehicle for DNA that could help train the body to fight off the new coronavirus. He said Vaxart is on track to start clinical studies in the second half this year.

Vaxart doesn't expect to create the first viable vaccine for COVID-19 — Latour thinks there will be many. Demand for a vaccine will be so high that the world won't have enough resources to get one vaccine in the hands of everyone who needs it, at least not initially.

"Get those early vaccines out," he said. "We could be right behind with this fantastic tablet and make life a lot easier and much more efficient in terms of implementing a large vaccination campaign and getting it to parts of the world where it's harder to get vaccines."

In order to make a vaccine pill effective, developers would have to figure out how to make it strong enough to not be killed by stomach acid before the vaccine can do its job, said Dr. Lee Riley, an infectious disease expert at UC Berkeley. But if effective, such a vaccine would be safe and easy to give to a lot of people, he said. A patch could work well because skin is the body's largest organ and it's good at producing a strong immune response, Riley said.

But finding a vaccine that works is only one part of the equation. Once proved effective, the product has to be made widely available — which will be a major challenge if it needs to reach billions of people.

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George Talbott, left, works on a coronavirus vaccine patch with Verndari CEO Dr. Daniel Henderson in Sacramento in May.

Photo: Paul Chinn / The Chronicle

“It will take years to be able to have a production capacity to make that many vaccines,” Riley said. “It’s not just coming up with a vaccine that works. It’s also the production that’s going to take some time.”

Dynavax Technologies of Emeryville is taking a slightly different approach to vaccine development than some of the other companies. Instead of building a vaccine on its own, Dynavax is lending a helping hand to others.

The company has created a federally-authorized vaccine for hepatitis B that uses a modifying ingredient to improve the immune response in patients. So Dynavax is providing that ingredient, called CpG 1018, to help other companies that are developing potential vaccines.

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“We have a technology that’s proven in our vaccine that can be possibly very valuable to helping address this issue, and therefore it has to be evaluated,” said Dynavax CEO Ryan Spencer. “We have, I think, a responsibility to be in the game here.”

At UCSF, immunology Professor Raul Andino is taking his time to study exactly how the coronavirus works before trying to devise a new way to protect people. He’s closely examining how the virus progresses in animals, and he thinks he’s at least six months away from moving into the clinic.

“While everybody is trying to jump ahead and get the answer in humans, basic studies are very important to understand the mechanisms by which this virus causes the disease,” Andino said.

He knows the world can’t wait for him to finish his work before advancing ways to make people immune to COVID-19. But his ultimate goal is still to create a live-attenuated vaccine, which uses a weakened form of a virus to create immunity.

That type of vaccine has proved broadly effective at combating other dangerous illnesses such as polio, mumps and smallpox, Andino said. Because using a weakened form of the virus is so similar to a natural infection, live-attenuated vaccines have the power to induce long-lasting immunity — but they require a sophisticated understanding of how the virus works.

“I understand everybody wants a vaccine yesterday,” he said. “But what I’m thinking of is the second generation of vaccines ... maybe a live-attenuated vaccine will be better in the long run.”

An ideal coronavirus vaccine might look like previous vaccines developed for hepatitis B and whooping cough that used certain proteins to provide protection, said Dr. Yvonne Maldonado, an epidemiologist and infectious disease specialist at Stanford University’s School of Medicine. Part of the challenge now is that doctors do not yet fully understand the virus that caused the current pandemic.

“It’s like the normal coronaviruses that cause colds in human beings, but it’s much more likely to cause serious disease as well,” she said. “We’re trying to understand why that is.”

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One way to speed up the vaccine development process may be to let volunteers be given a potential vaccine or placebo, then injected with the virus or placebo while researchers study the effects. A new campaign called 1 Day Sooner has sprung up in support of that goal. It's already registered thousands of people, including hundreds in California, who have said they're willing to participate in "challenge trials" — if and when they occur in humans.

Josh Morrison, a New York resident who co-founded the campaign, said the goal is to have a list of people who are willing to participate should researchers take the step of asking for volunteers. More screening would be required if that happens.

While such trials would only accept people who are at lower risk of developing severe or deadly cases of COVID-19, Morrison knows that asking people if they are willing to be injected with a live coronavirus may sound like a dicey proposition.

"This is definitely a significant risk ... but it's also a type of risk that is consistent with other risks we let people take," he said. "We think, if you have intelligent and well-educated volunteers, we should let those people make those choices if it's likely that you have a meaningful gain in vaccine development, which to us is as little as one day."

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