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Antibody Test, Seen as Key to Reopening Country, Does Not Yet Deliver

The tests, many made in China without F.D.A. approval, are often inaccurate. Some doctors are misusing them. The rollout is nowhere close to the demand.

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A law firm in Scottsdale, Ariz., tested employees who hoped, with the prick of a finger, to learn if they might be immune. In Laredo, Texas, community leaders secured 20,000 of the new tests to gauge how many residents had been infected. In Chicago, a hospital screened firefighters to help determine whether they could safely stay on the job.

In recent weeks, the United States has seen the first rollout of blood tests for coronavirus antibodies, widely heralded as crucial tools to assess the reach of the pandemic in the United States, restart the economy and reintegrate society.

But for all their promise, the tests — intended to signal whether people may have built immunity to the virus — are already raising alarms.

Officials fear the effort may prove as problematic as the earlier launch of diagnostic tests that failed to monitor which Americans, and how many, had been infected or developed the disease the virus causes. Criticized for a tragically slow and rigid oversight of those tests months ago, the federal government is now faulted by public health officials and scientists for greenlighting the antibody tests too quickly and without adequate scrutiny.

The Food and Drug Administration has allowed about 90 companies, many based in China, to sell tests that have not gotten government vetting, saying the pandemic warrants an urgent response. But the agency has since warned that some of those businesses are making false claims about their products; health officials, like their counterparts overseas, have found others deeply flawed.

Tests of “frankly dubious quality” have flooded the American market, said Scott Becker, executive director of the Association of Public Health Laboratories. Many of them, akin to home pregnancy tests, are easy to take and promise rapid results.

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And the federal guidance that does exist is so confusing that health care providers are administering certain tests unaware that they may not be authorized to do so. Some are misusing antibody test results to diagnose the disease, not realizing that they can miss the early stages of infection.

“People don’t understand how dangerous this test is,” said Michael T. Osterholm, an infectious disease expert at the University of Minnesota. “We sacrificed quality for speed, and in the end, when it’s people’s lives that are hanging in the balance, safety has to take precedence over speed.”

Even as government agencies, companies and academic researchers scramble to validate existing tests and create better ones, there are doubts they can deliver as promised. Most tests now available mistakenly flag at least some people as having antibodies when they do not, which could foster a dangerously false belief that those people have immunity.

And even if the tests do improve, their availability could be hampered by the same manufacturing shortages that have prevented the Covid-19 diagnostic tests from scaling up adequately.

As President Trump presses to reopen the country and several states are considering lifting lockdowns in the next few weeks, widespread screening is considered critical. On Friday, Mr. Trump cheered the F.D.A.’s emergency approval of some antibody tests, saying they would support efforts to get Americans back to work “by showing us who might have developed the wonderful, beautiful immunity.”

Epidemiologists are testing for antibodies in hot spots to better measure the extent of the outbreaks, and government officials intend to use those results to help decide when and how to return residents to daily life. But many scientists and political leaders say the country is nowhere close to deploying enough diagnostic and antibody tests at the speed and volume required.

“The more testing, the more open the economy,” Gov. Andrew M. Cuomo of New York said on Wednesday. He has pushed for the production of antibody tests as a central cog in plans to ease stay-at-home restrictions, saying that New York would eventually screen 100,000 people a day.

Recent testing around the country demonstrates the challenges of using the new products. At the Chicago hospital, for example, the city’s Public Health Department intervened, warning that it should not use antibody tests to determine whether emergency workers were actively infected.

Soon after it helped screen the Rose Law Group, the firm in Arizona, a lab stopped providing rapid tests to other clients, fearing they might not comply with federal guidelines, and switched to more sophisticated lab-based tests.

In Laredo, officials discovered the tests they received were woefully inadequate. The local health department found them to have a reliability of about 20 percent, far from the 93 to 97 percent the company had claimed. A police investigation led to a federal seizure of the tests.

“The city was disappointed, but during a time of crisis, we are doing everything possible to scour the earth to have tests available for the public,” said Rafael Benavides, the city’s public information officer.

“It’s a real mess,” Dr. Osterholm said. “This is the wild, wild West in terms of testing, and at a time when we need real definition of what these tests mean.”

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Medical Free-for-All

More than 90 companies have jumped into the market since the F.D.A. eased its rules and allowed antibody tests to be sold without formal federal review or approval.

Some of those companies are start-ups; others have established records. In a federal guidance document on March 16, the F.D.A. required them to validate their results on their own and notify the agency that they had done so.

Their products vary. Some test only for a transient antibody that spikes while the body is in the throes of an active infection. An antibody that peaks about four weeks after infection and typically marks longer-term immunity is a separate target. There are tests that look for both antibodies; others also look for a third involved in respiratory infections.

The most reliable ones involve a laboratory technique called Elisa that can indicate the amount of antibodies a person may have. Researchers are not certain that people who have recovered from Covid-19 have immunity, though it would follow the usual pattern for viral infections. Higher levels of antibodies generally mean a stronger physiological response, but it is unclear what levels are needed for immunity to the new coronavirus — or how long it might last.

“We’re really far from that,” Dr. Osterholm said. “We’re not even in the second inning of a nine-inning game at this point.”

Most of the tests offered are rapid tests that can be assessed in a doctor’s office — or, eventually, even at home — and provide simple yes-or-no results. Makers of the tests have aggressively marketed them to businesses and doctors, and thousands of Americans have already taken them, costing a patient roughly $60 to $115.

Rapid tests are by far the easiest to administer. But they are also the most unreliable — so much so that the World Health Organization recommends against their use.

A rapid antibody test for the novel coronavirus. The World Health Organization has warned about their unreliability.Credit...Omar Marques/Getty Images

Most are manufactured in China. Reports of countries that quickly bought millions have just as swiftly been followed by accounts of poor performance.

For example, Britain recently said the millions of rapid tests it had ordered from China were not sensitive enough to detect antibodies except in people who were severely ill. In Spain, the testing push turned into a fiasco last month after the initial batch of kits it received had an accuracy of 30 percent, rather than the advertised 80 percent. In Italy, local officials have begun testing even before national authorities have validated the tests.

“The problems mainly happen with rapid tests,” said Dr. Giorgio Palù, an Italian microbiologist and former president of the European Society for Virology. “They will never be able to tell the spread of the virus because they do not have the required sensitivity and specificity.”

Germany, which has emerged as a model among Western democracies in its efforts to curb the spread of the virus, is pursuing one of the most ambitious antibody studies, striving to test its entire population.

It is a leader in the technology, has made its own antibody tests and conducted extensive diagnostic screening from the beginning.

This month, the F.D.A. warned that some firms marketing their antibody tests in the United States were falsely claiming that they had formal federal approval, or that they could diagnose Covid-19.

In an effort to speed up access, the F.D.A. apparently did not fully consider how these tests would be administered. The agency released a guidance document saying that antibody tests could be performed at "point-of-care" settings, indicating that doctors, nurses and others could give them to patients in their offices. But agency officials also acknowledged that under federal law, if a test has not been authorized by the agency, it must be conducted in so-called high-complexity laboratories, like some large commercial facilities or public health labs. The officials decline to provide additional clarification.

"If you are getting an antibody test and it's being conducted in your physician's office, it's a red flag," said Kelly Wroblewski, director of the infectious disease programs for the Association of Public Health Laboratories.

No action has been taken against doctors, but as companies realized the ambiguity of the federal guidelines, some changed course, shifting to lab-based tests or pursuing formal federal approval, which would allow their products to be used at doctors' offices and even at home.

The F.D.A. has received requests for emergency-use authorization from 120 antibody-testing developers. So far it has granted formal approval to just four: Cellex, Ortho Clinical Diagnostics, Chembio Diagnostic Systems and the Mount Sinai Laboratory.

Mr. Becker, of the Association of Public Health Laboratories, said he was heartened to see more developers seeking the authorization, describing it as "the gold standard."

In a statement on Saturday, the F.D.A. commissioner, Dr. Stephen M. Hahn, said that "every step we have taken as part of our approach to Covid-19 testing has been a careful balancing of risks and benefits," adding, "We are continuing to learn and adapt based on the real-world experience and data we're seeing."

Everybody Wants One

Hospitals, municipalities and businesses have quickly moved into the first wave of antibody screening. They are acquiring kits from private suppliers, pairing up with research institutions or making their own lab-based tests.

The Hospital of the University of Pennsylvania began screening health care workers this past week as part of a clinical study of people who are infected but asymptomatic.

Eurofins, a network of clinical labs, is working with its subsidiary Boston Heart Diagnostics to test employees at 100 hospitals, including the V.A. New England Healthcare System, which serves about 265,000 patients a year. In Michigan, Beaumont Health is offering voluntary testing to its 38,000 employees and thousands of affiliates.

"Everybody's a little nervous about how protected they are really," said Dr. Matthew D. Sims, Beaumont's director of infectious diseases research. "We want to give everybody as much peace of mind as we can."

Physicians say antibody tests can be useful if given as part of a broader range of care.

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Dr. Ida Bergstrom, based in Washington, described the rapid tests as only "one tool" in the arsenal against the virus. Dr. Syed Ashraf advises patients in Northern Virginia that positive results, while not "a free license to run around and do whatever you feel like," can help clear someone to move forward.

Dene Callas, an advertising executive in Santa Monica, Calif., quickly accepted when her doctor offered to test her this month. An initial rapid test was invalid; a second one came back negative. Still, Ms. Callas believed she had contracted the virus and recovered: She had attended a conference in Las Vegas in January and fallen ill within days. A positive test, she said, would have made a difference. "I would be a little braver outside," she said. "I would be out there volunteering if I knew I had the antibodies."

Some large employers, including Goldman Sachs and Twitter, have looked into antibody tests but not bought any. Amazon has not focused on antibody screening, though it intends to roll out diagnostic testing for the hundreds of thousands of people in its warehouse and logistics network, according to people familiar with the plans.

Some smaller businesses, though, have pursued the new tests. At John Christner Trucking, a food transportation company near Tulsa, Okla., about 220 workers took rapid tests. They were concerned about exposure after two were infected with the virus. A small number came back positive, said Danny Christner, the chief executive. "I knew it wasn't a silver bullet, but it was some information that people could be aware of," he said.

The Chicago Public Health Department bought 5,500 rapid tests and put them to use in homeless shelters as a supplement to diagnostic testing. Those who were positive for the early antibodies were placed in hotel rooms rented by the city during the 48 hours it took to get diagnostic test results back, said Dr. Allison Arwady, commissioner of the department. The next step may be testing people in nursing homes, she said.

Sports leagues are also considering how antibody tests can figure into their plans. The N.B.A., with its season paused, has been approached about purchasing tests and is awaiting guidance from public health officials.

Major League Baseball employees and players will be tested as part of a 10,000-person nationwide study run by outside researchers to better understand the scale of infection. A players' union official said the testing was voluntary and not connected to beginning the season.

In Search of a Test That Works

While political leaders and some health officials say that antibody testing will be essential to reopening the country, it is unlikely to meet expectations anytime soon.

Less than 5 percent of the U.S. population may be infected, and even in hot zones like New York or New Orleans, the prevalence may not be higher than 10 to 15 percent, according to Dr. Osterholm. In China, early screening in hard-hit Wuhan indicates that only about 3 percent of the population has antibodies against the new coronavirus.

When the proportion of people exposed is that low, the tests' false positive rate — signaling antibodies where there are none — can limit the tests' utility.

Even Cellex's F.D.A.-authorized test has a false positive rate of about 5 percent. That is still a significant margin of error: In a community where 5 percent of people have had the virus, Dr. Osterholm said, there would be as many false positives as true ones.

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“What are you going to do with that? Are you going to say you’re not going to distance?” he said. “I don’t think that would give me peace of mind at all.”

Some tests on the market without federal approval are likely to have even higher false positive rates. It is unclear how these companies have validated their tests or how they stack up against one another.

Researchers at the National Institutes of Health are validating some of the tests in cooperation with the F.D.A. A Danish group published a small analysis of nine tests and found, as might be expected, that some performed better than others. A research group backed by the Chan Zuckerberg Initiative is working to assess all available tests using the same set of samples for each, with early results expected next week.

“There’s an urgent need to know which of these tests we can rely on — I think the only way we can know is head-to-head testing,” said Dr. Alexander Marson, one of the leaders of the project and a microbiologist at the University of California, San Francisco.
“The ideal outcome is not to pick a winner but to pick as many winners as possible so the world can have a diversified list of tests,” he added.

President Trump has said that once the federal government has finished validating the antibody tests, manufacturing will swiftly meet demand. But that may not be realistic.

Most companies are buying rapid tests from China, though they are unsure if and when they will become available. Early on, Chinese businesses could sell their products freely, but now, Chinese officials have signaled that only antibody tests approved by the country’s government can be exported. So far, China’s National Medical Products Administration has authorized only 11.

A start-up in Los Angeles, Scanwell Health, expected to receive a million tests each week from Innovita, one of the 11 companies. But it is still waiting for its first shipment of 10,000, which was scheduled to arrive three weeks ago.

Companies and health officials are also predicting shortages of the reagents and components required to assemble the tests.

“As many scientific challenges as there are right now,” said Scott Hensley, leading the University of Pennsylvania study, “there’s an equally large engineering challenge and scalability challenge to get these on the market.”