The United States badly bungled coronavirus testing—but things may soon improve

By Jon CohenFeb. 28, 2020 , 5:45 PM

A faulty reagent in a test kit distributed by the U.S. Centers for Disease Control and Prevention has hampered efforts to find and confirm COVID-19 cases.

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Speed is critical in the response to COVID-19. So why has the United States been so slow in its attempt to develop reliable diagnostic tests and use them widely?

The World Health Organization (WHO) has shipped testing kits to 57 countries. China had five commercial tests on the market 1 month ago and can now do up to 1.6 million tests a week; South Korea has tested 65,000 people so far. The U. S. Centers for Disease Control and Prevention (CDC), in contrast, has done only 459 tests since the epidemic began. The rollout of a CDC-designed test kit to state and local labs has become a fiasco because it contained a faulty reagent. Labs around the country eager to test more suspected cases—and test them faster—have been unable to do so. No commercial or state labs have the approval to use their own tests.

In what is already an infamous snafu, CDC initially refused a request to test a patient in Northern California who turned out to be the first probable COVID19 case without known links to an infected person.

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The problems have led many to doubt that the official tally of 60 confirmed cases in the United States is accurate. “There have been blunders, and there could be an underlying catastrophe that we don’t know about,” says epidemiologist Michael Mina, who helps run a microbiology testing lab at Brigham and Women’s Hospital. “It’s been very complicated and confusing for everyone with almost no clarity being provided by the CDC.”

The situation may soon improve. State labs and commercial diagnostic developers hope to win approval from the Food and Drug Administration (FDA) for their own tests, and FDA and CDC on Wednesday agreed on a workaround for the faulty CDC kit—which has a problem that is not essential to its proper functioning—so that it can now be used by at least some of the state labs that have it.

But there’s widespread discontent with the way the system has worked. “The U.S. government has not appropriately prioritized diagnostic tests and supported the laboratory response network to the degree they should have been supported over the years,” says Luciana Borio, who in previous jobs had lead roles in responding to emerging threats at the National Security Council and FDA.

If a new disease emerges, CDC normally “gets the ball rolling” with diagnostics because it has the expertise and the biosafety laboratories to handle dangerous novel pathogens, says Borio, who now works for In-Q-Tel, a not-for-profit venture capital firm. Typically, there are few confirmed viral samples from patients at the outset, which researchers need to validate their tests, and CDC has the capability to grow the virus for this critical quality assurance step. Once the agency has a working test, that goes out to state labs. Then, in a third phase, commercial labs take over and either produce their own tests or scale-up the CDC one. “I would have hoped to see that third phase by now,” Borio says.

In the case of SARS-CoV-2, as the virus causing COVID-19 is officially known, CDC’s sluggishness was apparent 1 month ago. On 26 January, the agency held an unusual Sunday teleconference for the media to provide an update about the rapidly growing outbreak. There were then five cases in the United States, but the CDC lab in Atlanta was still the only one in the country able to test for the virus, and it repeatedly had

backlogs. Asked why more labs weren't able to do the tests, Nancy Messonnier, who then was leading CDC's response, said it was a quality issue. "We hold ourselves to an incredibly high standard of precision in terms of laboratory testing," Messonnier said. "We wouldn't want to inadvertently make a mistake in patient care."

CDC finally started to send kits to state and local health labs on 5 February. But on 12 February, it revealed that several labs had difficulty validating the test because of a problem with one of the reagents.

The key problem with the kits is what's known as a negative control, says Kelly Wroblewski, director of infectious diseases at the Association of Public Health Laboratories (APHL). CDC's test uses the polymerase chain reaction (PCR) assay to find tiny amounts of the SARS-CoV-2 genome in, say, a nose swab. To make sure a test is working properly, kits also include DNA unrelated to SARS-CoV-2. The assay should not react to this negative control, but the CDC reagents did at many, but not all, state labs. The labs where the negative control failed were not allowed to use the test; they have to continue to send their samples to Atlanta.

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In principle, many hospital and academic labs around the country have the capability to carry out tests themselves. The PCR reaction uses so-called primers, short stretches of DNA, to find viral sequences. The CDC website posts the primers used in its test, and WHO publicly catalogs other primers and protocols, too. Well-equipped state or local labs can use these—or come up with their own—to produce what are known as a "laboratory-developed tests" for in-house use.

But at the moment, they're not allowed to do that without FDA approval. When the United States declared the outbreak a public health emergency on 31 January, a bureaucratic process kicked in that requires FDA's "emergency use approval" for any tests. "The declaration of a public health emergency did exactly what it shouldn't have. It limited the diagnostic capacity of this country," Mina says. "It's insane."

On 24 February, APHL asked FDA Commissioner Stephen Hahn for "enforcement discretion" to sidestep the emergency process and allow APHL members labs to use their own tests. On 26 February, Hahn replied that the CDC test could be modified to use just the primers that specifically detect SARS-CoV-2, essentially ignoring the faulty portion of the kits. FDA, in other words, would look the other way to make more widespread testing possible.

CDC has notified labs of FDA's decision in a letter, but the agency must still file an emergency use authorization with FDA for the protocol change. Once it does, it won't take long, Hahn promised in his letter to APHL: "FDA has been able to authorize tests for public health emergencies within as little as 1 day upon receipt of the complete validation."

In New York, the State Department of Health has designed its own test based on the CDC protocol and plans to seek emergency use authorization.

CDC provided an update about the situation in an email but did not respond to *Science*'s request for an interview with a scientist to discuss the details of the problem. Mina stresses he has great respect for CDC's competence overall, but says, "There's no good explanation for what's going on here."