The Way Forward For COVID-19 Testing In The US

By **Torrey Cope, Coleen Klasmeier, Diane McEnroe and Jaclyn Fonteyne** (May 11, 2020)

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The public debate over severe acute respiratory syndrome coronavirus 2, the pathogen responsible for COVID-19, has become dominated by questions about diagnostic testing. On April 24, President Donald Trump signed bipartisan legislation funding a national COVID-19 testing program with significant state and local responsibility for scale up, contact tracing and employer testing.[1]

Despite $25 billion allocated to COVID-19 testing, major challenges will confront authorities as they seek to make accurate testing available across the country. On April 27, the White House unveiled its blueprint for coronavirus testing through a partnership involving federal, state, local and tribal governments, and the private sector.

Background: Types and Public Health Significance of Diagnostic and Serology (Antibody) Tests

Many COVID-19 tests are based on reverse transcriptase-polymerase chain reaction, or RT-PCR, technology, which finds genetic material in biological specimens. RT-PCR tests indicate the presence of the virus during infection. There are also serology tests, which are blood-based tests that can be used to identify whether people have been exposed to a particular pathogen by looking at their immune response — that is, the presence of antibodies.

Serology tests do not identify active infection and are not properly used to diagnose COVID-19. They should, however, enable better quantification of COVID-19 cases, including individuals who may be or were asymptomatic or have recovered.

Robust information from appropriately widespread testing should enable authorities to relax requirements for social distancing. According to experts, an estimated 750,000 tests per week nationally would be needed to justify a shift to case-based interventions, provided there is also adequate supportive public health infrastructure such as contact tracing.[2]

Widespread and rapid diagnostic testing at the point of care would also be necessary, along with serological testing and nationwide surveillance, to safeguard against acceleration in case counts and a need to return to population-based physical distancing.[3] Determining population immunity through serological surveys has also been identified as a criterion for lifting remaining restrictions in the final stage of public health response.[4]

Reopening cannot occur in the absence of adequate testing — which has not materialized and appears unlikely to do so despite the nominal availability of a multitude of testing options.[5]

Testing Lapses and Public Health Challenges Related to Testing

Testing was almost completely unavailable in the early stages of the pandemic. The federal government did not seek to engage actively with commercial laboratories and indeed initially warned them against offering diagnostic assays. All testing was to have been conducted only through federally authorized state and local public health laboratories using a RT-PCR specific test developed by the Centers for Disease Control and Prevention.[6]

The deployment of the CDC test, however, was highly problematic,[7] leaving a testing gap that the government struggled to address. The U.S. Food and Drug Administration then invoked a statute providing for the distribution of medical countermeasures in emergency circumstances without requiring developers to follow ordinary regulatory procedures.

Currently "[t]here are no FDA-approved diagnostics for COVID-19."[8] The emergency use authorization pathway allows the FDA, in an emergency, to authorize unapproved medical products to diagnose, treat or prevent serious or life-threatening diseases where there are no adequate, approved and available alternatives.[9]

To grant an EUA, the FDA must find only that a diagnostic test may be effective — a lower standard than in nonemergency circumstances.[10] The FDA invoked its EUA power to expand testing capacity at the end of February.[11] In mid-March, the FDA extended the policy to allow some testing to proceed even without an EUA.[12] As of May 4, the FDA had authorized 56 COVID-19 tests for emergency use, including 47 molecular diagnostic tests and nine serological tests.[13]

Concerns have arisen with respect to the clinical performance of available tests for COVID-19. Test developers are required to validate their assays, and the FDA itself is supposed to be conducting its own evaluations of sensitivity and specificity. Nevertheless, reports have emerged of high false positive and false negative rates.

Indeed, the White House coronavirus response coordinator herself acknowledged that diagnostic testing is not completely reliable.[14] Sample collection problems also reduce the reliability of RT-PCR results, because specimens obtained from individual patients might not include enough viral material for detection.[15]

Poor handling of samples can generate inaccurate results or make testing impossible (e.g., sample degradation during transit).[16] The collection procedure is technically difficult, uncomfortable for patients and risky for health care personnel.[17]

The COVID-19 response effort is further behind in the area of serology tests. Many of these tests have been challenged in the European Union and elsewhere as unreliable, as they can yield a negative test result even in infected patients (e.g., if antibody has not yet developed in response to the virus) or may be falsely positive (e.g., if antibody to a coronavirus type other than the current pandemic novel strain is present).

They are also of limited value because they cannot rule out the presence of the virus. The FDA has issued four EUAs for serology tests, all of which must be performed in moderate complexity CLIA-certified clinical laboratories.[18]

A further threat to testing involves the global supply chain. The first serology test for which FDA granted an EUA is unavailable because its country of manufacture has restricted export to the U.S.[19] In addition, COVID-19 diagnostic testing involves several specific types of consumables.

Specimen collection items such as swabs are used to collect samples from individual

patients, and containers are used to transport them to the laboratory. The swabs used to collect nasopharyngeal samples for diagnostic testing are in critical shortage.[20]

Because the specimens are presumptively infectious, personnel handling them need personal protective equipment. Reagents — the so-called bottles of juice used to perform the test — are required every single time the test is performed. The lack of availability of these critical supplies means that laboratory capacity cannot be fully exploited.

Many Americans may wonder why they cannot access testing at their physician's office or order a kit from an online marketplace and obtain a prompt diagnosis themselves. Test kits are being developed for use at the point of care. But the FDA has not authorized any direct-to-consumer test to be completely used and performed at home for COVID-19.

The kits that have been allowed on the market for use by physicians in qualified health care settings are in short supply. Some point-of-care tests have to be run on a specific machine that may not have been purchased by every medical office or hospital. To date, no serology tests have been authorized for use by the FDA at the point of care or for home use.

Results reporting has also been an issue. Clinical laboratories processing significant numbers of specimens cannot always provide testing results immediately. Even if they are unaffected by supply chain disruptions, the tests are technically challenging to perform. Backlogs have been reported because of a sudden increase in orders that required corresponding adjustments in capacity.[21]

A related factor is the inability of some health care facilities to obtain results from the clinical laboratories that have excess testing capacity due to the inoperability of their electronic health record systems.[22] Delays in results reporting interfere with patient care, result in the unnecessary use of personal protective equipment because of false positive results, and delay access to investigational drugs under protocols requiring a diagnosis of COVID-19. They also deny decision-makers prompt access to information about the impact of the disease.

The Way Forward

The new law seeks to facilitate the development of a program of high-quality diagnostic testing for COVID-19 on a nationwide basis. Testing is one component of a multifaceted approach to bringing the spread of the virus under enough control to allow for the gradual relaxation of physical distancing and a return to more normal economic and social activity. Additional elements of a comprehensive strategy include contact tracing and public health surveillance.

State and local authorities will continue to have significant responsibility for COVID-19 response, including testing, despite the infusion of federal funding for a national testing program. Additional funding and policy development, in addition to scientific and technological advancements and regulatory actions, will likely be necessary in the coming weeks to address supply chain issues and other impediments to a well-functioning testing scheme for all Americans.

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[1] Paycheck Protection Program and Health Care Enhancement Act, Pub. L. No. 116-139 (116th Cong. 2020).

[2] See Scott Gottlieb et al., National Coronavirus Response: A Roadmap to Reopening, American Enterprise Institute (Mar. 28, 2020), https://bit.ly/2VLdfHW.

[3] Id.

[4] Mark McClellan, Scott Gottlieb et al., A National COVID-19 Surveillance System: Achieving Containment, Duke University Margolis Ctr. for Health Pol. (Apr. 7, 2020), https://bit.ly/3btwD2I.

[5] Id.

[6] On Feb. 18, 2020, the CDC warned clinical laboratories against performing any COVID-19 diagnostic testing in their facilities unless they were designated by CDC as a "qualified laboratory" for testing patient respiratory specimens meeting CDC criteria and used the CDC 2019-Novel Coronavirus (COVID-19) Real-Time RT-PCR Diagnostic Panel. CDC, Laboratory Advisory: Reminder: COVID-19 Diagnostic Testing (Feb. 18, 2020), https://bit.ly/2zoeO75.

[7] The Director of the Center for Devices and Radiological Health at the U.S. Food and Drug Administration (FDA) reportedly told the CDC that if it were subjected to the same scrutiny as a private clinical laboratory, "I would shut you down." Yasmeen Abutaleb et al., The U.S. was Beset by Denial and Dysfunction as the Coronavirus Raged, Washington Post (Apr. 4, 2020), https://wapo.st/2XX4PzI; Sheila Kaplan, C.D.C. Labs Were Contaminated, Delaying Coronavirus Testing, Officials Say, N.Y. Times (Apr. 18, 2020), https://nyti.ms/2S0TM4L.

[8] FDA, Coronavirus Disease 2019 (COVID-19) (updated May 2, 2020), https://bit.ly/2RWD9Y1.

[9] 21 U.S.C. § 360bbb-3.

[10] See FDA, Emergency Use Authorization of Medical Products and Related Authorities: Guidance for Industry and Other Stakeholders 7-8 (Jan. 2017) [hereinafter Emergency Use Authorization Guidance].

[11] FDA, Policy for Diagnostic Tests for Coronavirus Disease-2019 during the Public Health Emergency: Immediately in Effect Guidance for Clinical Laboratories, Commercial Manufacturers, and Food and Drug Administration Staff (Feb. 29, 2020).

[12] See FDA, Policy for Diagnostic Tests for Coronavirus Disease-2019 during the Public Health Emergency: Immediately in Effect Guidance for Clinical Laboratories, Commercial Manufacturers, and Food and Drug Administration Staff (updated Mar. 16, 2020), https://bit.ly/3bu0B6G.

[13] FDA, Emergency Use Authorizations (updated May 2, 2020), http://bit.ly/38NUJTt.

[14] Remarks by President Donald Trump, Vice President Mike Pence, and members of the

Coronavirus Task Force in press briefing (Apr. 20, 2020), https://bit.ly/2RWLRWc.

[15] Buddhisha Udugama et al., Diagnosing COVID-19: The Disease and Tools for Detection, ACSNano (Mar. 30, 2020), https://bit.ly/2KnJiYX ("Given the variability in the viral loads, a negative test result from respiratory samples does not rule out the disease").

[16] Elizabeth Pratt, 'False Negatives' in COVID-19 Testing: If You Have Symptoms, Assume You Have the Disease, Healthline (Apr. 13, 2020), https://bit.ly/34UVav7.

[17] Udugama, supra note 14 ("Both BAL and tracheal aspirates can be high risk for aerosol generation").

[18] FDA Emergency Use Authorization to Mt. Sinai Laboratory (Apr. 15, 2020), https://bit.ly/2wYHl2f; FDA Emergency Use Authorization to Chembio Diagnostic Systems, Inc. (Apr. 14, 2020), https://bit.ly/3eGc05c; FDA Emergency Use Authorization to Ortho-Clinical Diagnostics, Inc. (Apr. 14, 2020), https://bit.ly/2Vsx4EQ; FDA Emergency Use Authorization to Cellex Inc. (Apr. 1, 2020), https://bit.ly/3eFgSYv.

[19] See, e.g., Curt Devine et al., COVID-19 Antibody Tests Can Help People Rejoin Society, but Some are Stuck in China, CNN (last updated Apr. 17, 2020), https://cnn.it/3cG5nyf.

[20] Lauren Webber & Christina Jewett, Testing Swabs Run in Short Supply as Makers Try to Speed Up Production, NPR (Mar. 18, 2020), https://n.pr/2RYuMel. FDA recently announced a shift toward anterior nasal sample collection, which involves using a shorter, spun synthetic swab to collect a sample from the front of the nose.

[21] Alexis C. Madrigal & Robinson Meyer, Private Labs Are Fueling a New Coronavirus Testing Crisis, The Atlantic, Mar. 30, 2020.

[22] Amy Maxmen, Thousands of Coronavirus Tests Are Going Unused in US Labs, Nature, Apr. 9, 2020.