

COVID-19 TESTING

Testing Types, Recent Developments, and Policy Considerations

Introduction

Testing for the novel coronavirus disease 2019 (COVID-19) has become a pressing issue as policymakers and public health leaders seek to address the ongoing pandemic in the U.S. Early testing is paramount in the response to an infectious disease outbreak, providing valuable information to help direct appropriate local, state, and federal efforts. Testing allows healthcare workers to identify positive cases and helps public health officials and policymakers determine appropriate measures to control the spread of the virus, including isolating those who are ill, quarantining those who have been exposed, and employing contact tracing to identify others potentially infected. Testing also provides critical information about the effectiveness of mitigation efforts, such as social distancing, and a roadmap to determine how soon individuals may return to school or work or resume other daily activities.

Adequate COVID-19 testing has been an ongoing problem in the U.S., particularly compared to other countries such as Germany and South Korea which have been able to test broader swaths of their populations.¹ Multiple factors have affected our ability to test enough people, including early setbacks after initial test kits developed by the Centers for Disease Control and Prevention (CDC) and distributed to state public health labs were discovered to have faulty components.² Since then, federal authorities have sought to create additional mechanisms to expedite the development of tests, but significant barriers remain.

This explainer provides information on the types of tests used to identify COVID-19, recent testing developments, and policy considerations.



Background

COVID-19 testing can be grouped into two categories: molecular tests (to determine whether an individual is currently infected with COVID-19) and serology tests (to determine whether an individual was previously infected with COVID-19).

MOLECULAR TESTS

A molecular test is a type of test to identify individuals infected with COVID-19. Molecular tests usually involve inserting a swab into an individual's nasal passage to collect a sample. The sample is then sent to a lab for processing, although some lab companies have developed or are in the process of developing point-of-care molecular tests which provide rapid results.³

Molecular tests use a process called reverse transcription polymerase chain reaction, or RT-PCR, to find genetic material from the virus in a submitted sample. A positive test means that the individual is currently infected with the virus. Once the individual recovers from the infection and no longer has the virus in the nose or throat, the test will have a negative result.

This test cannot determine whether the patient has had an infection in the past or whether the patient is immune to reinfection. Current molecular tests are limited by a high rate of false negatives, that is, a negative test result in a patient who is actually infected. Early research from China indicates that the false-negative rate may be around 30%.⁴

SEROLOGICAL TESTS

Unlike molecular tests, serological tests can identify both individuals who are currently infected and individuals who have recovered from the virus.⁵ Serological tests, which require the collection of an individual's blood, determine whether a patient has developed antibodies to COVID-19.⁶

This test looks for two different types of antibodies: immunoglobulin M (IgM) and immunoglobulin G (IgG). With most types of infection, IgM antibodies appear within days to a few weeks after infection, and their presence indicates recent infection. IgG antibodies appear later — weeks to months after infection — and indicate past infection. This test also can sometimes detect whether the patient is immune to reinfection.

Some serological tests measure only the presence or absence of antibodies (qualitative) while other tests measure the amount of each type of antibody present (quantitative). Quantitative tests are generally more accurate in determining whether a patient is likely to be immune to reinfection with COVID-19.

Test Availability

U.S. FOOD AND DRUG ADMINISTRATION ACTIONS

On March 16, 2020, the U.S. Food and Drug Administration (FDA) issued updated guidelines (the original guidelines were released Feb. 29, 2020) intended to help rapidly expand testing capacity by facilitating the development and use of diagnostic tests during the public health emergency. The policy allows states to approve development and use of tests that have not been submitted to or approved by the FDA, if states are willing to assume liability. The guidance also permits commercial test developers to sell products without an emergency use authorization (EUA) from the FDA.

The guidance also addresses the development of serological tests. Until very recently, the only available tests for COVID-19 have been molecular tests. Under newer guidelines, the FDA will also allow developers of some serological tests to market their tests after performing necessary evaluations to determine their accuracy and reliability, and will waive prior FDA review if certain conditions are met.⁷ While over 250 test developers have alerted the FDA of serological tests available for use, some have falsely claimed these tests are FDA approved or authorized, or that the tests can be used to diagnose COVID-19. In early May 2020, the FDA issued updated guidance requiring test manufactures to meet minimum quality standards, along with submitting requests for EUAs for tests they have developed.⁸ Near the end of May, the FDA removed approximately 30 serological tests that should no longer be distributed for COVID-19, with possible reasons for removal including failure to submit a timely EUA or identification of significant problems with tests that could not be addressed in a timely manner.⁹

As of this explainer's June 4, 2020, publication date, 15 serological tests have received EUAs from the FDA. On April 4, the FDA granted an EUA for the first rapid antibody test for COVID-19, developed by a company called Cellex.¹⁰ On April 15, the FDA issued two additional EUAs for serological tests developed by ChemBio Diagnostic Systems and Ortho-Clinical Diagnostics. On April 16, an EUA was issued for a serological test developed by Mount Sinai Laboratory.¹¹

On April 24, three additional EUAs were issued for tests developed by Autobio Diagnostics Co. Ltd., DiaSorin Inc., and an additional serological assay developed by Ortho-Clinical Diagnostics. On April 26, an EUA was issued for a serological test developed by Abbott Laboratories Inc. On April 29, an additional EUA was issued for a serological test developed by Bio-Rad.¹² On April 30, Wadsworth Center & the New York State Department of Health received an EUA for a serological test. Since the beginning of May, five additional EUAs have been issued for serological tests, including tests developed by Roche Diagnostics, EUROIMMUN US Inc., Siemens Healthcare Diagnostics Inc., and Healgen Scientific LLC.¹³

On May 9, the first EUA was issued for an antigen test developed by Quidel Corporation.¹⁴ As opposed to molecular tests that use the RT-PCR process (discussed above) to look for the virus' genetic material in a sample, antigen tests detect molecules on the surface of the virus. Antigen tests are able to yield results more quickly than the molecular RT-PCR tests, much like rapid-result influenza tests. Although antigen tests are typically accurate in determining positive infections, these tests have a higher false negative rate than molecular RT-PCR tests.

TESTING IN ARKANSAS

To date, all of the COVID-19 tests being performed in Arkansas are molecular tests. The Arkansas Department of Health's (ADH) public health lab is able to process a limited number of tests, with the majority of tests being processed by commercial labs. On April 16, 2020, ADH issued a directive regarding the use of nucleic acid amplification tests (NAATs) for diagnosis of COVID-19 in physician offices, urgent care settings, and pharmacies. NAATs are molecular tests used to identify the virus in a clinical sample from a patient. The directive requires that all point-of-care NAATs used outside of Clinical Laboratory Improvement Amendments (CLIA)-approved labs have written approval from the Arkansas secretary of health and that all results from NAATs be reported electronically to ADH as soon as they are available.¹⁵ CLIA are federal regulatory standards that apply to all U.S. facilities or labs testing human specimens to diagnose, prevent, or treat disease.

Previously, on April 15, 2020, ADH issued a directive regarding the use of non-FDA-approved serological tests for COVID-19 diagnosis. Per the directive, ADH prohibits the use of serological tests that are not FDA-approved through the FDA's EUA mechanism or those that have not been approved by the Arkansas secretary of health. The directive also prohibits the use of these tests outside of CLIA labs.¹⁶

Initially, ADH's public health lab limited tests to Arkansans with possible high-risk exposure to COVID-19.¹⁷ On April 15, 2020, state Secretary of Health Dr. Nate Smith announced that because of expanded testing capability in commercial labs, the state would relax testing criteria for providers to include individuals with COVID-19 symptoms if a provider has adequate testing supplies.¹⁸ ADH recommends that Arkansans who believe they have been exposed to COVID-19 and develop a fever, cough, or shortness of breath contact their healthcare provider regarding testing. Healthcare providers may access testing through commercial labs, such as LabCorp or Quest.¹⁹

Conclusion

Testing for the COVID-19 virus got off to a slow start and is inadequate to determine how many Arkansans are infected with the virus. Until very recently, only molecular tests have been available. These tests cannot determine whether a person has been infected in the past or whether they are immune to reinfection. The FDA has approved 12 antibody tests under EUAs, and several others are in the pipeline. Antibody tests can determine past infections, and in some cases, immunity. Commercial labs have been providing more tests in recent weeks. Testing is expected to be more available over the coming weeks, and the recent announcement by ADH of expanded testing criteria is an important development. However, it is critical for policymakers and public health officials to continue pushing for additional resources for the state to reach adequate testing capacity.

¹ Bennhold, K. (2020). A German Exception? Why the Country's Coronavirus Death Rate is Low. The New York Times. Retrieved from <https://www.nytimes.com/2020/04/04/world/europe/germany-coronavirus-death-rate.html>.

² Pradhan, R. (2020). "CDC Coronavirus Testing Decision Likely to Haunt Nation for Months to Come." Kaiser Health News. Retrieved from <https://khn.org/news/cdc-coronavirus-testing-decision-likely-to-haunt-nation-for-months-to-come/>.

³ Billingsley, A. (2020). "The Latest in Coronavirus (COVID-19) Testing Methods and Availability." GoodRx. Retrieved from <https://www.goodrx.com/blog/coronavirus-covid-19-testing-updates-methods-cost-availability/>.

⁴ Yang Y, Yang M, Shen C, et al. (2020). Evaluating the Accuracy of Different Respiratory Specimens in the Laboratory Diagnosis and Monitoring of the Viral Shedding of 2019-nCoV Infections. medRxiv 2020.02.11.20021493; doi: <https://doi.org/10.1101/2020.02.11.20021493>.

⁵ U.S. Food & Drug Administration. (2020). FDA Statement: Coronavirus (COVID-19) Update: Serological Tests. Retrieved from <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-serological-tests>.

⁶ Billingsley, A., "The Latest in Coronavirus (COVID-19) Testing Methods and Availability."

⁷ U.S. Food & Drug Administration, Coronavirus (COVID-19) Update: Serological Tests.

⁸ U.S. Food & Drug Administration. (2020). Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency (Revised). Retrieved from <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-coronavirus-disease-2019-tests-during-public-health-emergency-revised>.

⁹ U.S. Food and Drug Administration. (2020). FAQs on Testing for SARS-CoV-2: What Tests Should No Longer Be Distributed for COVID-19? Retrieved from <https://www.fda.gov/medical-devices/emergency-situations-medical-devices/faqs-testing-sars-cov-2#nolonger>.

¹⁰ Otto, A. (2020). FDA Grants Emergency Authorization for First Rapid Antibody Test for COVID-19. The Hospitalist. Retrieved from <https://www.the-hospitalist.org/hospitalist/article/220225/coronavirus-updates/fda-grants-emergency-authorization-first-rapid>.

¹¹ U.S. Food and Drug Administration, (2020). Coronavirus (COVID-19) Update: Daily Roundup April 15, 2020. Retrieved from <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-daily-roundup-april-15-2020>.

¹² Center for Health Security. (2020). Serology-based tests for COVID-19. Johns Hopkins Bloomberg School of Public Health. Retrieved from <https://www.centerforhealthsecurity.org/resources/COVID-19/serology/Serology-based-tests-for-COVID-19.html>.

¹³ U.S. Food and Drug Administration. (2020). Emergency Use Authorizations. Retrieved from <https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations#coronavirus2019>.

¹⁴ U.S. Food and Drug Administration. (2020). Emergency Use Authorization, Quidel Corporation. Retrieved from <https://www.fda.gov/media/137886/download>.

¹⁵ Arkansas Department of Health. (2020). Directive Regarding the Use of Nucleic Acid Amplification Test for the Diagnosis of SARS-CoV-2 Infections in Physician Offices, Urgent Care Settings and Pharmacies. Retrieved from <https://www.healthy.arkansas.gov/images/uploads/pdf/NAAT-POCAssayUseDirectiveFinal4.16.20.pdf>.

¹⁶ Arkansas Department of Health. (2020). Directive Regarding Prohibition of the Use of Non-FDA Approved Serologic Tests for the Diagnosis of SARS-CoV-2 Infections. Retrieved from <https://www.healthy.arkansas.gov/images/uploads/pdf/Directive-ProhibitionNonFDASerologic4.15.20.pdf>.

¹⁷ Arkansas Department of Health. COVID-19 Guidance for Getting Tested. Accessed on April 13, 2020. Retrieved from <https://www.healthy.arkansas.gov/programs-services/topics/covid-19-guidance-for-getting-tested>.

¹⁸ Davis, A. (2020). State lines up health-worker bonuses. Arkansas Democrat Gazette. Retrieved from <https://www.arkansasonline.com/news/2020/apr/16/state-lines-up-health-worker-bonuses-20/>.

¹⁹ Arkansas Department of Health. COVID-19 Guidance for Healthcare Providers. Accessed April 13, 2020. Retrieved from <https://www.healthy.arkansas.gov/programs-services/topics/covid-19-guidance-for-healthcare-providers#labinfo>.