

Considerations for Implementation of SARS-CoV-2 Rapid Antigen Testing

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APHL recognizes the unique testing situation the US faces regarding the COVID-19 pandemic. This paper describes SARS-CoV-2 antigen tests including their benefits, limitations, use cases and outstanding data needs required to better inform their implementation. Currently available SARS-CoV-2 antigen tests have received FDA emergency use authorization for use only on individuals experiencing symptoms of COVID-19. On August 31, 2020, HHS announced PREP act coverage for COVID-19 screening tests at nursing homes, assisted living facilities, long-term-care facilities, and other congregate settings opening a regulatory pathway for the use of rapid antigen tests in asymptomatic people. Further, it was announced that rapid antigen tests would be deployed to states in large numbers for screening of various populations providing greatly expanded testing capacity. This paper also calls for additional evaluation of these tests to provide clinicians and public health professionals with additional evidence that will inform appropriate test interpretation.

Summary

Rapid antigen tests directly detect the presence or absence of an antigen. These tests are relatively inexpensive, offer a short turnaround time and are commonly used to diagnose patients in point-of-care settings such as doctors' offices. Currently available antigen tests for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have reported significantly lower sensitivity than most nucleic acid (i.e., molecular) tests but have reported high specificity. Please note, these comments refer to the ability to **detect viral infection** in a patient, which does not necessarily correlate with the **infectious or contagious** state (i.e., the ability to transmit virus) of the person being tested. At this time, there are limited data available on the correlation between SARS-CoV-2 antigen test positivity and the likelihood of them to be infectious (i.e., capable of transmitting infection to others).

There are also limited data available on the performance of antigen tests when used to test asymptomatic patients as well as their use in non-laboratory settings. However, HHS is in the process of deploying antigen tests to use in screening of residents and staff of long-term care facilities and other high priority asymptomatic populations.ⁱ

Rapid antigen tests are commonly used in the diagnosis of other respiratory pathogens including influenza virus and respiratory syncytial virus (RSV). Rapid antigen tests for some of these pathogens have proven challenging to interpret, notably influenza, where they have commonly produced false negative results due to their low sensitivity, as well as false positive results when disease prevalence is low. CDC therefore recommends the use of rapid antigen tests for influenza only during influenza season when the infection prevalence is high and primarily to inform treatment decisions (i.e., prescription of antivirals), aid in ongoing outbreak investigations, or to direct infection control actions.ⁱⁱ Based on experience with rapid influenza diagnostic tests (RIDTs) and currently available data, the following considerations are offered to assist public health officials and other healthcare providers in making decisions on the appropriate use of rapid antigen tests for SARS-CoV-2.

Overview of SARS-CoV-2 Rapid Antigen Tests

- Antigen tests are typically performed on nasopharyngeal, nasal or oral swab specimens directly or after the swabs have been added to viral transport media. Refer to **Table 1** for a list of authorized specimen types for currently available SARS-CoV-2 tests.
- Antigen tests target specific proteins of the virus of interest to indicate viral infection. Currently FDA authorized SARS-CoV-2 antigen tests target the SARS-CoV-2 nucleocapsid protein.

- Antigen tests produce rapid qualitative results for the detection of SARS-CoV-2. They do not provide a quantitative result.
- In populations experiencing high SARS-CoV-2 positivity rates, positive test results indicate detection of SARS-CoV-2 antigens and that individuals are infected and **presumed** to be infectious, though data supporting this correlation is lacking.
- Currently available SARS-CoV-2 antigen tests are less sensitive than molecular tests. False negative results can occur regardless of the overall prevalence of disease. If a false negative test is suspected, the individual should be tested with a more sensitive molecular test.
- Despite reported high specificity, **false positive results are possible** and are most likely to occur in populations where the prevalence of SARS-CoV-2 infection is low. If a false positive test is suspected, the individual should be retested with a molecular test.
- Currently available SARS-CoV-2 antigen tests have received FDA authorization for use on symptomatic patients only. Clinicians may order these tests to be used “off-label” on asymptomatic individuals. Tests used this way are considered to be “screening” tests and not diagnostic in nature.ⁱⁱⁱ

Scenarios Where SARS-CoV-2 Antigen Tests May Be Considered for Use

Due to the rapid time to result of antigen tests, SARS-CoV-2 antigen tests have utility in symptomatic patient populations with high pre-test probability that the patient has COVID-19 (i.e., symptomatic patients in high prevalence populations). Use of these tests should be reserved for instances where a positive result would direct immediate clinical decisions or infection control measures. Negative results may need to be confirmed in certain situations with a laboratory-based molecular test and downstream costs of that confirmatory testing should be considered when making implementation decisions. Below are some example scenarios in which SARS-CoV-2 antigen tests may reasonably be used.

- Deployed with strike teams to provide targeted testing in emergency or current outbreak situations.
- Triage of individuals with respiratory symptoms in an Emergency Department or similar setting.
- In correctional facilities, long-term care facilities or other high risk, congregate settings where recent cases have been confirmed.
- Off-hour testing in hospital settings when the patient will benefit from a rapid result and the laboratory will repeat the test by another method when staff are available.
- Symptomatic individuals in remote populations such as small rural hospitals, tribal nations or other jurisdictions with known high prevalence and limited alternative access to testing.

Scenarios Where the Utility of SARS-CoV-2 Antigen Tests Has Not Been Evaluated

Antigen tests are best suited for use in situations where a positive result indicates immediate, specific clinical action. In the following situations, the risk of both false positive and false negative results is high. Use of SARS-CoV-2 antigen tests in asymptomatic populations such as those described has not been evaluated. Additional data on performance of antigen tests in these scenarios are needed to better inform clinical management, infection control, follow-up testing and public health mitigation decisions.

- Screening of asymptomatic individuals, even when access to laboratory-based testing is not readily available.
- Screening of residents and staff of congregate settings or schools when there is no known outbreak or exposure.
Note: Asymptomatic individuals with a positive antigen test should not be moved to a COVID-19 ward or placed in a cohort with other COVID-19 positive individuals without PCR confirmation.
- Screening of healthcare workers, emergency responders and other essential personnel.
- Population-based surveillance studies.

Outstanding Data Needs

There has been growing dialogue around the use of antigen tests to screen asymptomatic individuals for SARS-CoV-2. HHS has deployed antigen tests to long-term care facilities and other congregate settings for routine screening of residents and staff members many of whom are likely to be asymptomatic. CDC has recommended the use of antigen tests in long-term care facilities and similar congregate settings^{iv} and issued guidance for their use in nursing homes.^v Although there is a potential advantage of quickly identifying individuals infected with SARS-CoV-2 to direct infection control actions, additional performance data are needed prior to large-scale role out of antigen tests as a screening tool. APHL has identified the following data needs:

- Independent evaluations of antigen tests in symptomatic and asymptomatic individuals to fully characterize their performance and inform proper interpretation of results in both populations.
- Studies to determine performance of antigen tests when done outside of the laboratory setting.
- Guidance on proper processes for recognizing, investigating and resolving potential false positives and false negative results.

Considerations for Public Health Laboratories When Deploying SARS-CoV-2 Rapid Antigen Tests in CLIA-Waived Settings

When public health laboratories are asked to deploy instruments and tests to non-laboratory settings in support of the COVID-19 response, they should consider providing assistance to support or ensure that the following are in place when feasible:

- A public health reporting mechanism when testing is not connected to a laboratory information system, preferably electronic reporting.
- A pathway for any follow up testing that may be required.
- Adequate training of staff that will be performing testing.
- Appropriate biosafety risk assessments and adequate biosafety procedures.
- Quality assurance processes including quality control schedules and proficiency testing, as applicable.

Table 1: Currently Available SARS-Cov-2 Antigen Tests

Test Name	Separate Instrument Required	Authorized for Use in Waived Settings	Specimen Types	Time to Result	Test Performance*	Learn More
Quidel Sofia 2 SARS Antigen FIA	Yes Sofia 2 FIA Analyzer	Yes	NP or Nasal Swabs Directly; Specimens should be collected within 5 days of symptom onset VTM is not recommended	15-30 minutes	Positive Percent Agreement: 96.7% (CI 83.3-99.4%) Negative Percent Agreement: 100% (CI 97.9%-100%)	IFU HCP
BD Veritor System for Rapid Detection of SARS-CoV-2	Yes BD Veritor Plus Analyzer	Yes	Nasal Swabs (supplied with kit) Directly Only	15 minutes	Positive Percent Agreement: 85% (CI 67%-93%) Negative Percent Agreement: 100% (CI 98%-100%)	IFU HCP
LumiraDx SARS-Cov-2 Ag Test	Yes LumiraDX Instrument	Yes	Nasal Swab; Should be collected within the first 12 days of symptom onset	12 minutes	Positive Percent Agreement: 97.6% (CI 91.6-99.3%) Negative Percent Agreement: 96.6% (CI 92.7%-98.4%)	IFU HCP
Abbott BinaxNOW COVID-19 Ag CARD	No	Yes	Direct nasal swab; collected within 7 days of symptom onset	15 minutes	Positive Percent Agreement: 97.1% (95% CI: 85.1%-99.9%) Negative Percent Agreement: 98.5% (95% CI: 92.0%-100%)	IFU HCP

* Test performance data taken from assay's IFU

i <https://www.cms.gov/files/document/covid-faqs-snf-testing.pdf>

ii https://www.cdc.gov/flu/professionals/diagnosis/clinician_guidance_ridt.htm

iii <https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/faqs-testing-sars-cov-2>

iv <https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antigen-tests-guidelines.html>

v <https://www.cdc.gov/coronavirus/2019-ncov/hcp/nursing-homes-antigen-testing.html>