

## UPDATE: Point of Care Antigen Test Use and Interpretation

<b>DATE:</b>	10/15/21
<b>TO:</b>	Health Alert Network
<b>FROM:</b>	Alison Beam, JD, Acting Secretary of Health
<b>SUBJECT:</b>	<b>UPDATE: Point of Care Antigen Test Use and Interpretation</b>
<b>DISTRIBUTION:</b>	Statewide
<b>LOCATION:</b>	n/a
<b>STREET ADDRESS:</b>	n/a
<b>COUNTY:</b>	n/a
<b>MUNICIPALITY:</b>	n/a
<b>ZIP CODE:</b>	n/a

**This transmission is a “Health Update” provides important information for a specific incident or situation; may not require immediate action.**

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This Health Update provides recommendations and considerations for point-of-care (POC) antigen testing and replaces the guidance provided in PA-HAN-548.

- Point of care (POC) antigen tests used to detect SARS-CoV-2 are widely available.
- The main advantage of using these antigen tests is the rapid turnaround time for results; however, these tests are not as sensitive as molecular tests [i.e., reverse transcription polymerase chain reaction (RT-PCR) and other nucleic acid amplification tests (NAATs)].
- In order to ensure accurate results, facilities conducting POC tests should become familiar with good laboratory practices. Some laboratory best practices and suggestions for preventing errors when using these tests are included in this message.
- Individuals using POC tests should understand antigen test performance characteristics in order to recognize potentially false negative or false positive results and to guide patient management.
- Assessment of the person being tested, which would include the likelihood they have the disease, were exposed to COVID-19, or received vaccine, should be considered when interpreting antigen test results and assessing the potential need for additional testing.
- The following message is being disseminated to address questions associated with antigen tests and assist with the use and interpretation of POC antigen test results.
- While some information contained in this HAN may be useful for long term care facilities, separate guidance for using antigen tests and the associated public health response in these facilities has been previously disseminated. Long term care facilities using antigen tests should refer to guidance disseminated in [HAN-547](#).
- If you have questions about this guidance, please call your local health department or **1-877-PA-HEALTH (1-877-724-3258)**.

Point of care (POC) antigen tests used to detect SARS-CoV-2 are widely available. The main advantage of using these antigen tests is the rapid turnaround time for results; however, these tests are not as sensitive as molecular tests.

This guidance is designed to describe what an antigen test is and how it differs from molecular testing, some best practices for sites conducting these tests, when POC antigen testing should be considered, when confirmatory testing may be needed, and circumstances that should be considered when interpreting antigen test results.

## **DESCRIPTION OF ANTIGEN TESTS**

Molecular tests look for pieces of nucleic acid from SARS-CoV-2, the virus that causes COVID-19, in the nose, throat, or other areas in the respiratory tract. Antigen tests look for pieces of proteins that are part of the SARS-CoV-2 virus. While both tests can be used to determine if a person has an active infection, antigen tests are less sensitive than molecular tests for detecting COVID-19 infections. The results of these antigen tests are impacted by pretest probability (i.e., the probability of a person having an infection before the test result is known) and need to be carefully interpreted.

Information on available antigen tests can be found at the following websites:

- <https://www.health.pa.gov/topics/disease/coronavirus/Pages/Guidance/Point-of-Care-Testing.aspx>
- <https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antigen-tests-guidelines.html>
- <https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas#individual-antigen>

## **Performance of Antigen Tests for SARS-CoV-2**

It is important for healthcare providers and testing personnel to understand the performance characteristics, including sensitivity, specificity, and positive and negative predictive values, of the particular antigen test being used, and to follow the manufacturer's instructions for use, which summarize performance characteristics.

The “gold standard” for clinical diagnostic detection of SARS-CoV-2 remains laboratory-based ([moderate- and high-complexity](#)) molecular tests. Thus, it may be necessary to confirm an antigen test result with a laboratory-based molecular test, especially if the result of the antigen test is inconsistent with the clinical context. Based on their instructions for use, some point-of-care molecular tests may not be used for confirmatory testing. Molecular tests that generate presumptive results are not appropriate for use in confirmatory testing.

The sensitivity of antigen tests varies but is generally lower than most laboratory-based molecular tests. The antigen level in specimens collected either before symptom onset, or late in the course of infection, may be below the tests' limit of detection. This may result in a negative antigen test result, while a more sensitive test, such as most molecular tests, may return a positive result. [Studies](#) have shown that antigen tests have comparable sensitivity to laboratory-based molecular tests when the viral load in the specimen is high and the person is likely to be most contagious.

The specificity of antigen tests is generally as high as most molecular tests, which means that false positive test results are unlikely when an antigen test is used according to the manufacturer's instructions. Despite the high specificity of antigen tests, false positive results will occur, especially when used in communities where the prevalence of infection is low – a circumstance that is true for all in vitro diagnostic (e.g., molecular and antigen) tests. In general, for all diagnostic tests, the lower the prevalence of infection in the community, the higher the proportion of false positive test results.

Positive and negative predictive values of all in vitro diagnostic tests (e.g., molecular and antigen tests) vary depending upon the pretest probability. Pretest probability considers both the prevalence of the target infection in the population that is being tested as well as the clinical context of the individual being tested.

- If the prevalence of infection in the [community](#) is high, and the person being tested is symptomatic, then the pretest probability is generally considered high.
- If the prevalence of infection in the [community](#) is low, and the person being tested is asymptomatic and has not had any known contact with a person with COVID-19, then the pretest probability is generally considered low.

While community transmission can impact testing performance, this should not be used as the sole basis for test interpretation. A consideration of the likelihood of infection which could include assessing if symptoms are compatible with a COVID-19 infection, determining if the individual had a known exposure to a COVID-19 case, or understanding if an alternative diagnosis is a more likely explanation for current symptoms should also be considered when interpreting test results.

## **CONSIDERATION FOR USE OF ANTIGEN TESTS**

### Clinical Laboratory Improvement Amendments (CLIA) Certificate

Any entity utilizing Point-of-Care (POC) tests for COVID-19 must have a Pennsylvania laboratory permit and a CLIA Certificate. If you already have a Pennsylvania laboratory permit and CLIA Certificate, you must notify the Department of your intent to implement COVID-19 antigen testing to ensure that this test is added to the list of tests that you are approved to perform before beginning to perform the testing.

Please see [Understanding Clinical Laboratory Regulation in Pennsylvania](#) for more information. If you have questions about laboratory permits or CLIA certification, please notify [RA-DHPACLIA@pa.gov](mailto:RA-DHPACLIA@pa.gov) to assure laboratory compliance.

### Reporting

All entities conducting testing to identify SARS-CoV-2, the virus that causes COVID-19, are required to report positive, inconclusive/indeterminate, and negative results to PA-NEDSS within 24 hours of test completion. There are a number of mechanisms that have been established to ensure reporters can be compliant in providing the results of POC tests. Details on how to report to PA-NEDSS can be found in [PA-HAN-534](#).

### Laboratory Best Practices and Preventing Errors

All testing for SARS-CoV-2, including rapid antigen testing, is directly impacted by the integrity of the specimen, which depends on specimen collection and handling. To reduce the potential for inaccurate results related to testing errors, implement the following:

- Ensure that users are properly trained to complete POC testing.
  - Maintain training records and ensure procedural compliance through routine auditing.
  - CDC provides materials on [good laboratory practice](#) and offers an online training with professional continuing education credits for their [Ready, Set, Test](#) training program.
- Follow manufacturer's instructions for specimen collection, processing, storage, and handling of the specimen. Not following the manufacturer's instructions can cause some swabs to have limited amounts of viral genetic or antigenic material for detection, leading to false negative results.
  - Antigen test manufacturers offer different training modalities for sites to familiarize themselves with the appropriate use of these products. Sites are encouraged to utilize these training opportunities and carefully review these materials prior to antigen test use.
- Wear appropriate PPE when collecting and handling specimens per [PA-HAN-524](#). It is critical that gloves are changed and hand hygiene is performed between each specimen collection and handling. Handling specimens without changing gloves or performing hand hygiene in between creates the potential for cross-contamination.
- Minimize delays between specimen collection and processing. Delays can affect the accuracy of the result.
- Conduct calibration of the machine, if applicable, and ensure positive and negative control procedures are performed as per the manufacturer's instructions. Carefully handle positive control solutions. Once control procedures are complete, clean and disinfect hands, work surfaces, and the instrument (if applicable) to assure the positive control does not contaminate clinical specimens.
- For batch testing methods, carefully plan a systematic approach to specimen receipt, labeling, rotation into the instrument (if applicable), removal, and recording the results. For each step of the process, the plan should address ways to minimize contamination and errors in results reporting, such as mixing up specimens from two individuals.

### **Testing Considerations and Antigen Test Interpretation**

This guidance is geared towards the interpretation of antigen testing within the community setting. While some information contained in this HAN may be useful for long term care facilities, separate guidance for using antigen tests and the associated public health response in these facilities has been previously disseminated. Long term care facilities using antigen tests should refer to guidance disseminated in [HAN-547](#).

Figures 1a and 1b has been developed to assist with antigen interpretation. Careful review of the language in this document along with footnotes that accompany the figures are recommended.

#### **Testing a symptomatic person in a community setting**

In a community setting, when testing a person who has symptoms compatible with COVID-19, the healthcare provider generally can interpret a positive antigen test to indicate that the person is infected with SARS-CoV-2; this person should follow guidance for isolation located in [HAN 535](#).

A positive antigen test result for a symptomatic person *may* need confirmatory testing if the person has a low likelihood of SARS-CoV-2 infection. For example, a low likelihood of SARS-CoV-2 infection would be a person who has had no known exposure to a person with COVID-19 within the last 14 days or is fully vaccinated or has had a SARS-CoV-2 infection in the last 3 months.

A negative antigen test result for a symptomatic person *should be* confirmed with a laboratory-based molecular test. In this case, an alternative to confirmatory molecular testing is serial antigen testing that is performed every 3–7 days for 14 days.

A negative antigen result for a symptomatic person *may not* need confirmatory testing if the person has a low likelihood of SARS-CoV-2 infection (see low likelihood example provided above).

A symptomatic person who has received a negative antigen test result and then a positive confirmatory molecular test should follow guidance for isolation located in [HAN 535](#).

A symptomatic person who has received a negative antigen test result and then a negative confirmatory molecular test should follow guidance for quarantine in [HAN 583](#) if they have had close contact or suspected exposure to a person with COVID-19 within the last 14 days. If that same person has not had any known exposure to COVID-19, then they do not need to quarantine.

### Testing an asymptomatic person in a community setting

Asymptomatic people who are fully vaccinated do not need to pursue testing in many cases. When testing an asymptomatic person in a community setting for COVID-19, the healthcare provider generally can interpret a positive antigen test to indicate that the person is infected with SARS-CoV-2; this person should follow guidance for isolation located in [HAN 535](#).

A positive antigen test result from an asymptomatic person *may* need confirmatory testing if the person has a low likelihood of SARS-CoV-2 infection. For example, a low likelihood of SARS-CoV-2 infection would be a person who has had no known exposure to a person with COVID-19 within the last 14 days or is fully vaccinated or has had a SARS-CoV-2 infection in the last 3 months.

When testing an asymptomatic person for COVID-19, the healthcare provider generally can interpret a negative antigen result to indicate that a SARS-CoV-2 infection is not present. However, a negative antigen test result *may* need confirmatory testing if that asymptomatic person has a high likelihood of SARS-CoV-2 infection. For example, a high likelihood of SARS-CoV-2 infection would be a person who has had close contact or suspected exposure to COVID-19 within the last 14 days and the person is not fully vaccinated and has not had a SARS-CoV-2 infection in the last 3 months.

An asymptomatic person who has received a negative antigen test result should follow guidance for quarantine in [HAN 583](#) if they have had close contact or suspected exposure to a person with

COVID-19 within the last 14 days; fully vaccinated people and those who have had a SARS-CoV-2 infection in the last 3 months do not need to quarantine. Those who are not fully vaccinated and have not had COVID-19 in the last 3 months should consider serial antigen testing if they have had contact with a person who has COVID-19 within the last 14 days. Serial antigen testing should be performed every 3–7 days for 14 days.

### Confirmatory Testing When Using Antigen Tests for SARS-CoV-2

As the antigen testing algorithms indicate, confirmatory testing may be needed regardless of the symptom or exposure status of the person being tested. Confirmatory testing should take place as soon as possible after the antigen test, and not longer than 48 hours after the initial antigen testing. If more than 48 hours separate the two specimen collections, or if there have been opportunities for new exposures, a laboratory-based molecular test should be considered a separate test – not a confirmation of the earlier test. If the results are discordant between the antigen test and the confirmatory molecular test, in general the confirmatory test result should be interpreted as definitive for the purpose of clinical diagnosis.

CDC recommends laboratory-based molecular tests for confirmatory testing. CDC does not recommend molecular tests that use oral specimens (e.g., saliva) for confirmatory testing and instead suggests the use of specimens that are considered optimal for detection, such as nasopharyngeal, nasal mid-turbinate, and anterior nasal swabs. Additional information is available in CDC's guidance for [Nucleic Acid Amplification Tests \(NAATs\)](#).

Several studies have documented persistent or intermittent detection of virus using RT-PCR after recovery; in these cases, the people did not seem to be infectious to others. Thus, if the person being tested has recently had COVID-19 and completed their period of isolation, it is possible for that person to receive a negative antigen test result and a positive confirmatory molecular test, potentially indicating a persistent detection of SARS-CoV-2 after recovery from COVID-19. For this reason, repeat testing after the initial diagnostic test is not recommended during the period of isolation or as a test of cure.

If confirmatory testing is not available, clinical discretion can determine whether to recommend that the patient isolate or quarantine.

### Serial Testing When Using Antigen Tests

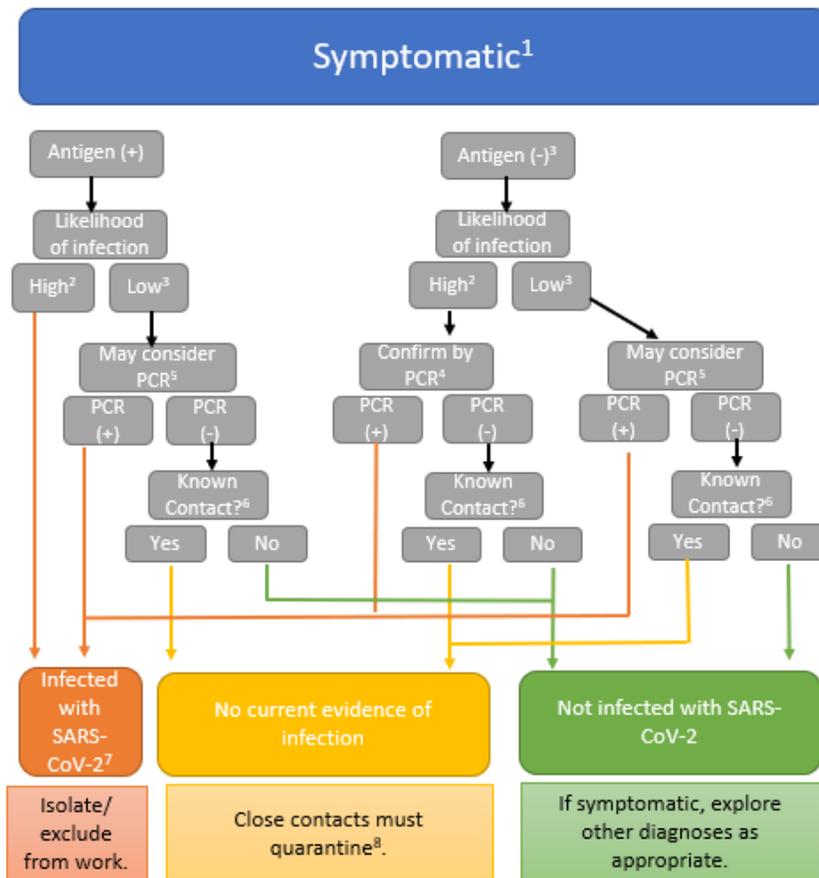
Depending on the circumstances and setting, it may be useful to implement serial antigen testing for persons who receive a negative antigen test result. Serial antigen testing within a congregate living setting, such as a long-term care facility or a correctional or detention facility, could quickly identify someone with a SARS-CoV-2 infection and prevent further transmission. It may not be necessary to perform confirmatory testing with a molecular test when conducting serial antigen testing on those who have received a negative antigen test result.

[Modeling evidence](#) shows that outbreak control depends largely on the frequency of testing, the speed of reporting, and the application of interventions, and is only marginally improved by the sensitivity of the test. [Additional evidence](#) shows that serial antigen testing every 3 days, or twice per week, will almost always identify SARS-CoV-2 during early stages of infection, and thus significantly reduce disease transmission. Thus, if resources allow, serial antigen testing is a potentially important public health practice along with other prevention strategies.

## FIGURE 1A AND 1B- CONSIDERATIONS FOR ANTIGEN TEST RESULTS INTERPRETATION

The following figures were developed to assist partners with the interpretation of antigen tests. The figures considers additional laboratory results which may be available or the need to request additional laboratory testing. While this information can be used as a guide, there may be additional circumstances (e.g., confidence in laboratory testing procedures, assessment of clinical picture, specimen collection practices, burden of COVID-19 in the surrounding community, etc.) that may alter the interpretation from the below table. Separate guidance ([HAN-547](#)) regarding the use of antigen testing in long-term care facilities is available and should be used to guide actions in those settings. This table is subject to change as additional information about antigen testing is learned.

**Figure 1A – Symptomatic**



1: Symptomatic people with COVID-19 have had a wide range of symptoms reported – ranging from mild symptoms to severe illness. Symptoms may appear 2-14 days after exposure to the virus. Anyone can have mild to severe symptoms. Additional guidance is located in [PA-HAN 535](#) and from the [CDC](#).

2: A high likelihood of SARS-CoV-2 infection would be a person who has had close contact or suspected exposure to COVID-19 within the last 14 days and the person is not fully vaccinated **and** has not had a SARS-CoV-2 infection in the last 3 months.

3: A low likelihood of SARS-CoV-2 infection would be a person who has had no known exposure to a person with COVID-19 within the last 14 days or is fully vaccinated or has had a SARS-CoV-2 infection in the last 3 months.

4: An antigen test should be confirmed by a PCR. This is important when the index of suspicion for disease does not match the antigen test result (e.g., a person with COVID compatible symptoms that tests negative on an antigen). The time of the confirmatory PCR should also be considered - see HAN section [Confirmatory Testing When Using Antigen Tests for SARS-CoV-2](#). In certain circumstances, serial antigen testing can be used when PCR is not available ([additional detail in the HAN](#)). If PCR testing or serial testing is not performed, clinical judgement should be used when determining the appropriate public health action.

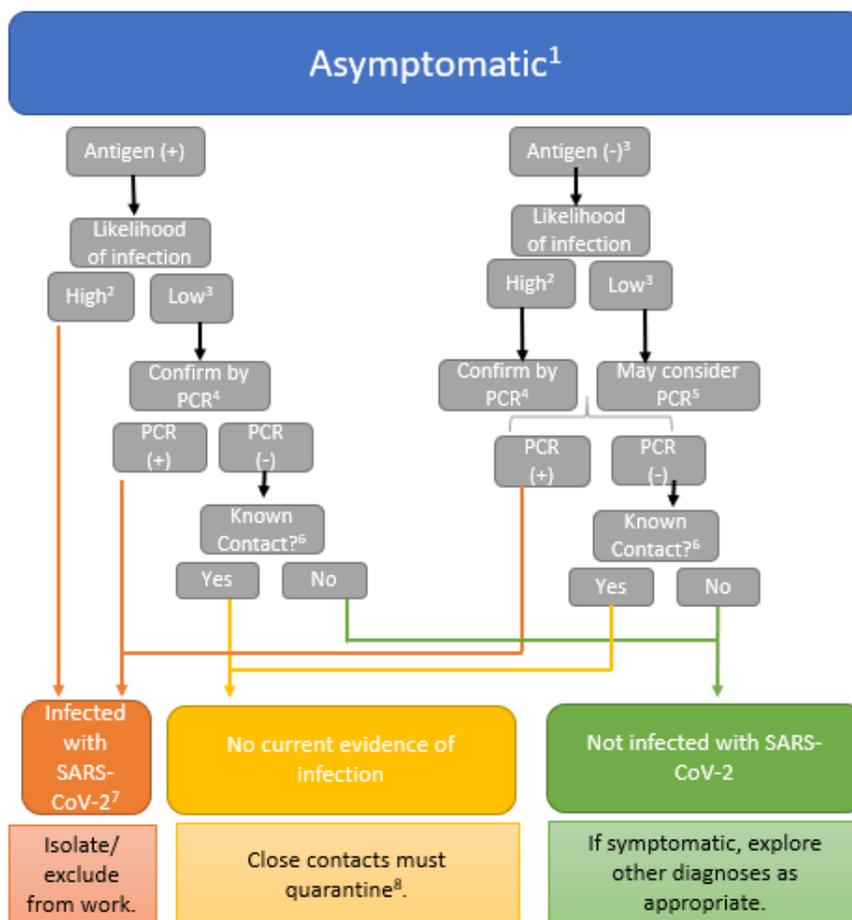
5: An antigen test may need to be confirmed by PCR when the likelihood of infection is low.

6: Close contact is defined in [PA-HAN 533](#).

7: Isolation is necessary. See [PA-HAN 535](#).

8: Quarantine is necessary. See [PA-HAN-583](#).

**Figure 1B - Asymptomatic**



1: Asymptomatic people who are fully vaccinated do not need to pursue testing in many cases. Additional guidance regarding testing for those who are [fully vaccinated](#) is available. Asymptomatic people who are not fully vaccinated may be tested routinely as part of work requirements or if they have been exposed to a case of COVID-19. Asymptomatic people who have had a SARS-CoV-2 infection in the last 3 months should generally not be tested unless symptoms develop (CDC has additional guidance on testing for those [within 90 days of their initial infection](#)).

2: A high likelihood of SARS-CoV-2 infection would be a person who has had close contact or suspected exposure to COVID-19 within the last 14 days and the person is not fully vaccinated **and** has not had a SARS-CoV-2 infection in the last 3 months.

3: A low likelihood of SARS-CoV-2 infection would be a person who has had no known exposure to a person with COVID-19 within the last 14 days **or** is fully vaccinated or has had a SARS-CoV-2 infection in the last 3 months.

4: An antigen test should be confirmed by a PCR. This is important when the index of suspicion for disease does not match the antigen test result (e.g., a person with COVID compatible symptoms that tests negative on an antigen). The time of the confirmatory PCR should also be considered - see HAN section [Confirmatory Testing When Using Antigen Tests for SARS-CoV-2](#). In certain circumstances, serial antigen testing can be used when PCR is not available ([additional detail in the HAN](#)). If PCR testing or serial testing is not performed, clinical judgement should be used when determining the appropriate public health action.

5: An antigen test may need to be confirmed by PCR when the likelihood of infection is low.

6: Close contact is defined in [PA-HAN 533](#).

7: Isolation is necessary. See [PA-HAN 535](#).

8: Quarantine is necessary. See [PA-HAN-583](#).

## **Resources**

- PADOH Point of Care Testing
  - <https://www.health.pa.gov/topics/disease/coronavirus/Pages/Guidance/Point-of-Care-Testing.aspx>
- CDC Interim Guidance for Rapid Antigen Testing for SARS-CoV- 2
  - <https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antigen-tests-guidelines.html>

If you have questions about this guidance, please call your local health department or **1-877-PA-HEALTH (1-877-724-3258)**.

Categories of Health Alert messages:

**Health Alert:** conveys the highest level of importance; warrants immediate action or attention.

**Health Advisory:** provides important information for a specific incident or situation; may not require immediate action.

**Health Update:** provides updated information regarding an incident or situation; unlikely to require immediate action.

This information is current as of October 15, 2021 but may be modified in the future. We will continue to post updated information regarding the most common questions about this subject.