

COVID-19: Demystifying Testing for the SARS-CoV-2 Virus



Frequently Asked Questions About COVID-19 Testing

Testing for COVID-19, caused by the SARS-CoV-2 virus, is rapidly evolving. As pharmacists work on the front line of the COVID-19 response, it is important to understand testing options, how to know which tests are recognized by FDA, and what qualifies a test to be provided in a pharmacy setting. The FDA's [FAQs on Diagnostic Testing for SARS-CoV-2](#) serves as a primary source for information on approval of COVID-19 tests.

What types of specimen are used to determine if someone has COVID-19?

Testing for SARS-CoV-2 relies on two main types of specimen: respiratory or blood.

- Respiratory specimens may be collected via the following methods for each of the listed sites. The nasopharyngeal swab has been the preferred and most common respiratory specimen collection technique during the United States' initial response to the COVID-19 pandemic.
 - > Swab: nasopharyngeal, oropharyngeal, nasal, throat
 - > Aspirate: nasopharyngeal, nasal, lower respiratory tract
 - > Sputum
 - > Bronchoalveolar lavage
- Blood specimens range from a drop from a fingerstick to a more extensive blood draw by a trained phlebotomist, depending on the assay used in the test.

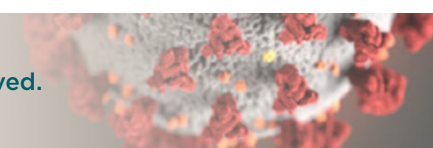
Who collects the specimen for COVID-19 testing?

Predominantly, trained health care professionals—including some pharmacists—have been collecting testing specimens, with the greatest number of specimens being collected by nasopharyngeal swab. On March 24, the CDC made changes to allow for self-collection of nasal and nasal turbinate swabs as an alternative to nasopharyngeal swabs. Current guidance on specimen collection is available through the CDC's [Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens from Persons for Coronavirus Disease 2019 \(COVID-19\)](#).

How do assays used in COVID-19 testing work?

Molecular assays and serologic assays are two broad categories for specific testing mechanisms.

- **Molecular assays:** Molecular tests detect the presence of a virus by locking onto sequences of genetic material of interest—in this case, portions of SARS-CoV-2 RNA, then amplifying that portion until there's enough for detection. Because SARS-CoV-2 is an RNA virus, molecular assays that require DNA for the amplification and detection to occur (e.g., polymerase chain reaction) are predicated on the reverse transcription of RNA into complementary DNA. Strictly speaking, a PCR test could render a positive result if it finds viral fragments, even if whole viable virus is not present.



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- **Serologic assays:** The [Johns Hopkins Center for Health Security](#) explains serology-based tests as “blood-based tests that can be used to identify whether people have been exposed to a particular pathogen.” Serology-based tests analyze the serum component of whole blood, which includes antibodies against specific antigens that are recognized by the immune system as foreign. Serology-based tests can be used to diagnose infection by detecting if the patient has had an immune response to a pathogen—in this case, SARS-CoV-2. The Johns Hopkins Center for Health Security has resources that succinctly describe serology-based testing mechanisms, both [generally](#) and [specifically in COVID-19](#).

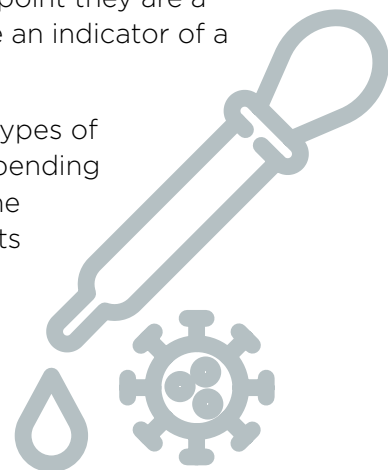
APhA’s 15 on COVID-19 episode on 4/10/2020 provides a deeper explanation of the assays used in COVID-19 testing.

Do these tests determine if someone has COVID-19 now, or if they had it in the past?

In short, it depends on the tests currently available. Some tests detect active infection, while others may differentiate between active infection and acquired immunity. Molecular assays detect active infection because they are designed to detect and amplify pieces of the pathogen—in this case, SARS-CoV-2. Certain serology-based tests can detect active infection and acquired immunity because they are designed to detect the different antibody types a person has made in response to the antigens on the surface of the pathogen. The [antibodies](#) of note in serology-based COVID-19 tests include:

- Immunoglobulin M (IgM) are antibodies made in first response to a new antigen and, when present without IgG, represent early and acute infection. In brief, anti-SARS-CoV-2 IgM antibodies could be an indicator of acute infection.
- Immunoglobulin G (IgG) are antibodies that protect against antigens the body has already been exposed to, serving as the body’s “memory” and signifying acquired immunity. If an infection persists long enough, IgG antibodies may be detectable during the latter stage of the infection. IgG antibodies typically persist after the infection resolves, at which point they are a key element of convalescent serum. Anti-SARS-CoV-2 IgG antibodies could be an indicator of a current or prior infection.

Another factor to consider is whether the test is quantitative or qualitative. Both types of tests can detect the presence or absence of pathogen, antigen, or antibodies (depending on the type of test) in the specimen. Qualitative tests return results indicating if the sample is positive or negative for what it is trying to detect, while quantitative tests specify how much of the virus component or antibody is present in the sample. Quantitative tests are the only way to determine if a person definitely has SARS-CoV-2 or has sufficient, lasting immunity to SARS-CoV-2.



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What types of tests are available or being studied for COVID-19 testing?

Tests that are being used or studied for use in COVID-19 have various analytic methods, type of specimen collected, analysis time needed, and other considerations. The table below includes a brief overview of the main analysis methods used:

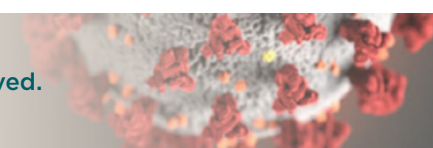
Type of Assay	Specimen Type in SARS-CoV-2	Typical Time for Analysis	Notes
Molecular assays Example: reverse-transcriptase polymerase chain reaction (RT-PCR)	Respiratory	A few hours to 2 days	<ul style="list-style-type: none">• Gold standard for sensitivity• Must be analyzed in a certified laboratory• Detects pathogen presence
Rapid molecular assays Example: rapid RT-PCR (RT-qPCR or rRT-PCR)	Respiratory	15–30 minutes	<ul style="list-style-type: none">• Can be conducted at point-of-care• Detects pathogen presence
Serology assays Examples: lateral flow assay, enzyme-linked immunosorbent assay (ELISA), neutralization (“neut”) assay	Blood	10 minutes to 5 days	<ul style="list-style-type: none">• Can be conducted at point-of-care• Detects antibodies to determine active infection (IgM) vs. established infection or acquired immunity (IgG)

How does FDA authorize COVID-19 tests?

FDA’s [Policy for Diagnostic Tests for Coronavirus Disease-2019](#) “describes policies intended to help rapidly expand testing capacity by facilitating the development and use of SARS-CoV-2 diagnostic tests during the public health emergency.” There are three main paths for COVID-19 tests to being “approved” for use:

- Obtaining an emergency use authorization (EUA) from the FDA
- Developing the test under the [authorities of the State](#), in which the laboratory operates, and the State takes responsibility for, COVID-19 testing by laboratories in its State
- Using serological testing without an EUA

The policies and guidance above do not apply to [home-based tests](#) and self-collection of samples to be sent to laboratories. Manufacturers of those tests should work directly with FDA early in the development process.



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What is an EUA?

During times of emergency, the FDA is authorized to grant [Emergency Use Authorizations](#) (EUAs), which “allow unapproved medical products or unapproved uses of approved medical products to be used ... to diagnose, treat, or prevent serious or life-threatening diseases or conditions when there are no adequate, approved, and available alternatives.” COVID-19 tests that are considered in vitro diagnostics must receive an EUA to be considered approved for use in COVID-19, and the FDA provides an [EUA template](#) indicating required information for test kit manufacturers to facilitate the process. Serologic testing for COVID-19 must work with FDA to receive appropriate approval from FDA, but an EUA may not be the channel for that approval.

Which tests have EUA status?

The full and current list of diagnostics that have received an FDA EUA are available under the [In Vitro Diagnostics EUA section](#) of the FDA’s Emergency Use Authorizations page. The FDA also publishes a [list of commercial manufacturers](#) that have notified the FDA of their intent to submit an EUA for a validated test, and the commercial manufacturer may begin selling the test prior to EUA submission.

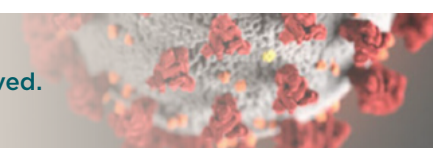
What is CLIA? How does CLIA normally affect tests provided in pharmacies?

The [FDA notes](#) that “the Clinical Laboratory Improvement Amendments (CLIA) regulate laboratory testing and require clinical laboratories to be certified by the Centers for Medicare and Medicaid Services (CMS) before they can accept human samples for diagnostic testing.” The [CDC expands](#) on this explanation, stating “the CLIA regulations establish quality standards for laboratory testing performed on specimens from humans, such as blood, body fluid, and tissue, for the purpose of diagnosis, prevention, or treatment of disease, or assessment of health.” The FDA, CMS, and CDC are jointly responsible for CLIA tests, and each has a [specific role](#).

When diagnostic tests undergo full FDA approval, they are [categorized](#) based on complexity as high complexity, moderate complexity, or waived, which determines where the tests can be analyzed. High and moderate complexity tests can only be analyzed in laboratories certified under CLIA. When a diagnostic test is granted a CLIA waiver, analysis can be done in other settings able to provide CLIA-waived tests, such as pharmacies. CMS and state authorities are responsible for enforcement of CLIA requirements.

Do COVID-19 tests receive CLIA waivers so they can be provided in pharmacy settings?

In the EUA process that is allowing COVID-19 testing in the U.S. market, the FDA specifies in which settings the test may be used. When the FDA authorizes a point-of-care test (i.e., one that has been authorized for use in “patient care settings”), [that test is considered to be CLIA waived](#) for the duration of the emergency declaration, and patient care settings that have CLIA Certificates of Waiver or Certificates of CLIA Compliance may provide those tests. Most COVID-19 tests that have EUAs can only be analyzed in laboratories certified for high or moderate complexity. However, a few have also been approved for “patient care settings”—including pharmacies with CLIA Certificates of Waiver—that have access to a specified instrument/device that analyzes the specimen.



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How can a pharmacy obtain a CLIA Certificate of Waiver?

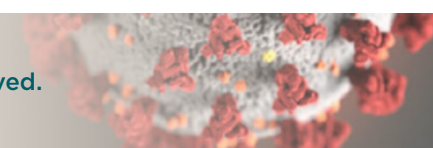
CMS manages the process to obtain a CLIA Certificate of Waiver, and some states have additional regulations or guidance related to the process. CMS's [How to Obtain a CLIA Certificate of Waiver](#) details the process and include FAQs and helpful links to State agencies. It is important to check the State Pharmacy Practice Act and other State guidance on CLIA waivers.

Which COVID-19 tests with EUAs can be provided in a pharmacy?

The table below includes information (current as of April 7, 2020) about three diagnostic tests with EUAs, indicating the test can be analyzed in patient care settings possessing a specific instrument. As new tests are authorized and added to the FDA's [list of tests with EUAs](#), pharmacists can determine the approved testing locations by reviewing the first page of a test's Letter of Authorization. If the "Authorized Laboratories and Other Authorized Testing Locations" section indicates "patient care settings," the test may be provided in pharmacies that have CLIA Certificates of Waiver.

Reminder: serology-based tests do not require EUAs and are not included in the table below. The Johns Hopkins Center for Health Security has a resource that lists [serology-based tests that are approved or being studied](#) for COVID-19.

Diagnostic Test (Manufacturer)	Diagnostic Method	Patient Care Setting Instrument Required	Specimen Collected via		
			Nasopharyngeal	Nasal	Throat
ID NOW COVID-19 (Abbott)	Molecular	ID NOW Instrument	Swab	Swab	Swab
Accula SARS-Cov-2 Test (Mesa Biotech Inc.)	Molecular	Accula Dock or Silaris Dock	—	Swab	Swab
Xpert Xpress SARS-CoV-2 test (Cepheid)	RT-PCR	GeneXpert Dx and GeneXpert Infinity Systems	Swab	Wash/Aspirate	—



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Can pharmacists order and administer COVID-19 tests?

On 4/8/2020, U.S. Department of Health & Human Services (HHS) Office of the Assistant Secretary for Health (OASH) released [Guidance for Licensed Pharmacists, COVID-19 Testing, and Immunity under the PREP Act](#), which authorized “licensed pharmacists to order and administer COVID-19 tests, including serology tests, that the Food and Drug Administration (FDA) has authorized.” The guidance also noted that pharmacists ordering and administering tests pharmacists “will qualify as ‘covered persons’ under the [PREP Act](#),” which provides liability immunity for any loss related to countermeasures to COVID-19. The guidance did not address state scope of practice considerations, the need for pharmacies to have CLIA Certificates of Waiver, payment for services, and many other factors that could facilitate or limit pharmacists’ ability to order and administer tests for COVID-19. APhA is advocating and collaborating with key decisionmakers to gain clarity on the many factors that will affect pharmacists’ ability to order and administer tests.

What serologic tests are available within patient care settings that are following the FDA’s Policy for Diagnostic Tests for Coronavirus Disease-2019, but are not pursuing EUAs?

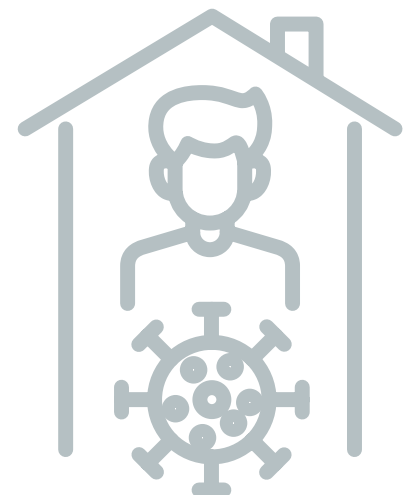
The FDA is allowing development and distribution of serological tests without going through the EUA process. However, such serology tests to identify antibodies to SARS-CoV-2 must be validated, and the FDA must be notified of the validation and the testing reports must include specific statement (e.g., that the test has not been reviewed by the FDA). FDA [maintains a list](#) of serology tests whose manufacturers have notified the FDA of the test’s validation but do not intend to pursue EUAs. Note: the list and policy do not apply to home testing.

What home-based tests are available for COVID-19?

As of April 9, 2020, there are no home-based tests for SARS-CoV-2 authorized by the FDA.

How can pharmacists identify fraudulent tests for COVID-19?

APhA’s [COVID-19 Fraudulent Medical Devices and Scams](#) includes red flags pharmacists can look for and tips for protecting pharmacists and patients from frauds and scams during the COVID-19 pandemic.



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