

COVID-19, PCR, Respiratory Specimen (Lab Tests and Diagnostic Procedures)

Comment

The FDA has noted that unauthorized **fraudulent** COVID-19 test kits are being sold online. The FDA advises consumers and health professionals to be cautious of websites and stores selling products that claim to prevent, diagnose, treat, or cure COVID-19 ([FDA Fraudulent 2020](#)). Consumers and health care professionals can help by reporting suspected fraud to the [FDA's Health Fraud Program](#) or the [Office of Criminal Investigations](#).

The molecular tests for SARS-CoV-2 are designed to detect specific genetic sequences found in the genome of the virus. As the virus can mutate over time resulting in genetic variations, the FDA is alerting the health care community that false negative results may occur with any SARS-CoV-2 molecular test if a mutation occurs in the part of the virus' genome assessed by a particular test. Currently the FDA has identified six molecular tests that may be impacted by viral mutation and have reduced sensitivities ([FDA SARS-CoV-2 Mutations](#) 2021):

- **Accula SARS-CoV-2 Test** manufactured by Mesa Biotech Inc. Performance may be affected when patient sample has genetic variant at position 28881 to 28883 (GGG to AAC), and also 28877 to 28878 (AG to TC). This impact does not appear to be significant, however; the FDA is alerting health care providers.
- **TaqPath COVID-19 Combo Kit** (also labeled as TaqPath COVID-19 Combo Kit Advanced) manufactured by Thermo Fisher Scientific, Inc. One of three targets in this assay has significantly reduced sensitivity due to mutations including mutations in the B.1.1.7 variant. As this assay detects multiple genetic targets, the overall sensitivity should not be impacted. When certain mutations are present, the pattern of detection may help with early identification of new variants.
- **Linea COVID-19 Assay Kit** manufactured by Applied DNA Sciences, Inc. One of the two targets in this assay has significantly reduced sensitivity due to mutations, including a mutation in the B.1.1.7 variant. As this assay detects multiple genetic targets, the overall sensitivity should not be impacted. When certain mutations are present, the pattern of detection may help with early identification of new variants.
- **Xpert Xpress SARS-CoV-2, Xpert Xpress SARS-CoV-2 DoD, Xpert Omni SARS-CoV-2** manufactured by Cepheid. These tests are impacted by a single point mutation in the target area of the test. They look for both the N2 and E target regions within viral RNA. Two independent single point mutations reduce test sensitivity for detecting the N2 target. The E target is still detected when enough virus is present, and a *presumptive positive* result is reported with the **Xpert Xpress SARS-CoV-2** and **Xpert Xpress SARS-CoV-2 DoD** tests. With the **Xpert Omni SARS-CoV-2** test, detection of the E target without detecting the N2 target is reported as *positive*. As the testing is designed to detect multiple genetic targets, and the mutations do not lead to false negative results, the FDA states the impact on test performance does not appear to be significant.

- For more information see [FDA SARS-CoV-2 Mutations: Impact on COVID-19 Tests](#).

Prior receipt of a COVID-19 vaccine will **not** affect viral testing for SARS-CoV-2.

Related Information

- [COVID-19 Antibody \(IgG\), Quantitative, Serum or Plasma](#)
- [COVID-19 Antibody \(IgG\), Semi-quantitative, Serum or Plasma](#)
- [COVID-19 Antibody \(IgG\), Serum, Plasma, or Whole Blood](#)
- [COVID-19 Antibody Total, Oral Fluid](#)
- [COVID-19 Antibody Total, Serum, Plasma, or Whole Blood](#)
- [COVID-19 Antibody, IgG/IgM Rapid Test, Serum, Plasma, or Whole Blood](#)
- [COVID-19 Antigen, Upper Respiratory Specimen](#)
- [COVID-19 Neutralization Antibody, Serum or Plasma](#)
- [COVID-19, PCR, Saliva](#)
- [Influenza and SARS-CoV-2 Antigen, Upper Respiratory Specimen](#)
- [Influenza SARS-CoV-2 Multiplex Assay, PCR, CDC](#)
- [Respiratory Panel, PCR, Nasopharyngeal](#)

Overview

At the end of 2019, a novel coronavirus was identified as the cause of several cases of pneumonia in Wuhan City, Hubei Province, China. Initially linked to a large seafood and animal market suggesting animal-to-human spread, person-to-person transmission was quickly confirmed (Li Q 2020). The virus spread rapidly worldwide and in January 2020, the World Health Organization (WHO) declared the outbreak a "public health emergency of international concern." On March 11, 2020, the WHO publicly characterized COVID-19 as a pandemic. Currently, more than 200 million infections have been confirmed globally in over 200 countries and territories with over 4 million deaths ([WHO 2021](#)).

The novel virus has been named **severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)** and the disease it causes has been named **coronavirus disease 2019, or COVID-19**. The virus spreads by contact with respiratory fluids (droplets or aerosol) produced when an infected person exhales (eg, breathes, speaks, coughs, sneezes, or sings). These droplet/aerosol particles can be

- inhaled directly into lungs
- directly deposited on exposed mucous membranes (eyes, mouth, nose)
- transferred to mucous membranes by hands contaminated with virus-containing respiratory fluids or by indirectly touching surfaces with virus on them ([CDC SARS-CoV-2 Transmission 2021](#))

COVID-19 symptoms typically appear within 2 to 14 days (median of 5 days) of exposure and include **fever, chills, fatigue, cough, shortness of breath, myalgia, recent loss of taste or smell,**

vomiting or diarrhea, and/or sore throat. Sickness ranges from a mild respiratory illness to severe disease including respiratory failure, septic shock, or other organ failure. Most fatalities have occurred in patients with underlying comorbidities, with overall global fatalities around 2 to 3 percent ([WHO situation rept 2021](#)). The CDC currently estimates that about 30% of COVID-19 infections are asymptomatic, and 50% of transmission occurs prior to symptom onset ([CDC Pandemic Planning 2021](#)).

The Center of Disease Control and Prevention (CDC) developed a nucleic acid amplification/real time Reverse Transcription-Polymerase Chain Reaction (rRT-PCR) assay to diagnose SARS-CoV-2 in respiratory specimens. In the early stages of disease dissemination, the CDC was the only lab conducting the SARS-CoV-2 testing; however, with the rapid spread of the viral infection, in February 2020 the FDA issued an Emergency Use Authorization (EUA) allowing qualified laboratories (as designated by CDC) to perform testing. Those facilities included US state and local public health laboratories, Department of Defense (DOD) laboratories, and select reference and international laboratories. Currently, under FDA guidance, there has been local, hospital-based SARS-CoV-2 test development. The developed tests may be based on the CDC, WHO, or manufacturer assays, or created de novo. The laboratories must perform an assay validation and pursue an FDA Emergency Use Authorization. See [Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency \(Revised\)](#).

As the pandemic has progressed many FDA EUA nucleic acid amplification tests have entered the market, including:

- Batch testing platforms with various turnaround times (useful for large facilities or reference laboratories that have bigger sample volumes)
- Rapid, point-of-care tests which can provide results in 5 to 45 minutes ([FDA, Cepheid 2020c](#); [Abbott NOW COVID-19 PI 2020](#))
- Self-contained, single-use, fully-integrated, automated RT-PCR disposable kits for laboratory diagnostics ([FDA Visby 2021b](#))
- Nucleic acid testing on pooled specimens of symptomatic or asymptomatic individuals (can save time and money)
- Saliva testing
- At home self-collection devices to be sent into specific testing facilities
- Prescription tests that can be self-collected and performed at home or at point-of-care ([FDA, Lucira 2020g](#))
- Over-the-counter (nonprescription), at-home, isothermal nucleic acid amplification test for use with a compatible mobile smart device ([FDA, Cue 2021](#)).
- Serial Screening (testing an individual multiple times on a routine basis using upper respiratory specimens). The qualitative nucleic acid test(s) can be used for individuals with or without symptoms, providing better testing solutions for schools, workplaces, and communities when establishing SARS-CoV-2 screening protocols (FDA, BD SARS-COV-2 2021).

Also, available (via EUA) are molecular respiratory panels that include SARS-CoV-2 and several other well-known respiratory pathogens. These panels are intended for qualitative identification and

differentiation of nucleic acid from multiple organisms (including influenza A and B) and assist health care providers in discerning various infectious agents that produce similar symptoms to COVID-19. Panel testing can also assist in diagnosing coinfections which have been noted in some COVID-19 patients (Ding 2020; Kim 2020).

As each of these assays has unique specificities regarding specimen, collection, transport and processing, it is important that health care providers understand testing options available and follow manufacturer instructions for proper specimen collection, processing, and transport. The information below covers the specimens and collection procedures required by the CDC.

Use/Indications

Aid in the diagnosis of coronavirus disease (COVID-19); detect current infection

Nucleic acid amplification testing was also originally recommended for determining resolution of infection, a test-based strategy which required serial tests and improvement of symptoms to determine when an individual with SARS-CoV-2 infection was no longer infectious and transmission-based precautions could be discontinued. However, the CDC has changed to a symptom-based strategy with recommendations based on severity of illness (eg, 10 days from onset of symptoms for mild to moderate illness **and** 24 hours fever free without fever-reducing medications **and** symptoms have improved). It was found in the majority of cases, the test-based strategy actually prolonged the isolation of patients who continue to shed detectable SARS-CoV-2 RNA but are no longer infectious (virus is no longer replication-competent).

A test-based strategy is still considered useful in some instances when transmission-based precautions could be discontinued earlier than if the symptom-based strategy was used, or for some patients with severe illness or immunocompromised (chemotherapy, transplant, untreated HIV infection, combined primary immunodeficiency disorder, prednisone treatments, advanced age, diabetes mellitus, end-stage renal disease). These patients may produce replication-competent virus for longer than 20 days after symptom onset ([CDC Discontinuation 2021](#); Baang 2021; Aydillo 2020).

Special Instructions

With the rapid spread and newly acquired knowledge of COVID-19 along with the increased availability of tests, the CDC and IDSA testing recommendations are continuously changing, see

[Overview of Testing for SARS-CoV-2 \(COVID-19\)](#) and

[Infectious Diseases Society of America Guidelines on the Diagnosis of COVID-19](#) (IDSA [Hanson 2020]).

Note: Testing for other respiratory pathogens by the provider should be done as part of the initial work-up (as indicated) and should not delay specimen shipping to CDC or qualified laboratory.

Test Includes

Qualitative detection of nucleic acid (RNA) from SARS-CoV-2

Specimen

Upper Respiratory Tract Specimen

For initial COVID-19 testing, the CDC recommends collecting an upper respiratory specimen. This includes ([CDC 2020f](#)):

- Nasopharyngeal (NP) specimen collected by a trained health care professional. **Or**
- Oropharyngeal (OP) specimen collected by a trained health care professional. **Or**
- Nasal mid-turbine (NMT) specimen collected by a trained health care professional or by a supervised or unsupervised onsite self-collection (using flocked tapered swab), or self-collected at home following kit instructions. Both nares should be swabbed. **Or**
- Anterior nares (nasal swab; NS) specimen collected by a trained health care professional, or by a supervised or unsupervised onsite self-collection (using a flocked or spun polyester swab), or self-collected at home following kit instructions. Both nares should be swabbed using the same swab. **Or**
- Nasopharyngeal wash/aspirate or nasal wash/aspirate (NW) specimen collected by health care professional. **Or**
- Saliva, self-collection at home or at testing site
- **Note:** The IDSA recommends collecting an NP swab, NMT swab, anterior nasal swab, saliva, or a combined anterior nasal/oropharyngeal swab rather than an oropharyngeal swab alone for nucleic acid testing in symptomatic patients ([IDSA \[Hanson 2020\]](#)).

Lower Respiratory Tract Specimen

- Bronchoalveolar lavage (BAL), tracheal aspirate, pleural fluid, lung biopsy
- Sputum - for patients who develop a productive cough; induction of sputum is **not** recommended.

Note: SARS-CoV-2 RNA has also been detected in stool, blood, and semen (Li D 2020).

Container(s)

- Confer with testing laboratory for proper specimen container and collection.
- Lower respiratory specimen: Sterile, screw-cap plastic container
- Nasal mid-turbinate (NMT) specimen: Flocked tapered swab
- Nasal swab or anterior nares (NS) specimen: Flocked or spun polyester swab
- Nasopharyngeal or oropharyngeal specimen: Use only synthetic fiber swab with plastic or wire shaft. Do not use calcium alginate swab or cotton swab with wooden shaft.
- Nasopharyngeal wash/aspirate or nasal wash/aspirate specimen: Sterile viral transport media tube
- Saliva: Sterile, screw-cap plastic container

Volume / Minimum Volume

- 1 NP swab or 1 OP swab or 1 NS swab or 1 NMT swab
- Saliva: 1-5 mL
- Fluids: 2-3 mL

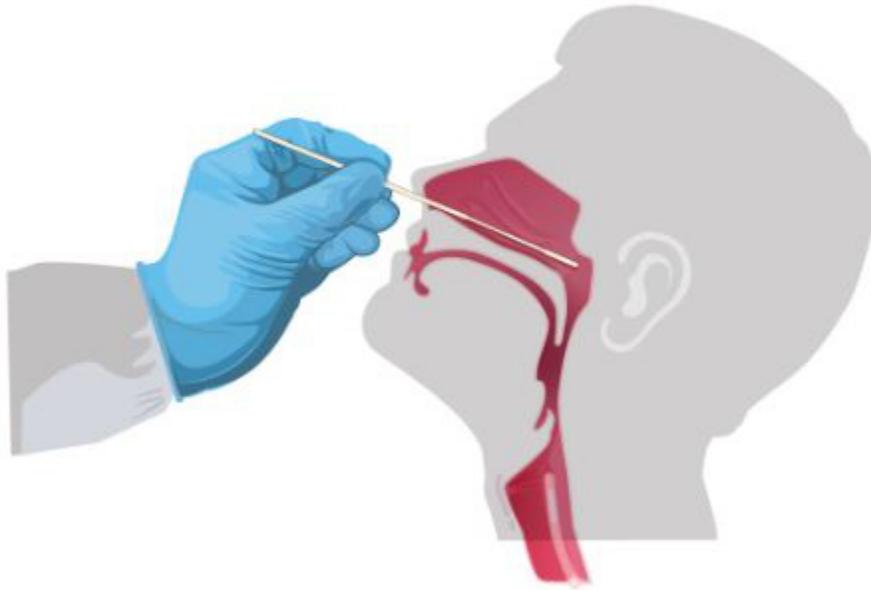
Collection

Prior to specimen collection, patient identity should be confirmed using two independent identifiers; use of a patient identification arm band or similar system is recommended. Specimen label(s) should include the two independent identifiers and the date of collection. There should be a method to identify the individual collecting the specimen. The specimen container(s) should be labeled in the presence of the patient after specimen is collected. Container(s) should **not** be pre-labeled. Use computer-generated label(s), if available, to avoid transcription errors.

Collect specimen from patient as soon as possible, regardless of time of symptom onset. Health care professionals collecting specimens should use proper infection control techniques and wear personal protective equipment, including an N95 respirator (or facemask if respirator is not available), eye protection, gloves, and a gown.

Upper Respiratory Tract Specimen

- **NP swab:** Tilt patient's head back 70 degrees. Insert a minitip swab with flexible (wire or plastic) shaft through the nostril parallel to the palate (not upwards) until resistance is detected or the distance is equivalent to that from the ear to the nostril of the patient, indicating contact with the nasopharynx. Swab should reach depth equal to distance from nostrils to outer opening of the ear. Gently rub and roll swab. Leave swab in place for several seconds to absorb secretions. Slowly remove swab while rotating it. Specimens can be collected from both sides using the same swab, but it is not necessary to collect from both sides if the minitip is saturated with fluid from the first collection. If a deviated septum or blockage create difficulty in obtaining the specimen from one nostril, use the same swab to obtain the specimen from the other nostril. Place swab immediately into sterile tubes containing 2 to 3 mL of viral transport media (VTM), Amies transport medium, phosphate-buffered saline, or sterile saline. If both are collected, NP and OP specimens should be placed in the same vial at collection site. **Note:** Some point of care assays are designed to analyze the specimen **directly (without medium)**; use swabs provided and follow manufacturers instructions for swab storage and processing. See [CDC Nasopharyngeal Specimen Collection Steps](#).



CDC 2020f

- **OP (throat) swab:** Avoiding the tongue, teeth, and gums, insert swab into the posterior of pharynx and tonsillar areas. Rub swab over both tonsillar pillars and posterior oropharynx. Place swab immediately into sterile tubes containing 2 to 3 mL of viral transport media (VTM), Amies transport medium, phosphate-buffered saline, or sterile saline. If both are collected, NP and OP specimens should be placed in the same vial at collection site. **Note:** Some point of care assays are designed to analyze the specimen **directly (without medium)**; use swabs provided and follow manufacturers instructions for swab storage and processing.
- **NMT swab (deep nasal swab):** Use a flocked tapered swab. Tilt patient's head back 70 degrees. While gently rotating, insert swab less than one inch (about 2 cm) into nostril (until resistance is met at turbinates). Rotate the swab several times against nasal wall and repeat in other nostril using the same swab. Place swab immediately into sterile tubes containing 2 to 3 mL of viral transport media (VTM), Amies transport medium, phosphate-buffered saline, or sterile saline. **Note:** Some point of care assays are designed to analyze the specimen **directly (without medium)**; use swabs provided and follow manufacturers instructions for swab storage and processing. See [CDC Nasal Mid-turbinate Specimen Collection Steps](#).
- **NS (anterior nares):** Using a flocked or spun polyester swab, insert the tip of swab 0.5 to 0.75 inch (1 to 1.5 cm) inside the nostril (naris) and firmly sample the nasal membrane by rotating the swab in a circular path against the nasal wall at least 4 times. Take approximately 15 seconds to collect the sample. Be sure to collect any nasal drainage that may be present on the swab. Sample both nostrils with same swab. Place swab immediately into sterile tubes containing 2 to 3 mL of viral transport media (VTM), Amies transport medium, phosphate-buffered saline, or

sterile saline. **Note:** Some point of care assays are designed to analyze the specimen **directly (without medium)**; use swabs provided and follow manufacturers instructions for swab storage and processing. See [CDC How to collect Your Anterior Nasal Swab Sample for COVID-19 Testing](#).

- **NP wash/aspirate or nasal wash/aspirate (NW):** Sterile collection by health care provider. Attach catheter to suction apparatus. Have the patient sit with head tilted slightly backward. Instill 1 to 1.5 mL of non-bacteriostatic saline (pH 7.0) into one nostril. Insert the tubing into the nostril parallel to the palate (not upwards). Catheter should reach depth equal to distance from nostrils to outer opening of ear. Begin gentle suction/aspiration and remove catheter while rotating it gently. Place specimen in a sterile viral transport media tube.
- **Saliva:** Supervised, patient self-collection into sterile, leakproof container

Lower Respiratory Tract Specimen

- **BAL, tracheal aspirate, pleural fluid, lung biopsy:** Sterile collection by health care provider. Collect 2 to 3 mL into sterile, leakproof, screw-cap container. Collection of lower respiratory specimens is advised if collected later in the course of disease or in patients with a negative upper respiratory test and a strong clinical suspicion of COVID-19 infection (WHO 2020b).
- **Sputum:** Patient should be educated on difference between sputum and saliva. Patient should rinse mouth with water then expectorate deep cough sputum directly into sterile, leakproof screw-cap container. Health care personnel should apply standard precautions and wear an N95 or equivalent or higher respirator when collecting specimens. **Note:** Sputum induction is **not** recommended.

For more information see: [CDC Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens for COVID-19](#).

See [Guidelines for submitting specimens to CDC](#) for laboratory testing for SARS-CoV-2.

Processing and Storage

- For all specimens: Refrigerate at 2°C to 8°C and ship overnight on ice pack to CDC (or qualified laboratory). Specimens are stable 72 hours.
- For longer storage, freeze specimen(s) at -70°C.
- For state, local, or reference laboratories, follow specific shipping guidelines.

Stability

- Refrigerated: 72 hours
- Frozen (-70°C): Not established

Methodology

Nucleic acid amplification testing (NAAT), with reverse-transcription polymerase chain reaction (RT-PCR) to detect SARS-CoV-2 RNA

Other types of NAAT include isothermal amplification, CRISPR-based assays, and next-generation sequencing (Brandsma 2020; Joung 2020).

Normal Values/Findings

Not detected

Note: If a negative result is obtained from a patient with a high index of suspicion, the World Health Organization (WHO) recommends resampling with repeat nucleic acid testing; the collection of additional specimens, including the lower respiratory tract may be necessary (WHO 2020b).

All positives must be reported to local/state health departments.

Interpretative Information

- A positive result indicates the presence SARS-CoV-2 RNA; results must be correlated with patient history and clinical symptoms. Positive results do not rule out infection with other pathogens (bacteria or coinfection with other viruses).
- A Not Detected test result means that SARS-CoV-2 RNA was not present in the specimen above the limit of detection, thus a negative result does not rule out the possibility of COVID-19 and should not be used as the sole basis for patient management decisions.

Limitations

Factors that can lead to a false-negative result include:

- Poor specimen quality; small amount of patient specimen
- Specimen collected early or late in the infection process. A study of PCR-based SARS-CoV-2 tests, funded by the National Institute of Allergy and Infectious Diseases (NIAID) and the CDC, found the median false-negative rate on the first day of symptom onset was 38%, and decreased to 20% three days after symptom onset. This percentage began to increase on day 4, and 16 days after symptom onset the false-negative rate was up to 66% (Kucirka 2020).
- Inadequate processing, storage, or shipping of specimen
- Technical reasons inherent in the test (eg, virus mutation, PCR inhibition) (FDA novel coronavirus EUA 2020b)

False positive results are rare but can occur due to technical error or reagent contamination

Diagnostic Role

Gold standard confirmation of acute SARS-CoV-2 infection is based on the detection of unique viral sequences by nucleic acid amplification tests (NAATs). These assays' targets include regions on the nucleocapsid (N), envelope (E), spike (S), and RNA-dependent RNA polymerase (RdRp) genes (WHO 2020b). Although this testing is both sensitive and specific, an accurate result is dependent on the type and quality of the specimen and the duration of illness at the time of testing.

The viral load tends to be higher in lower respiratory tract (LRT) specimens; Wang et al found RT-PCR viral loads highest in bronchoalveolar lavage (BAL) specimens (93%), followed by sputum (72%), nasal

swab (63%), and pharyngeal swab (32%) (Wang 2020b). As such an LRT specimen may be recommended when an upper respiratory tract (URT) specimen is negative for SARS-CoV-2. Some studies have shown that viral loads are higher in nasal/nasopharyngeal specimens compared to oropharyngeal specimens (Covid Investigation Team 2020; Zou 2020) while other studies do not find a difference (Wölfel 2020).

SARS-CoV-2 may be detected in the URT 1 to 3 days prior to development of symptoms (Furukawa 2020; WHO 2020b); the viral concentration is highest around the time of symptom onset and then gradually declines (He 2020; Zou 2020). Although it is important to test the suspected positive patient as soon as possible, the duration of the illness at specimen collection must be considered when interpreting results.

It is important to note that the various NAATs available have different limits of detection (LOD), thus varying sensitivities. Specimens tested on different platforms could have different results. For more information see [SARS-CoV-2 Reference Panel Comparative Data](#).

Laboratory/Diagnostic Pearls

- Severe Acute Respiratory Syndrome (SARS) was identified in 2003 and Middle East Respiratory Syndrome (MERS) was identified in 2012. As these syndromes are also caused by viruses in the coronavirus family, researchers are incorporating information learned from these previous infections to aid in understanding SARS-CoV-2.
- For biosafety reasons it is not recommended to perform viral isolation in cell culture for SARS-CoV-2 or perform initial characterization of viral agents recovered in cultures of specimens from patients.
- Studies indicate SARS-CoV-2 may persist on surfaces for a few hours up to several days dependent on conditions (eg, type of surface, temperature or humidity of the environment). Warmer temperatures and exposure to sunlight reduces viral survival time ([CDC 2020e](#)).
- Concentrations of SARS-CoV-2 RNA in upper respiratory specimens declines after onset of symptoms as does the recovery of replication-competent virus. In patients with mild to moderate disease, replication-competent virus has not been recovered after 10 days following symptom onset. In patients with severe COVID-19 disease or some immunocompromised patients replication-competent virus has been recovered 10 to 20 days post symptom onset. Some severely immunocompromised have had replication-competent virus recovered at much longer than 20 days post symptom onset (Baang 2021; Aydillo 2020), thus making a case for test-based strategy for determining resolution of infection in these patients.
- Current data indicate that low levels of SARS-CoV-2 may persist for up to 3 months in the respiratory tracts of persons recovered from COVID-19 infection. This latent shedding has **not** been found to be replication competent. If tested within 3 months of initial infection, individuals may continue to have a positive test result, however; infectiousness is unlikely ([CDC 2021 Interim guidance on duration](#)).

Additional Information

FDA recommendations for clinical laboratory and health care providers who use molecular testing to detect SARS-CoV-2 (SARS-CoV-2 Viral Mutations 2021):

- Be aware that genetic variants of SARS-CoV-2 arise regularly and false negative test results can occur.
- Be aware that tests that use multiple genetic targets to determine a final result are less likely to be impacted by increased prevalence of genetic variants.
- Consider negative results in combination with clinical observations, patient history, and epidemiological information.
- Consider repeat testing with a different test (with different genetic targets) if COVID-19 is still suspected after receiving a negative test result.

For more information, interim guidance has been issued by the United States [CDC](#) and the [World Health Organization](#).

See: [Guidance for Healthcare Workers about COVID-19 \(SARS-CoV-2\) Testing](#)

See: [Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens for COVID-19](#)

See: [Information for Laboratories](#)

See: [Interim Laboratory Biosafety Guidelines for Handling and Processing Specimens Associated with Coronavirus Disease 2019 \(COVID-19\)](#)

See: FDA [Emergency Use Authorizations](#)

Index Terms

2019 Novel Coronavirus; 2019-nCoV; COVID-19 PCR; COVID-19, Qualitative, PCR; Covid19; nCoV, 2019; Novel Coronavirus, 2019; Qualitative COVID-19; SARS-CoV-2; Severe Acute Respiratory Syndrome Coronavirus 2; Wuhan

Applies to

Pandemic; Pneumonia of Unknown Etiology

References

Abbott Diagnostics. ID NOW COVID-19 [product information] <https://www.fda.gov/media/136525/download>. Scarborough, Maine; April 2020.

Abbott Laboratories. Abbott Provides Update on ID NOW™. <https://abbott.mediaroom.com/2020-05-14-Abbott-Provides-Update-on-ID-NOW-TM>. Published May 14, 2020b. Accessed May 18, 2020.

Abbott Laboratories. Detect COVID-19 in as little as 5 minutes. Abbott Laboratories website. <https://www.abbott.com/corpnewsroom/product-and-innovation/detect-covid-19-in-as-little-as-5-minutes.html>. Updated March 27, 2020c. Accessed March 30, 2020.

Aydillo T, Gonzalez-Reiche AS, Aslam S, van de Guchte A, Khan Z, Obla A, Dutta J, van Bakel H, Aberg J, García-Sastre A, Shah G, Hohl T, Papanicolaou G, Perales MA, Sepkowitz K, Babady NE, Kamboj M. Shedding of Viable SARS-CoV-2 after Immunosuppressive Therapy for Cancer. *N Engl J Med*. 2020 Dec 24;383(26):2586-2588. doi: 10.1056/NEJMc2031670. Epub 2020 Dec 1. [\[PubMed 33259154\]](#)

Baang JH, Smith C, Mirabelli C, Valesano AL, Manthei DM, Bachman MA, Wobus CE, Adams M, Washer L, Martin ET, Lauring AS. Prolonged Severe Acute Respiratory Syndrome Coronavirus 2 Replication in an Immunocompromised Patient. *J Infect Dis.* 2021 Jan 4;223(1):23-27. doi: 10.1093/infdis/jiaa666. [\[PubMed 33089317\]](#)

Bai Y, Yao L, Wei T, et al. Presumed Asymptomatic Carrier Transmission of COVID-19 [published online February 21, 2020]. *JAMA.* 2020;10.1001/jama.2020.2565. [\[PubMed 32083643\]](#)

Brandsma E, Verhagen HJMP, van de Laar TJW, Claas ECJ, Cornelissen M, van den Akker E. Rapid, sensitive and specific SARS coronavirus-2 detection: a multi-center comparison between standard qRT-PCR and CRISPR based DETECTR. *J Infect Dis.* 2020 Oct 10;jiaa641. doi: 10.1093/infdis/jiaa641. Epub ahead of print. [\[PubMed 33038252\]](#)

Burke RM, Killerby ME, Newton S, et al. Symptom Profiles of a Convenience Sample of Patients with COVID-19 - United States, January-April 2020. *MMWR Morb Mortal Wkly Rep.* 2020;69(28):904-908. Published 2020 Jul 17. [\[PubMed 32673296\]](#)

Centers for Disease Control and Prevention (CDC). CDC Tests for 2019-nCoV. <https://www.cdc.gov/coronavirus/2019-ncov/about/testing.html>. Updated August 5, 2020a. Accessed December 12, 2020.

Centers for Disease Control and Prevention (CDC). Coronavirus Disease 2019 (COVID-19). Interim Guidance on Duration of Isolation and Precautions for Adults with COVID-19. <https://www.cdc.gov/coronavirus/2019-ncov/hcp/duration-isolation.html>. Updated February 13, 2021. Accessed February 15, 2021.

Centers for Disease Control and Prevention (CDC). Coronavirus Disease 2019 (COVID-19). Overview of Testing for SARS-CoV-2. <https://www.cdc.gov/coronavirus/2019-nCoV/hcp/clinical-criteria.html>. Updated October 21, 2020c. Accessed December 12, 2020.

Centers for Disease Control and Prevention (CDC). COVID-19 Pandemic Planning Scenarios. <https://www.cdc.gov/coronavirus/2019-ncov/hcp/planning-scenarios.html>. Updated March 19, 2021. Accessed March 23 2021.

Centers for Disease Control and Prevention (CDC). COVID-19. Scientific Brief: SARS-CoV-2 Transmission. <https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/sars-cov-2-transmission.html>. Updated May 7, 2021. Accessed July 30, 2021.

Centers for Disease Control and Prevention (CDC). Discontinuation of Transmission-Based Precautions and Disposition of Patients with COVID-19 in Healthcare Settings (Interim Guidance). <https://www.cdc.gov/coronavirus/2019-ncov/hcp/disposition-hospitalized-patients.html>. Updated February 14, 2021. Accessed February 15, 2021.

Centers for Disease Control and Prevention (CDC). Environmental Protection Agency (EPA). Guidance for cleaning and disinfecting public spaces, workplaces, businesses, schools, and homes. https://www.cdc.gov/coronavirus/2019-ncov/community/pdf/reopening_america_guidance.pdf. Published September 16, 2020e.

Centers for Disease Control and Prevention (CDC). Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens for COVID-19. <https://www.cdc.gov/coronavirus/2019-nCoV/lab/guidelines-clinical-specimens.html>. Updated November 30, 2020f. Accessed December 12, 2020.

COVID-19 Investigation Team. Clinical and virologic characteristics of the first 12 patients with coronavirus disease 2019 (COVID-19) in the United States. *Nat Med*. 2020 Jun;26(6):861-868. doi: 10.1038/s41591-020-0877-5. Epub 2020 Apr 23. [\[PubMed 32327757\]](#)

Ding Q, Lu P, Fan Y, Xia Y, Liu M. The clinical characteristics of pneumonia patients coinfecting with 2019 novel coronavirus and influenza virus in Wuhan, China [published online March 20, 2020]. *J Med Virol*. [\[PubMed 32196707\]](#)

Furukawa NW, Brooks JT, Sobel J. Evidence Supporting Transmission of Severe Acute Respiratory Syndrome Coronavirus 2 While Presymptomatic or Asymptomatic. *Emerg Infect Dis*. 2020 Jul;26(7):e201595. doi: 10.3201/eid2607.201595. Epub 2020 Jun 21. [\[PubMed 32364890\]](#)

Hanson KE, Caliendo AM, Arias CA, Hayden MK, Englund JA, Lee MJ, et al. Infectious Diseases Society of America Guidelines on the Diagnosis of COVID-19: Molecular Diagnostic Testing. Infectious Diseases Society of America. 2020; Version 2.0.0. <https://www.idsociety.org/practice-guideline/covid-19-guideline-diagnostics/>. Accessed March 18, 2021.

He X, Lau EHY, Wu P, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. *Nat Med*. 2020 May;26(5):672-675. doi: 10.1038/s41591-020-0869-5. Epub 2020 Apr 15. Erratum in: *Nat Med*. 2020 Sep;26(9):1491-1493. [\[PubMed 32296168\]](#)

Joung J, Ladha A, Saito M, et al. Detection of SARS-CoV-2 with SHERLOCK One-Pot Testing. *N Engl J Med*. 2020 Oct 8;383(15):1492-1494. doi: 10.1056/NEJMc2026172. Epub 2020 Sep 16. [\[PubMed 32937062\]](#)

Kim D, Quinn J, Pinsky B, Shah NH, Brown I. Rates of Co-infection Between SARS-CoV-2 and Other Respiratory Pathogens [published online April 15, 2020]. *JAMA*. [\[PubMed 32293646\]](#)

Kucirka LM, Lauer SA, Laeyendecker O, Boon D, Lessler J. Variation in False-Negative Rate of Reverse Transcriptase Polymerase Chain Reaction-Based SARS-CoV-2 Tests by Time Since Exposure. *Ann Intern Med*. Published online May 13, 2020. doi:10.7326/M20-1495. [\[PubMed 32422057\]](#)

Lippi G, Simundic AM, Plebani M. Potential preanalytical and analytical vulnerabilities in the laboratory diagnosis of coronavirus disease 2019 (COVID-19) [published online March 16, 2020]. *Clin Chem Lab Med*. [\[PubMed 32172228\]](#)

Li D, Jin M, Bao P, Zhao W, Zhang S. Clinical Characteristics and Results of Semen Tests Among Men With Coronavirus Disease 2019. *JAMA Netw Open*. 2020;3(5):e208292. Published 2020 May 1. [\[PubMed 32379329\]](#)

Li Q, Guan X, Wu P, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia [published online January 29, 2020]. *N Engl J Med*. [\[PubMed 31995857\]](#)

Patel A, Jernigan DB; 2019-nCoV CDC Response Team. Initial Public Health Response and Interim Clinical Guidance for the 2019 Novel Coronavirus Outbreak - United States, December 31, 2019-February 4, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(5):140-146. Published February 7, 2020. [\[PubMed 32027631\]](#)

Pixel by Lab Corp. Introducing Self-Collection Kits for COVID-19 Testing. <https://www.pixel.labcorp.com/blog/introducing-self-collection-kits-covid-19-testing>. Published April 2020. Accessed April 22, 2020.

QIAstat-Dx Respiratory SARS-CoV2 Panel Instructions for Use (Handbook). Germantown, MD: QIAGEN; March 2020.

Sethuraman N, Jeremiah SS, Ryo A. Interpreting Diagnostic Tests for SARS-CoV-2 [published online ahead of print, 2020 May 6]. *JAMA*. 2020;10.1001/jama.2020.8259. [\[PubMed 32374370\]](#)

US Food & Drug Administration (FDA). BD SARS-CoV-2 Reagents for BD MAX™ System [product information]. <https://www.fda.gov/media/136816/download>. 2021. Accessed April 28, 2021.

US Food & Drug Administration (FDA). Beware of Fraudulent Coronavirus Tests, vaccines and Treatments. https://www.fda.gov/consumers/consumer-updates/beware-fraudulent-coronavirus-tests-vaccines-and-treatments?utm_campaign=FDA%20MedWatch%20-%20Fraudulent%20Coronavirus%20Tests%2C%20Vaccines%20and%20Treatments&utm_medium=email&utm_source=Eloqua. Current November 20, 2020a. Accessed December 2, 2020.

US Food & Drug Administration (FDA). CDC 2019-Novel Coronavirus (2019-nCoV) Real-Time RT-PCR Diagnostic Panel [Emergency Use Only]. <https://www.fda.gov/media/134922/download> Effective December 1, 2020b. Accessed January 26, 2021.

US Food & Drug Administration (FDA). Cepheid. Xpert® Xpress SARS-CoV-2 Test [Emergency Use Authorization]. <https://www.fda.gov/media/136314/download>. Published September 2020c. Accessed January 5, 2021.

US Food & Drug Administration (FDA). Coronavirus (COVID-19) Update: Daily Roundup [News Release]. <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-daily-roundup-april-21-2020>. Published April 21, 2020d. Accessed April 22, 2020.

US Food & Drug Administration (FDA). Coronavirus (COVID-19) Update: FDA Informs Public About Possible Accuracy Concerns with Abbott ID NOW Point-of-Care Test. <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-informs-public-about-possible-accuracy-concerns-abbott-id-now-point>. Published May 14, 2020e. Accessed May 18, 2020.

US Food & Drug Administration (FDA). Cue Health. The Cue™ COVID-19 Test for Home and Over The Counter (OTC) Use [Emergency Use Authorization]. <https://www.fda.gov/media/146470/download>. Published March 5, 2021. Accessed March 11, 2021.

US Food & Drug Administration (FDA). Genetic Variants of SARS-CoV-2 May Lead to False Negative Results with Molecular Tests for Detection of SARS-CoV-2 - Letter to Clinical Laboratory Staff and Health Care Providers. https://www.fda.gov/medical-devices/letters-health-care-providers/genetic-variants-sars-cov-2-may-lead-false-negative-results-molecular-tests-detection-sars-cov-2?utm_medium=email&utm_source=govdelivery. Published January 8, 2021. Accessed January 12, 2021.

US Food & Drug Administration (FDA). Infinity BiologiX. SARS-CoV-2 ASSAY [EUA Summary]. <https://www.fda.gov/media/137776/download>. Published November 13, 2020f. Accessed December 16, 2020.

US Food & Drug Administration (FDA). Lucira Health, Inc. Lucira COVID-19 All-In-One Test Kit [Emergency Use Authorization]. <https://www.fda.gov/media/143810/download>. Published November 17, 2020g. Accessed December 12, 2020.

US Food & Drug Administration (FDA) SARS-CoV-2 Viral Mutations: Impact on COVID-19 Tests. <https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-viral-mutations-impact-covid-19-tests>. Current June 3, 2021. Accessed June 8, 2021.

US Food and Drug Administration (FDA). Visby Medical. COVID-19 Point of Care [Emergency Use Authorization]. <https://www.fda.gov/media/145917/download>. February 2021. Accessed February 17, 2021.

Wang C, Horby PW, Hayden FG, Gao GF. A novel coronavirus outbreak of global health concern [published online January 24, 2020] [published correction appears in *Lancet* January 29, 2020]. *Lancet*. 2020a Feb 15;395(10223):470-473. [\[PubMed 31986257\]](#)

Wang W, Xu Y, Gao R, et al. Detection of SARS-CoV-2 in Different Types of Clinical Specimens. *JAMA*. 2020b May 12;323(18):1843-1844. doi: 10.1001/jama.2020.3786. [\[PubMed 32159775\]](#)

Wölfel R, Corman VM, Guggemos W, et al. Virological assessment of hospitalized patients with COVID-2019. *Nature*. 2020 May;581(7809):465-469. doi: 10.1038/s41586-020-2196-x. Epub 2020 Apr 1. [\[PubMed 32235945\]](#)

World Health Organization (WHO). Coronavirus disease 2019 (COVID-19). Situation reports. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports/>. Updated July 8, 2021. Accessed July 9, 2021.

World Health Organization (WHO). Coronavirus disease (COVID-19) technical guidance: Laboratory testing for 2019-nCoV in humans. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/laboratory-guidance>. Updated February 7, 2020a. Accessed February 13, 2020.

World Health Organization (WHO). Diagnostic testing for SARS-CoV-2 [interim guidance]. <https://www.who.int/publications/i/item/diagnostic-testing-for-sars-cov-2>. Published September 11, 2020b. Accessed December 9, 2020.

World Health Organization (WHO). Laboratory testing for coronavirus disease 2019 (COVID-19) in suspected human cases. <https://www.who.int/publications-detail/laboratory-testing-for-2019-novel-coronavirus-in-suspected-human-cases-20200117>. Published March 2, 2020c. Accessed March 9, 2020.

Young BE, Ong SWX, Kalimuddin S, et al. Epidemiologic Features and Clinical Course of Patients Infected With SARS-CoV-2 in Singapore [published online ahead of print, 2020 Mar 3]. *JAMA*. [\[PubMed 32125362\]](#)

Zou L, Ruan F, Huang M, et al. SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients. *N Engl J Med*. 2020;382(12):1177-1179. [\[PubMed 32074444\]](#)

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