

Influenza and SARS-CoV-2 Antigen, Upper 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 Beware of Fraud 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](#).

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

Related Information

- [COVID-19 Antigen, Upper Respiratory Specimen](#)
- [COVID-19, PCR, Respiratory Specimen](#)
- [COVID-19, PCR, Saliva](#)
- [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 400 million infections have been confirmed globally in over 200 countries and territories with over 6 million deaths ([WHO 2022](#)).

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](#)).

Both molecular (current gold standard) and antigen testing have been developed for the diagnosis of SARS-CoV-2 infection. Because COVID-19 infection symptoms can be similar to influenza and other respiratory infections caused by various pathogens, several molecular panels have been developed for qualitative differentiation of nucleic acid from multiple organisms. The FDA has also issued emergency use authorizations (EUA) for Influenza/SARS-CoV-2 Antigen testing. See FDA [EUA](#). These assays provide simultaneous detection and differentiation of SARS-CoV-2 and Influenza A/B viral proteins in nasopharyngeal (NP) and nasal swab (NS) specimens.

Antigen tests are generally less sensitive than nucleic acid amplification tests (NAAT) but due to ease of use, quick turnaround, reduced cost, and point of care availability, this type of assay is useful for quick diagnosis of symptomatic patients.

Use/Indications

Aid in the diagnosis of infection with SARS-CoV-2, influenza A, and/or influenza B; the detection of organism nucleocapsid protein antigens also provides epidemiological and surveillance information.

Test Includes

Rapid qualitative detection, differentiation, and identification of nucleocapsid protein from SARS-CoV-2, influenza A and/or influenza B directly from nasopharyngeal (NP) or nasal (NS) swab specimen in symptomatic patient.

- Quidel Sofia 2 Flu + Sars Antigen: Rapid qualitative detection, differentiation, and identification of nucleocapsid protein from SARS-CoV-2, influenza A and/or influenza B directly from nasopharyngeal (NP) or nasal (NS) swab specimen within 5 days of symptom onset. **Note:** The assay does not differentiate between SARS-CoV-2 and SARS-CoV. If differentiation of specific SARS or influenza A subtypes and strains is needed, additional testing, in consultation with state or local public health departments, is necessary.
- Status COVID-19/Flu: Rapid qualitative detection, differentiation, and identification of nucleocapsid protein from SARS-CoV-2, influenza A and/or influenza B directly from nasopharyngeal (NP) swab specimen within 5 days of symptom onset. **Note:** The assay does not differentiate between SARS-CoV-2 and SARS-CoV. If differentiation of specific SARS or influenza A subtypes and strains is needed, additional testing, in consultation with state or local public health departments, is necessary.
- BD Veritor SARS-CoV-2 & Flu A+B: Rapid qualitative detection, differentiation, and identification of nucleocapsid protein from SARS-CoV-2, influenza A and/or influenza B directly from nasal swab specimen within 6 days of symptom onset. Designed for point of care use. Specimen must be tested within one hour of collection.

Specimen

Note: Manufacturer dependent; follow kit instructions for proper specimen.

Nasopharyngeal (NP) specimen collected by a trained health care professional

Anterior nares (nasal swab; NS) specimen collected by a trained health care professional, or by a supervised or unsupervised onsite self-collection

Container(s)

- NP specimen: Swab provided in kit or nylon flocked nasopharyngeal swab
- NS specimen: Swab provided in kit

Volume / Minimum Volume

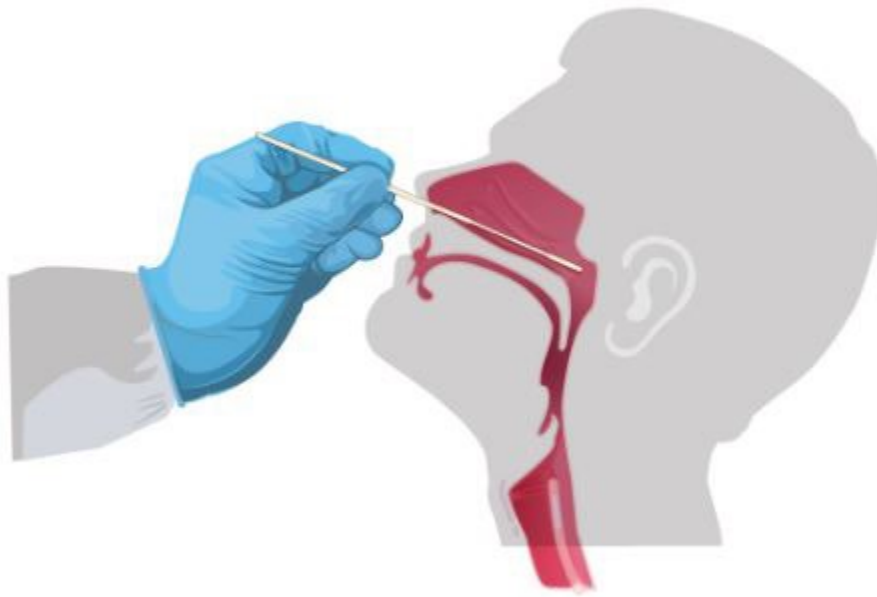
1 nasopharyngeal or 1 nasal swab

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.

Specimen should be collected within 5 to 6 days of symptom onset. Follow manufacturer's recommendations.

Nasopharyngeal swab: Tilt patient's head back 70 degrees. Using swab provided in kit or a nylon flocked NP swab, 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 in clean, dry transport tube and transport to laboratory immediately. Sample should be tested as possible after collection. See [CDC Nasopharyngeal Specimen Collection Steps](#).



CDC Interim Guidelines for Collecting 2021

Nasal swab (anterior nares): Patient should be instructed to blow their nose prior to collection (manufacturer dependent). Using swab provided in kit, insert the swab into nostril that visually shows the most secretion. While gently rotating, push the swab until resistance is met at the level of the turbinates (less than one inch into the nostril). Rotate the swab several times against the nasal wall then remove it from the nostril. Place in clean, dry transport tube and transport to laboratory immediately. Sample should be tested as possible after collection. Note: Dual nares sampling may be preferred. Follow manufacturer instructions for correct collection procedure. See [CDC How to collect Your Anterior Nasal Swab Sample for COVID-19 Testing](#).

Processing and Storage

- Testing should be performed immediately after collection.

Stability

- Room temperature: 1 to 48 hours (manufacturer dependent)
- Refrigerated: 8 to 48 hours (manufacturer dependent)

Causes for Rejection

Specimen placed in transport media; inadequate/inappropriate specimen collection, storage, or transport can interfere with test results

Methodology

- Quidel Sofia 2 Flu + Sars Antigen: Lateral Flow/Fluorescent Immunoassay (FIA), instrument read
- Status COVID-19/Flu: Lateral Flow, visual read
- BD Veritor SARS-CoV-2 & Flu A+B: Rapid immunochromatographic Digital Immunoassay, instrument read

Normal Values/Findings

Negative or not detected

Positive results are indicative of active infection

All positive SARS-CoV-2 results must be reported to local/state health departments.

Interpretative Information

- A positive result indicates the presence of SARS and/or influenza viral antigens; 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).
 - **Note:** Coinfection with Influenza A, B and/or SARS-CoV-2 is rare. If results are positive for more than one antigen, retesting is recommended (Status 2021).
- A negative test result means that SARS and/or influenza viral antigens were not present in the specimen above the limit of detection, thus a negative result does not rule out the possibility of either infection and should not be used as the sole basis for patient management decisions.
 - A negative SARS result should be treated as presumptive and should be confirmed with an FDA-authorized molecular assay if necessary, for clinical management and infection control.
 - A negative result for influenza A or B is presumptive and should be confirmed with an FDA-authorized molecular assay or by viral culture if necessary, for clinical management and including infection control .

Limitations

- Inadequate specimen collection, improper specimen handling and/or transport can cause false testing results.
- Antigen levels below the assay detection limit can yield false-negative results.
- Specimen obtained outside of recommended collection time window (from symptom onset) is more likely to be negative when compared to a PCR assay.
- Use of viral transport media (VTM) or universal transport media (UTM) can interfere with antigen tests designed for direct testing; false positive, false negative, or invalid results can occur. Follow test kit instructions for proper specimen collection and transport.
- Positive results do not rule out coinfections with other pathogens.

- Both viable and nonviable influenza A, influenza B, SARS-CoV, and SARS-CoV-2 are detected; positive results do not differentiate between SARS-CoV and SARS-CoV-2.
- Individuals who received nasally administered influenza A vaccine may have positive influenza A test results for up to three days after vaccination.
- Monoclonal antibodies can fail to detect, or detect with less sensitivity, viruses that have undergone minor amino acid changes in the target epitope region.

Diagnostic Role

Similar to COVID-19 illness (and other respiratory infections caused by various pathogens), the most common symptoms of influenza are fever, cough, shortness of breath, fatigue, headache, myalgia, and arthralgia. Because treatment is available for some viral infections it is important to identify the correct pathogen and also investigate possible coinfection - which has been noted in some COVID-19 patients (Ding 2020; Kim 2020).

Laboratory/Diagnostic Pearls

- Children tend to shed influenza virus more abundantly and for longer periods of time than adults. Testing samples from adults may yield lower sensitivity than testing samples from children (FDA Sofia2 2020).
- During peak activity when prevalence of disease is high, false negative test results are more likely; during periods of low disease prevalence, false positive test results are more likely.

Additional Information

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

See: [Flu Symptoms and Diagnosis](#)

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

COVID-19, Influenza Antigen; Flu SC2; Influenza A Antigen; Influenza B Antigen; SARS-CoV-2, Influenza Antigen

Applies to

Pandemic; Seasonal Influenza

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Last Updated 3/22/22



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