Coronavirus Disease (COVID-19) 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. Currently the only way to be tested for COVID-19 is through licensed health care providers. 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 2020). Any concerns regarding fraudulent products, including tests, should be sent to: FDA-COVID-19-Fraudulent-Products@fda.hhs.gov.

Related Information

- Coronavirus Disease (COVID-19) Antibody (IgG) Serum or Plasma
- Coronavirus Disease (COVID-19) Antibody Total Serum or Plasma
- Coronavirus Disease (COVID-19) Antibody, IgG/IgM Rapid Test, Whole Blood, Serum, or Plasma
- Coronavirus Disease (COVID-19), PCR, Respiratory Specimen
- Coronavirus Disease (COVID-19), PCR, Saliva
- Influenza SARS-CoV-2 Multiplex Assay, CDC

Overview

At the end of 2019, a novel coronavirus was identified as the cause of several cases of pneumonia in Wuhan City, Huber 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 42 million infections have been confirmed globally in over 200 countries and territories with over 1.1 million deaths (WHO situation rept 2020).

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 (COVID-19)**. The virus is thought to spread mainly by respiratory droplets produced when an infected person coughs or sneezes. The droplets can land in the mouths, noses and eyes of nearby people, or possibly be inhaled into the lungs. Touching a contaminated surface and transferring to eyes, nose or mouth is also thought to be a mode of transmission although not as dominant as by respiratory droplets. 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 3 percent (WHO situation rept 2020). The CDC currently estimates that about 40% of COVID-19 infections are asymptomatic, and 50% of transmission occurs prior to symptom onset (CDC Pandemic Planning 2020). Currently, there is no vaccine or specific treatment; care is supportive.

Although molecular nucleic acid polymerase chain reaction tests have become the current gold standard method for diagnosis of SARS-CoV-2 infection (see COVID-19, Respiratory Specimen), antigen testing is also being developed as a simpler and more rapid turnaround (~15 minutes) method. The FDA has issued an emergency use authorizations (EUAs) for the direct detection of SARS-CoV-2 viral proteins in nasopharyngeal (NP) and nasal swab (NS) specimens (See FDA EUA). These assays are authorized for use by trained laboratory personnel and individuals trained in point of care settings.

Use/Indications

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

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), Considerations for COVID-19 Diagnostics (Molecular or Antigen) Testing and

Infectious Diseases Society of America Guidelines on the Diagnosis of COVID-19.

Note: Testing for other respiratory pathogens by the provider should be done as part of the initial work-up and should not delay specimen shipping to CDC or qualified laboratory. If a patient tests positive for another respiratory pathogen, after clinical evaluation and consultation with public health authorities, they may no longer be considered a person under investigation (PUI).

Test Includes

Quidel Sofia® SARS Antigen FIA: Qualitative detection of the nucleocapsid protein antigen from SARS-CoV and SARS-CoV-2 in NP or NS specimens directly, within first five days of symptom onset. **Note:** This assay detects both viable (live) and nonviable SARS-CoV and SARS-CoV-2. It does **not** differentiate between the two viruses.

BD Veritor™ System: Qualitative detection of SARS-CoV-2 nucleocapsid antigens in nasal swabs (NS) directly, within first five days of symptom onset. **Note:** This assay detects both viable (live) and nonviable SARS-CoV-2.

LuminraDx™ SARS-CoV-2 Ag Test: Qualitative detection of the nucleocapsid protein antigen from SARS-CoV and SARS-CoV-2 directly in nasal swab (NS) specimen within 12 days of symptom onset. **Note:** This assay detects both viable (live) and nonviable SARS-CoV and SARS-CoV-2. It does **not** differentiate between the two viruses.

BinaxNOW™ COVID-19 Ag CARD: Qualitative detection of the nucleocapsid protein antigen from SARS-CoV and SARS-CoV-2 directly from nasal swab (NA) specimen within 7 days of symptom onset. **Note:** This assay detects both viable (live) and nonviable SARS-CoV and SARS-CoV-2. It does **not** differentiate between the two viruses.

CareStart™ COVID-19 Antigen: Qualitative detection of nucleocapsid protein antigen from SARS-CoV-2 in nasopharyngeal swab specimen directly or in transport media within 5 days of symptom onset. This assay detects both viable (live) and nonviable SARS-CoV-2.

Specimen

Nasopharyngeal swab or nasal swab tested directly or placed in viral transport media (follow manufacturer requirements)

Container(s)

- Confer with testing laboratory for proper specimen container and collection.
- NP specimen: Swab provided in kit or nylon flocked nasopharyngeal swab
- NS specimen: Swab provided in kit

Volume / Minimum Volume

1 NP swab 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 prelabeled. Use computer-generated label(s), if available, to avoid transcription errors.

Specimen should be collected by trained health care professional using proper infection control techniques and wearing personal protective equipment, including an N95 respirator (or facemask if respirator is not available), eye protection, gloves, and a gown.

- **NP swab:** Insert swab into nostril that displays the most secretion under visual inspection. Keep the swab near the septum floor of the nose while gently pushing the swab into the posterior nasopharynx. Rotate the swab several times then remove from nostril. Refer to manufacturer instructions as most kits require direct testing only, however; viral transport media maybe be allowed for some specimens.
- **NS (anterior nares):** Insert swab into nostril that displays the most secretion under visual inspection. Using gentle rotation, 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 and remove from nostril. Follow instructions with kit as some manufacturers recommend sampling both nostrils with the same swab. Refer to manufacturer instructions as most kits require direct testing only, however; viral transport media maybe be allowed for some specimens.

Processing and Storage

- Refer to manufacturer instructions.

Stability

Swab without VTM

- Some kits state specimen must be tested within one hour of collection; storage is not appropriate.
- Room temperature: 24-48 hours (manufacturer dependent)
- Refrigerated: 24-48 hours (manufacturer dependent)

Swab in VTM (manufacturer dependent, follow instructions with kit)

Methodology

Quidel Sofia and Sofia®2: Lateral Flow Immunofluorescent Assay for the detection of SARS-CoV and SARS-CoV-2. This methodology does not differentiate between the two viruses.

BD Veritor™: Chromatographic Digital Immunoassay for the detection of SARS-CoV-2

LumiraDx™: Microfluidic Immunofluorescence Assay for the detection of SARS-CoV and SARS-CoV-2. This methodology does not differentiate between the two viruses.

BinaxNOW™: Lateral flow immunoassay for detection of SARS-CoV and SARS-CoV-2.This methodology does not differentiate between the two viruses.

CareStart™: Lateral flow immunochromatographic assay for qualitative detection of SARS-CoV-2

Normal Values/Findings

Negative

Interpretative Information

- A positive result indicates presence of viral antigens. Result should be correlated with patient history and other diagnostic information. All positives must be reported to local/state health departments.
- A negative result should be treated as presumptive and confirmed with a molecular assay, if necessary, for clinical management, including infection control (Sofia® 2020; Veritor™ 2020).

Limitations

- Antigen levels below the assay detection limit can yield false-negative results.
- Use of viral transport media can dilute specimen and result in decreased test sensitivity; direct testing of specimen is recommended.
- Positive results do not rule out coinfections with other pathogens.
- Both viable and nonviable virus is detected
- In some test kits, positive results do not differentiate between SARS-CoV and SARS-CoV-2, consult package insert
- Monoclonal antibodies can fail to detect, or detect with less sensitivity, SARS-CoV-2 viruses that have undergone minor amino acid changes in the target epitope region.
- Presence of biotin can cause false negative results (CareStart™ 2020)

Statistical Validity

The sensitivity of rapid antigen testing is typically lower than RT-PCR testing; 84% to 97% compared to RT-PCR. Specificity is comparable to RT-PCR at 100% (CDC Rapid Ag Testing 2020)

Laboratory/Diagnostic Pearls

- PUI: Any person who is under investigation for having SARS-CoV-2 that causes COVID-19 or who was under investigation but tested negative.
- 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 PUI.
- 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) (WHO Q&A 2020).
- High SARS-CoV-2 viral loads (more in nose than throat) can be detected soon after symptom onset (within first week) and can also be found in the asymptomatic patient (Zou 2020). Viral shedding may continue for days after symptom relief and recovery (Lan 2020). Median range of viral shedding among hospitalized patients has been documented as 12 to 20 days (Zhou 2020; Young 2020).
- 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, although it has not been found to be replication competent. If tested within 3 months of initial infection, the individuals may continue to have a positive test result, however; there is no evidence that they are contagious (CDC Duration of Isolation 2020).

Additional Information

For more information, interim guidance has been issued by the United States CDC and the World Health Organization.

See: Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens from Persons Under Investigation (PUIs) for Coronavirus Disease 2019 (COVID-19).

See: Information for Laboratories

See: COVID-19 Testing and Reporting by Laboratories: Q & A

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

See: For Healthcare Professionals

See: FDA Emergency Use Authorizations

The CDC has developed a serologic test for detection of antibodies to SARS-CoV-2. This will assist in determining how much of the US population has been exposed to the virus. This test is not designed for testing individuals who want to know if they have been previously infected with SARS-CoV-2; however, commercially manufactured serologic tests for COVID-19 antibodies are becoming increasingly available.

Index Terms

2019 Novel Coronavirus; 2019-nCoV; Antigen Test for COVID-19; COVID-19 Antigen; COVID-19 Antigen Test; COVID-19 Direct Detection; COVID-19 Rapid Antigen Testing; nCoV, 2019; Novel Coronavirus, 2019; Qualitative COVID-19; SARS-CoV-2; SARS-CoV-2 Antigen Test; Severe Acute Respiratory Syndrome Coronavirus 2; Wuhan

Applies to

Pandemic; Person Under Investigation (PUI); Pneumonia of Unknown Etiology; Sofia 2 SARS Antigen FIA

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