

## Coronavirus Disease (COVID-19) Neutralization Antibody, Serum or Plasma (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](#)). Consumers and health care professionals can help by reporting suspected fraud to the [FDA's Health Fraud Program](#) or the [Office of Criminal Investigations](#).

### 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 \(COVID-19\) Antigen, Upper Respiratory Specimen](#)
- [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, 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 79 million infections have been confirmed globally in over 200 countries and territories with over 1.7 million deaths ([WHO situation report 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 larger respiratory droplets (and less commonly, small aerosol droplets) produced when an infected person exhales (eg, breathes, speaks, coughs, sneezes, or sings). 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 efficient 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 2 to 3 percent ([WHO situation report 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.

SARS-CoV-2 infection is diagnosed by direct detection of nucleic acid or the slightly less sensitive direct detection of SARS-CoV-2 nucleocapsid protein antigen. These tests are supported by antibody detection (total, IgG, and/or IgM) assays which provide evidence of immune response. Most of the current clinical lab tests detect the presence of binding antibodies. Binding antibodies (or nonneutralizing antibodies) recognize and bind to a pathogen or virus, but do not necessarily decrease the infection or cause destruction. Neutralizing antibodies interfere with pathogen entrance into host cells thus preventing pathogen replication.

Following infection with SARS-CoV-2, most individuals mount a cell-mediated response and production of SARS-CoV-2-specific antibodies. Some of these antibodies are specific to the receptor-binding domain (RBD) of the viral spike protein and are associated with neutralizing activity (Premkumar 2020; Wölfel 2020). Neutralization tests determine the ability of the antibodies to prevent infection in vitro. Traditional neutralization tests involve the use of live virus or pseudovirus incubated with serum or plasma containing the "suspect" antibodies. Testing can take up to 5 days and must be performed in a BSL-3 or BSL-2 laboratory. This assay is a modified ELISA detection assay that mimics virus neutralization by using purified SARS-CoV-2 receptor binding domain (RBD) conjugated to horseradish peroxidase and purified human ACE2 receptor to detect antibodies that prevent the binding of RBD to the ACE2 receptor. Results can be available in approximately 60 minutes.

#### Use/Indications

Identifying adaptive immune response, indicating recent or prior SARS-CoV-2 infection. At this time it is not known whether presence of neutralizing antibodies indicates immunity and caution is urged about its utility at this point in the pandemic.

#### Test Includes

Qualitative direct detection of total neutralizing antibodies to SARS-CoV-2. This test focuses on antibodies specific for the "spike" protein that prevent the virus from binding to the ACE2 receptor and entering host cells thus preventing viral replication. The assay mimics the binding of the virus to the ACE2 receptor by using just the purified protein.

#### Specimen

Serum or plasma

#### Container(s)

- Serum separator tube or lavender top (EDTA) tube

#### Volume / Minimum Volume

Tube filled to capacity or 1 mL blood (0.5 mL serum or plasma)

#### 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.

Routine venipuncture, using appropriate personal protective equipment; transport to laboratory immediately.

#### Processing and Storage

- Allow serum separator tube to clot for 30 minutes at room temperature. Centrifuge and transfer serum into clean, plastic vial. Run assay immediately or freeze specimen at -20°C.
- Centrifuge lavender top (EDTA) tube within 30 minutes of collection and transfer plasma into clean, plastic vial. Run assay immediately or freeze specimen at -20°C.

#### Methodology

Modified ELISA assay; detection of neutralizing antibodies that block interaction of purified SARS-CoV-2 receptor binding domain (RBD) with purified human ACE2

#### Normal Values/Findings

Negative; neutralizing antibodies for SARS-CoV-2 not detected

Positive; neutralizing antibodies for SARS-CoV detected

#### Interpretative Information

Results of the test should not be interpreted as having any level of immunity from the virus or protection from reinfection. Results should not be used to diagnose or exclude acute SARS-CoV-2 infection.

#### Limitations

- Negative results do not rule out SARS-CoV-2 infection.
- False positive results may be due to cross-reaction with non-SARS-CoV-2 coronavirus strains including HKU1, NL63, OC43, 229E.
- False positive results may be due to cross-reaction with SARS-CoV-1 neutralizing antibodies.
- This test should not be used for blood donor screening.
- It is not known at this time if the presence of SARS-CoV-2 antibodies confers immunity to reinfection.

#### Diagnostic Role

Understanding the antibody response to SARS-CoV-2 is still in the early stages and clinical utility is not completely established. When more information is acquired, the potential of serology testing may include:

- Identification of convalescent plasma donors; selecting optimal units for therapy
- Determining seroprevalence or immunity levels in the community
- Possible verification of vaccine response
- Humoral protective immunity in recovered patients (Tan 2020)
- Investigation of asymptomatic infection rate (Tan 2020)

Note: At this time, it is unknown for how long antibodies persist following infection and if the presence of antibodies confers protective immunity.

#### Additional Information

A coronavirus contains 4 structural proteins: Spike (S), envelope (E), membrane (M), and nucleocapsid (N) proteins. S protein plays the most important roles in viral attachment, fusion, and entry to host cells, and serves as a target for development of antibodies, entry inhibitors, and vaccines. The S protein binds to the host cell receptor ACE2 through the receptor-binding domain (RBD), mediating viral entry into host cell; viral replication follows.

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

See: [Interim Guidelines for COVID-19 Antibody Testing](#)

See: [Information for Laboratories](#)

See: [Frequently Asked Questions about Coronavirus \(COVID-19\) for Laboratories](#)

See: [For Healthcare Professionals](#)

See: FDA [Emergency Use Authorizations](#)

#### Index Terms

COVID Neutralization Antibody; COVID-19 Blocking Antibody Test; cPass™ Neutralization Antibody Detection; SARS-CoV-2 Neutralizing Antibody Test; Surrogate Virus Neutralization Test; sVNT

#### Applies to

Pandemic; Pneumonia of Unknown Etiology; RBD; Spike Protein Receptor Binding Domain

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