CLINITEST®

Rapid COVID-19 Antigen Test

SIEMENS Healthineers

INTENDED USE

The CLINITEST® Rapid COVID-19 Antigen Test is an *in vitro* immunochromatographic assay for the qualitative detection of nucleocapsid protein antigen from SARS-CoV-2 in direct nasopharyngeal (NP) swab or nasal swab specimens directly from individuals who are suspected of COVID-19 by their healthcare provider. It is intended to aid in the rapid diagnosis of SARS-CoV-2 infections and can be used by healthcare professionals up to ten days post symptom onset, or to screen asymptomatic individuals or individuals from areas of low infection prevalence. Negative results from patients with symptom onset beyond ten days should be treated as presumptive and confirmation with a molecular assay, if necessary, for patient management, may be performed. The CLINITEST Rapid COVID-19 Antigen Test does not differentiate between SARS-CoV and SARS-CoV-2. The test also provides individuals with the option to self-collect their nasal sample under the supervision of a healthcare professional.

SUMMARY AND EXPLANATION

The novel coronaviruses belong to the β genus. COVID-19 is an acute respiratory infectious disease. People are generally susceptible. Currently, the patients infected by the novel coronavirus are the main source of infection; asymptomatic infected people can also be an infectious source. Based on the current epidemiological investigation, the incubation period is 1 to 14 days, mostly 3 to 7 days. The main manifestations include fever, fatigue, and dry cough. Nasal congestion, runny nose, sore throat, myalgia, and diarrhea are found in a few cases.

This test is for detection of SARS-CoV-2 nucleocapsid protein antigen. Antigen is generally detectable in upper respiratory specimens during the acute phase of infection. Rapid diagnosis of SARS-CoV-2 infection will help healthcare professionals to treat patients and control the disease more efficiently and effectively.

PRINCIPLE OF THE TEST

The CLINITEST Rapid COVID-19 Antigen Test is an immunochromatographic membrane assay that uses highly sensitive monoclonal antibodies to detect nucleocapsid protein from SARS-CoV-2 in direct nasopharyngeal (NP) swab or nasal swab. The test strip is composed of the following parts: namely sample pad, reagent pad, reaction membrane, and absorbing pad. The reagent pad contains the colloidal-gold conjugated with the monoclonal antibodies against the nucleocapsid protein of SARS-CoV-2; the reaction membrane contains the secondary antibodies for nucleocapsid protein of SARS-CoV-2. The whole strip is fixed inside a plastic device. When the sample is added into the sample well, conjugates dried in the reagent pad are dissolved and migrate along with the sample. If SARS-CoV-2 nucleocapsid antigen is present in the sample, a complex forms between the anti-SARS-2 conjugate and the virus will be captured by the specific anti-SARS-2 monoclonal antibodies coated on the test line region (T). Absence of the test line (T) suggests a negative result. To serve as a procedural control, a red line will always appear in the control line region (C) indicating that proper volume of sample has been added and membrane wicking has occurred.

MATERIALS PROVIDED

20 Test Cassettes
2 Extraction Buffer Vials
20 Sterile Swabs
20 Extraction Tubes and Tips
1 Workstation
1 Package Insert

MATERIALS REQUIRED BUT NOT PROVIDED

1. Clock, timer, or stopwatch

WARNINGS AND PRECAUTIONS

1. For *in vitro* diagnostic use only.
2. The test device should remain in the sealed pouch until use.
3. Do not use kit past its expiration date.
4. Swabs, tubes, and test devices are for single use only.
5. Solutions that contain sodium azide may react explosively with lead or copper plumbing. Use large quantities of water to flush discarded solutions down a sink.
6. Do not interchange or mix components from different kit lots.
7. Testing should only be performed using the swabs provided within the kit.
8. To obtain accurate results, do not use visually bloody or overly viscous samples.
9. Wear appropriate personal protection equipment and gloves when running each test and handling patient specimens. Change gloves between handling of specimens suspected of COVID-19.
10. Specimens must be processed as indicated in the SPECIMEN COLLECTION and SAMPLE PREPARATION PROCEDURE sections of this Product Insert. Failure to follow the instructions for use can result in inaccurate results.
11. Proper laboratory safety techniques should be followed at all times when working with SARS-CoV-2 patient samples. Patient swabs used Test Strips and used extraction buffer vials may be potentially infectious. Proper handling and disposal methods should be established by the laboratory in accordance with local regulatory requirements.
12. Inadequate or inappropriate specimen collection and storage can adversely affect results.
13. Humidity and temperature can adversely affect results.
14. Dispose of test device and materials as biohazardous waste in accordance with federal, state, and local requirements.

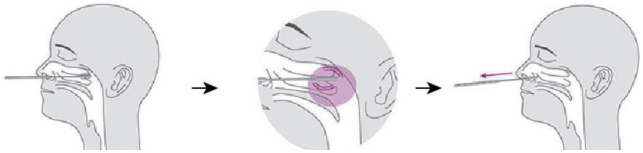
STORAGE AND STABILITY

1. The kit can be stored at room temperature or refrigerated (2-30°C).
2. Do not freeze any of the test kit components.
3. Do not use test device and reagents after expiration date.
4. Test devices that have been outside of the sealed pouch for more than 1 hour should be discarded.
5. Close the kit box and secure its contents when not in use.

SPECIMEN COLLECTION

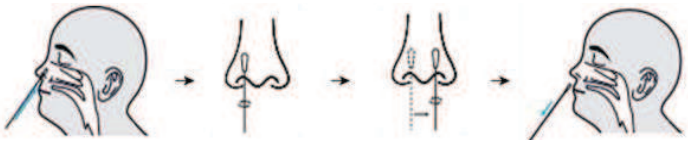
1. Nasopharyngeal Swab

1) Using the sterile swab provided in the kit, carefully insert the swab in the patient's nostril.
2) Swab over the surface of the posterior nasopharynx and rotate the swab several times.
3) Withdraw the swab from the nasal cavity. The specimen is now ready for preparation using the extraction buffer provided in the test kit.



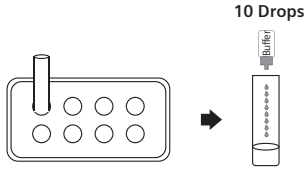
2. Nasal Swab

1) Using the sterile swab provided in the kit, carefully insert the swab into one nostril of the patient. The swab tip should be inserted up to 2-4 cm until resistance is met.
2) Roll the swab 5 times along the mucosa inside the nostril to ensure that both mucus and cells are collected.
3) Using the same swab, repeat this process for the other nostril to ensure that an adequate sample is collected from both nasal cavities.
4) Withdraw the swab from the nasal cavity. The specimen is now ready for preparation using the extraction buffer provided in the test kit.

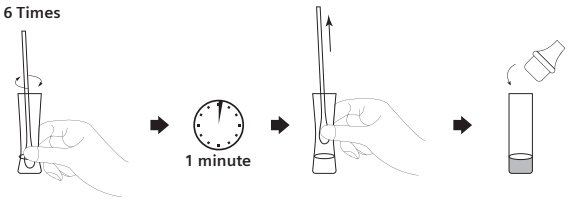


SAMPLE PREPARATION PROCEDURE

1. Insert the test extraction tube into the workstation provided in the kit. Make sure that the tube is standing upright and reaches the bottom of the workstation.
2. Add 0.3 mL (approximately 10 drops) of the sample extraction buffer into the extraction tube.



3. Insert the swab into the extraction tube which contains 0.3 mL of the extraction buffer.
4. Roll the swab at least 6 times while pressing the head against the bottom and side of the extraction tube.
5. Leave the swab in the extraction tube for 1 minute.
6. Squeeze the tube several times from the outside to immerse the swab. Remove the swab.



SPECIMEN TRANSPORT AND STORAGE

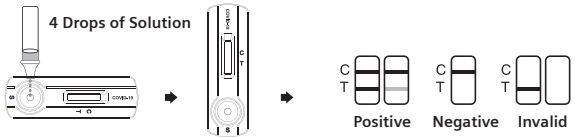
Do not return the sterile swab to the original paper packaging.

Specimen should be tested immediately after collection. If immediate testing of specimen is not possible, insert the swab into an unused general-purpose plastic tube. Ensure the breakpoint swab is level with the tube opening. Bend the swab shaft at a 180 degrees angle to break it off at the breaking point. You may need to gently rotate the swab shaft to complete the breakage. Ensure the swab fits within the plastic tube and secure a tight seal. The specimen should be disposed and recollected for retesting if untested for longer than 1 hour.

TEST PROCEDURE

Allow the test device, test sample and buffer to equilibrate to room temperature (15-30°C) prior to testing.

1. Just prior to testing remove the test device from the sealed pouch and place it on a flat surface.
2. Push the nozzle which contains the filter onto the extraction tube. Ensure the nozzle has a tight fit.
3. Hold the extraction tube vertically and add 4 drops (approximately 100 µL) of test sample solution tube into the sample well.
4. Start the timer.
5. Read the results at 15 minutes. Do not interpret the result after 20 minutes.



INTERPRETATION OF RESULTS

1. POSITIVE:

The presence of two lines as control line (C) and test line (T) within the result window indicates a positive result.

2. NEGATIVE:

The presence of only control line (C) within the result window indicates a negative result.

3. INVALID:

If the control line (C) is not visible within the result window after performing the test, the result is considered invalid. Some causes of invalid results are because of not following the directions correctly or the test may have deteriorated beyond the expiration date. It is recommended that the specimen be re-tested using a new test.

NOTE:

1. The intensity of color in the test line region (T) may vary depending on the concentration of analyses present in the specimen. Therefore, any shade of color in the test line region (T) should be considered positive. This is a qualitative test only and cannot determine the concentration of analytes in the specimen.
2. Insufficient specimen volume, incorrect operating procedure or expired tests are the most likely reasons for control band failure.

QUALITY CONTROL

A procedural control is included in the test. A red line appearing in the control line region (C) is the internal procedural control. It confirms sufficient specimen volume and correct procedural technique. Control standards are not supplied with this test. However, it is recommended that positive and negative controls are sourced from a local competent authority and tested as a good laboratory practice, to confirm the test procedure and verify the test performance.

LIMITATIONS

1. The etiology of respiratory infection caused by microorganisms other than SARS-CoV-2 will not be established with this test. The CLINITEST Rapid COVID-19 Antigen Test can detect both viable and non-viable SARS-CoV-2. The performance of the CLINITEST Rapid COVID-19 Antigen Test depends on antigen load and may not correlate with viral culture results performed on the same specimen.
2. Failure to follow the Test Procedure may adversely affect test performance and/or invalidate the test result.
3. If the test result is negative and clinical symptoms persist, additional testing using other clinical methods is recommended. A negative result does not at any time rule out the presence of SARS-CoV-2 antigens in specimen, as they may be present below the minimum detection level of the test or if the sample was collected or transported improperly.
4. As with all diagnostic tests, a confirmed diagnosis should only be made by a physician after all clinical and laboratory findings have been evaluated.
5. Positive test results do not rule out co-infections with other pathogens.
6. Positive test results do not differentiate between SARS-CoV and SARS-CoV-2.
7. The amount of antigen in a sample may decrease as the duration of illness increases. Specimens collected after day 10 of illness are more likely to be negative compared to a RT-PCR assay.
8. Negative results from patients with symptom onset beyond ten days, should be treated as presumptive and confirmation with a molecular assay, if necessary, for patient management, may be performed.
9. Negative results do not rule out SARS-CoV-2 infection and should not be used as the sole basis for treatment or patient management decisions, including infection control decisions.

PERFORMANCE CHARACTERISTICS

1. Clinical Sensitivity, Specificity and Accuracy

Nasopharyngeal Swab

Clinical Performance of the CLINITEST Rapid COVID-19 Antigen Test was evaluated by being involved in 7 sites within the US where patients were enrolled and tested. Testing was performed by 24 Healthcare Workers that were not familiar with the testing procedure. A total of 865 fresh nasopharyngeal swab samples were collected from symptomatic and asymptomatic individuals and tested, which included 119 positive samples and 746 negative samples. The CLINITEST Rapid COVID-19 Antigen Test results were compared to US FDA Emergency Use Authorized RT-PCR assays for SARS-CoV-2 in nasopharyngeal swab specimens.

Overall study results are shown in **Table 1**.

Table 1: CLINITEST Rapid COVID-19 Antigen Test (Nasopharyngeal Swab) vs PCR

Method		PCR		Total Results
CLINITEST Rapid COVID-19 Antigen Test (Nasopharyngeal Swab)	Results	Positive	Negative	
	Positive	117	3	120
	Negative	2	743	745
Total		119	746	865

Relative Sensitivity: 98.32% (95% CI* 94.06% to 99.80%)
Relative Specificity: 99.60% (95% CI* 98.83% to 99.92%)
Accuracy: 99.42% (95%CI* 98.66% to 99.81%)

*Confidence Intervals

Nasal Swab

A total of 237 fresh nasal swab samples were collected from symptomatic and asymptomatic individuals and tested, which included 109 positive samples and 128 negative samples. The CLINITEST Rapid COVID-19 Antigen Test results were compared to results of USFDA Emergency Use Authorized RT-PCR assays for SARS-CoV-2 in nasopharyngeal swab specimens. Overall study results are shown in **Table 2**.

Table 2: CLINITEST Rapid COVID-19 Antigen Test (Nasal Swab) vs PCR

Method		PCR		Total Results
CLINITEST Rapid COVID-19 Antigen Test (Nasal Swab)	Results	Positive	Negative	
	Positive	106	0	106
	Negative	3	128	131
Total		109	128	237

Relative Sensitivity: 97.25% (95% CI*: 92.17% to 99.43%)
Relative Specificity: 100% (95% CI*: 97.69% to 100%)
Accuracy: 98.73% (95%CI*: 96.35% to 99.74%)

*Confidence Intervals

2. Limit of Detection (LOD)

LOD studies determine the lowest detectable concentration of SARS-CoV-2 at which approximately 95% of all (true positive) replicates test positive. Heat inactivated SARS-CoV-2 virus, with a stock concentration of 4.6×10^5 $TCID_{50}$ / mL, was spiked into negative specimen and serially diluted. Each dilution was ran in triplicate on the CLINITEST Rapid COVID-19 Antigen Test. The Limit of Detection of the CLINITEST Rapid COVID-19 Antigen Test is 1.15×10^2 $TCID_{50}$ / mL (**Table 3**).

Table 3: Limit of Detection (LOD) Study Results

Concentration	No. Positive/Total	Positive Agreement
1.15×10^2 $TCID_{50}$ / mL	180/180	100%

3. High Dose Hook Effect

No high dose hook effect was observed when testing up to a concentration of 4.6×10^5 $TCID_{50}$ / mL of heat inactivated SARS-CoV-2 virus.

4. Cross Reactivity

Cross reactivity with the following organisms has been studied. Samples positive for the following organisms were found negative when tested with the CLINITEST Rapid COVID-19 Antigen Test.

Pathogens	Concentration
Respiratory syncytial virus Type A	5.5×10^{7} PFU/mL
Respiratory syncytial virus Type B	2.8×10^{5} $TCID_{50}$/mL
Novel influenza A H1N1 virus (2009)	1×10^{6} PFU/mL
Seasonal influenza A H1N1 virus	1×10^{5} PFU/mL
Influenza A H3N2 virus	1×10^{6} PFU/mL
Influenza A H5N1 virus	1×10^{6} PFU/mL
Influenza B Yamagata	1×10^{5} PFU/mL
Influenza B Victoria	1×10^{6} PFU/mL
Rhinovirus	1×10^{6} PFU/mL
Adenovirus 3	$5\times10^{7.5}$ $TCID_{50}$/mL
Adenovirus 7	2.8×10^{6} $TCID_{50}$/mL
EV-A71	1×10^{5} PFU/mL
Mycobacterium tuberculosis	1×10^{3} bacteria/mL
Mumps virus	1×10^{5} PFU/mL
Human coronavirus 229E	1×10^{5} PFU/mL
Human coronavirus OC43	1×10^{5} PFU/mL
Human coronavirus NL63	1×10^{6} PFU/mL
Human coronavirus HKU1	1×10^{6} PFU/mL
Parainfluenza virus 1	7.3×10^{6} PFU/mL
Parainfluenza virus 2	1×10^{6} PFU/mL
Parainfluenza virus 3	5.8×10^{6} PFU/mL
Parainfluenza virus 4	2.6×10^{6} PFU/mL
Haemophilus influenzae	5.2×10^{6} CFU/mL
Streptococcus pyogenes	3.6×10^{6} CFU/mL
Streptococcus pneumoniae	4.2×10^{6} CFU/mL
Candida albicans	1×10^{7} CFU/mL
Bordetella pertussis	1×10^{4} bacteria/mL
Mycoplasma pneumoniae	1.2×10^{6} CFU/mL
Chlamydia pneumoniae	2.3×10^{6} IFU/mL
Legionella pneumophila	1×10^{4} bacteria/mL
Staphylococcus aureus	3.2×10^{8} CFU/mL
Staphylococcus epidermidis	2.1×10^{8} CFU/mL

5. Interfering Substance

The following substances, naturally present in respiratory specimens or that may be artificially introduced into the nasal cavity or nasopharynx, were evaluated with the CLINITEST Rapid COVID-19 Antigen Test at the concentrations listed below and were found not to affect test performance.

Substance	Concentration
Human blood (EDTA anticoagulated)	20% (v/v)
Mucin	5 mg/mL
Oseltamivir phosphate	5 mg/mL
Ribavirin	5 mg/mL
Levofloxacin	5 mg/mL
Azithromycin	5 mg/mL
Meropenem	5 mg/mL
Tobramycin	2 mg/mL
Phenylephrine	20% (v/v)
Oxymetazoline	20% (v/v)
0.9% sodium chloride	20% (v/v)
A natural soothing ALKALOL	20% (v/v)
Beclomethasone	20% (v/v)
Hexadecadrol	20% (v/v)
Flunisolide	20% (v/v)
Triamcinolone	20% (v/v)
Budesonide	20% (v/v)
Mometasone	20% (v/v)
Fluticasone	20% (v/v)
Fluticasone propionate	20% (v/v)