For Emergency Use Authorization only
For prescription use only
For in vitro diagnostic use only

COVCLEAR COVID-19 RAPID ANTIGEN TEST

INTENDED USE

The CovClear COVID-19 Rapid Antigen Test is a lateral flow immunochromatographic assay intended for the qualitative detection of the nucleocapsid protein antigen from SARS-CoV-2 in nasal swab specimens directly collected.

Testing is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C 263a, to perform moderate or high complexity tests and as applicable and for Point of Care (POC) testing.

This test is intended for use in individuals with or without symptoms or other epidemiological reasons to suspect a COVID-19 infection. Results are for the identification of the SARS-CoV-2 nucleocapsid protein antigen. The antigen is generally detectable in nasal swab specimens during the acute phase of infection. Positive results indicate the presence of viral antigens, but the clinical correlation with patient history and other diagnostic information is necessary to determine infection status. Positive results do not rule out a bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause of disease. Laboratories within the United States and its territories are required to report all results to the appropriate public health authorities.

Negative results are presumptive and confirmation with a molecular assay, if necessary, for patient management may be performed. 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. Negative results should be considered in the context of a patient's recent exposures, history and the presence of clinical signs and symptoms consistent with COVID-19.

The CovClear COVID-19 Antigen Test is intended for use by medical professionals or trained operators who are proficient in performing tests and trained clinical laboratory personnel or individuals trained in Point of Care settings. The CovClear™ COVID-19 Antigen Test is only for use under the Food and Drug Administration's Emergency Use Authorization (EUA).

PRINCIPLES OF THE TEST

The CovClear COVID-19 Rapid Antigen Test is a lateral flow immunochromatographic assay for the detection of extracted nucleocapsid protein antigens specific to SARS-CoV-2 in nasal swab specimens directly collected.

The CovClear COVID-19 Rapid Antigen Test is comprised of five components: polyester swab, lateral flow assay strip, polypropylene vials, locking caps, and chase buffer solution. Each assay strip contains a nitrocellulose membrane coated with antibodies against the SARS-CoV-2 nucleocapsid protein at the test line. A green line will appear at the test line in the presence of the SARS-CoV-2 nucleocapsid protein. The nitrocellulose membrane is also coated with a printed control line that will appear as a blue line until the assay strip has been exposed to the swab sample where it will then appear red. This color change from blue to red will indicate that the test was run successfully.

Nasal swabs require a sample preparation step in which the sample is extracted from the swab and into the chase buffer solution. The assay strip is then placed into the chase buffer solution. When the swab sample migrates up the assay strip the gold nanoparticles labeled with anti-SARS-CoV-2 antibodies will bind the SARS-CoV-2 viral antigens to form an antibody-antigen immune complex. The immune complex is then captured by the test line on the nitrocellulose membrane as it migrates through the strip.

Test results are interpreted between 3 and 20 minutes. The presence of two colored lines, red at the control line and green at the test line, indicates a COVID-19 positive sample. The presence of one red-colored line indicates a COVID-19 negative sample. A blue-colored line or no line at 20 minutes after running the assay indicates an invalid test.

WARNINGS AND PRECAUTIONS

- For prescription and in vitro diagnostic use only.
- The test has been validated but the FDA's independent review of this validation is pending.
- This test is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostic tests for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.
- This test has been authorized only for the detection of proteins from SARS-CoV-2, not for any other viruses or pathogens.
- Immediately use after removing the assay strip from packaging.
- In order to obtain accurate results, the test must follow this package insert.
- Do not interpret the test result before 3 minutes and after 20 minutes of starting the test.
- Do not use if the test device package or its contents are damaged.
- Do not use the kit contents beyond the expiration date.
- Do not eat, drink, or smoke in the area where the specimens and kit contents are handled.
- Use appropriate precautions in the collection, handling, storage, and disposal of samples and used kit contents.
- If the chase buffer contacts the skin or eye, flush with copious amounts of water.
- Handle all specimens as though they contain infectious agents.
- Observe normal precautions against microbiological hazards and proper disposal of specimens.
- Do not interchange kit contents from different lots.
- Do not re-use any contents in the kit as they are single use only.

REAGENTS AND MATERIALS PROVIDED

Materials Provided

KIT COMPONENT	AMOUNT PER KIT
Lateral Flow Assay Strip	50
Chase Buffer Ampule	50
Vial	50
Locking Cap	50
Individually Wrapped Swab	50
Instructions for Use	1

Materials not provided with your test

- Timer

STORAGE AND STABILITY

The reagents and materials in the CovClear COVID-19 Rapid Antigen Test are stable until the expiration date printed on the packaging. Do not use beyond the expiration date. Store at 15°C to 30°C (60°F to 86F) sealed. Do not freeze any contents of the kit.

SPECIMEN COLLECTION AND HANDLING

The CovClear COVID-19 Rapid Antigen Test only uses a direct nasal swab specimen. Only use the swab provided in the kit. It is essential that correct specimen collection and preparation methods be followed.

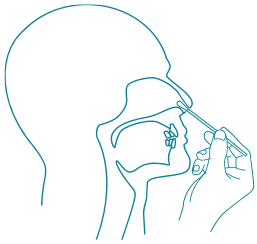
LOWER NOSTRIL SWAB SAMPLE COLLECTION

Procedural Notes:

- Process the test sample immediately after collection.
- Use only provided nasal swab for specimen collection.
- Do not touch the tip (specimen collection area) of the swab.
- Collect samples as soon as possible after the onset of symptoms.

1

Remove a swab from the pouch.



2

Place the dry swab into one of the patient's nostrils until it reaches resistance.

3

Slowly rotate the swab 7 times over the inside surface of the nostril.

4

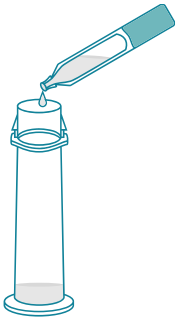
Slowly remove the swab from the nostril while still rotating.

Repeat steps 2-4 on other nostril using the same swab.

DIRECT SWAB TEST PROCEDURE

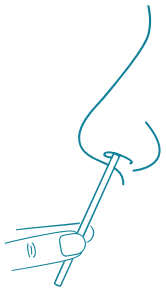
Procedural Notes:

- The test kit should be at room temperature (15-30°C) prior to use.
- Remove the assay strip, vial and locking cap, swab, chase buffer ampules from the kit immediately before testing.
- The CovClear COVID-19 Rapid Antigen Test kit IS INTENDED to be used only with a direct nasal swab specimen.
- The CovClear COVID-19 Rapid Antigen Test kit IS NOT INTENDED for testing other liquid samples such as nasal wash or aspirate samples as results can be compromised by over dilution.



1

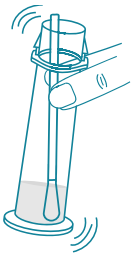
Pour entire buffer solution ampule into empty vial



2

Following the Lower Nostril Sample Collection Procedure, insert dry swab into one nostril until you meet resistance. Swirl 7 times.

Repeat with the same swab in other nostril.

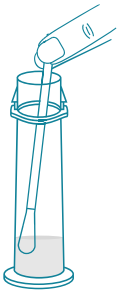


3

Place swab into prepared vial with buffer solution.

Slightly swirl the vial and swab for 30 seconds.

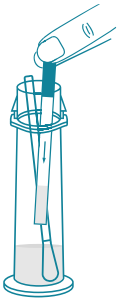
NOTE: DO NOT place the cap on the vial. DO NOT REMOVE SWAB.



4

Press tip against side of vial to squeeze liquid from swab for 10 seconds. Then place swab back into the buffer solution.

NOTE: DO NOT REMOVE SWAB



5

Place new test strip, arrow pointing down, into vial with the swab.

NOTE: Touch test strip on the colored end only.

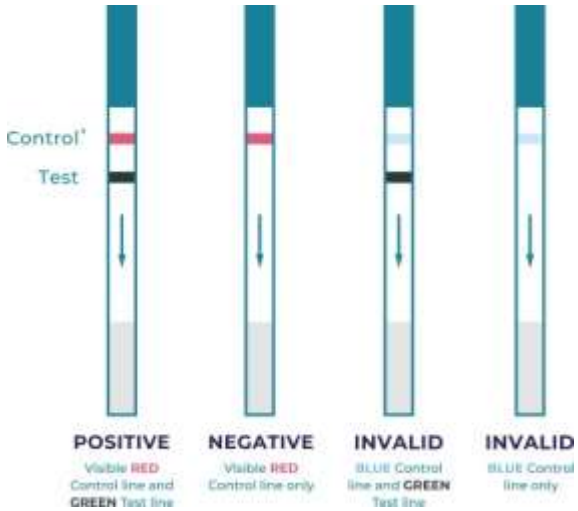
6

Place cap securely onto the vial with the test strip and swab inside.

NOTE: Cap will permanently lock in place. DO NOT tip vial over as this will invalidate the test.

READ RESULTS AT 20 MINUTES.

INTERPRETATION OF RESULTS



NOTE: The test results should be read and interpreted 20 minutes after the sample application and the reading and interpretation of the results should not exceed 20 minutes. The test results should not be interpreted using any instruments.

NOTE: Before use, a blue control line will be visible. It will transition to red when a valid test is performed.

NOTE: The color intensity in the test line (i.e. green-colored line) will vary depending on the amount of SARS-CoV-2 nucleocapsid protein antigen present in the sample. Any faint colored line in the test region should be considered as positive.

POSITIVE: Two distinct colored lines appear: One red-colored line representing the control line and one green-colored line representing COVID-19 positive result.

NEGATIVE: One red-colored line indicates a negative result.

INVALID: If the red-colored line is not visible, the result is invalid. If the test is invalid, a new test should be performed with a new sample collection.

Persons who test positive with the CovClear COVID-19 Rapid Antigen Test should seek follow-up care with their physician or healthcare provider as additional testing and public health reporting may be necessary. Positive results do not rule out bacterial infection or co-infection with other viruses. Persons who test negative and continue to experience COVID-19 like symptoms of fever, cough and/or shortness of breath may still have SARS-CoV-2 infection and should seek follow-up care with their physician or healthcare provider.

LIMITATIONS

- Failure to follow the instructions for use may adversely affect test performance and/or invalidate the test result.
- If the differentiation of specific SARS viruses and strains is needed, additional testing, in consultation with state or local public health departments, is required.
- Results from antigen testing should not be used as the sole basis to diagnose or exclude SARS-CoV-2 infection or to determine infection status.
- This test will indicate the presence of SARS-CoV-2 nucleocapsid protein antigen in the specimen from both viable and non-viable SARS-CoV-2 virus. Test performance depends on the amount of virus (antigen) in the sample and may or may not correlate with viral culture results performed on the same sample.
- The detection of SARS-CoV-2 nucleocapsid antigen is dependent upon proper specimen collection, handling, storage, and preparation. Failure to observe proper procedures in any one of these steps can lead to incorrect results.
- Results from the device should be correlated with the clinical history, epidemiological data and other data available.
- This device has been evaluated for use with human specimen material only.
- False-negative results may occur if the concentration of the target antigen in the clinical specimen is below the detection limits of the device.
- This test cannot rule out diseases caused by other bacterial or viral pathogens.

CONDITIONS FOR AUTHORIZATION OF LABORATORY

The CovClear COVID-19 Antigen Test Letter of Authorization, along with the authorized Fact Sheet for Healthcare Providers, the authorized Fact Sheet for Patients, and authorized labeling are available on the FDA website:

https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas

To assist clinical laboratories using the CovClear COVID-19 Antigen Test ("your product" in the conditions below), the relevant Conditions of Authorization are listed below:

A. Authorized laboratories[1] using your product will include with test result reports, all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.
B. Authorized laboratories using your product will use your product as outlined in the authorized labeling. Deviations from the authorized procedures, including the authorized instruments, authorized extraction methods, authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and authorized materials required to use your product are not permitted.
C. Authorized laboratories that receive your product will notify the relevant public health authorities of their intent to run your product prior to initiating testing.
D. Authorized laboratories using your product will have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
E. Authorized laboratories will collect information on the performance of your product and report to DMD/OHT7-OIR/OPEQ/CDRH (via email: CDRH-EUA- Reporting@fda.hhs.gov) and EMPOWERED DIAGNOSTICS, LLC (Technical Support at +1-954-354-2768) any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of your product of which they become aware.

F. All operators using your product must be appropriately trained in performing and interpreting the results of your product, use appropriate personal protective equipment when handling this kit, and use your product in accordance with the authorized labeling.

G. EMPOWERED DIAGNOSTICS, LLC authorized distributors, and authorized laboratories using your product will ensure that any records associated with this EUA are maintained until otherwise notified by FDA. Such records will be made available to FDA for inspection upon request

[1] The letter of authorization refers to, "Laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet the requirements to perform high complexity tests."

PERFORMANCE CHARACTERISTICS

Clinical Performance

A total of 75 subjects were tested in one investigational site to evaluate the point of care clinical performance of the CovClear COVID-19 Rapid Antigen Test. Every subject was administered a CovClear COVID-19 Rapid Antigen Test as per the test instructions. Every subject also had a nasal swab sample collected by clinical study site staff for testing at Genova Laboratories using the EUA approved Thermo Fisher TaqPath COVID-19 SARS-CoV-2 Test. Samples for the CovClear COVID-19 Rapid Antigen Test and the lab-based PCR test were collected in a randomized manner. 28 asymptomatic patients were evaluated for this clinical trial.
Age distribution of the 75 subjects is presented below.

Age Distribution Per Age Group

Age Group	N (Total Number of Subjects)	N% (Number of subjects per group / Total Tested)
<18 Years of Age	0	0%
18-24 Years of Age	18	24%
25-29 Years of Age	8	11%
30-49 Years of Age	25	33%
50-64 Years of Age	21	28%
65+ Years of Age	3	4%
Total	75	100%

The following table summarizes the Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) for CovClear COVID-19 Rapid Antigen Test when compared to an FDA EUA high sensitivity PCR SARS-CoV-2 assay.

CovClear COVID-19 Antigen (retrospective samples) Performance against the Comparator Method

CovClear COVID-19 Rapid Antigen Test	Comparator		
	Positive	Negative	Total
Positive	49	0	49
Negative	1	25	26
Total	50	25	75
Positive Percent Agreement (PPA)	98% (95% CI:91.0%-99.8%)		
Negative Percent Agreement (NPA)	100% (95% CI:90.5%-100%)		

Analytical Sensitivity: Limit of Detection (LoD)

The LoD for direct swab was established using heat-inactivated SARS-CoV-2 isolate Hong Kong/VM20001061/2020). The strain was spiked into 0.5% saline solution. The estimated LoD found from the initial two- fold serial dilution test was confirmed by testing 20 replicates. The confirmed LoD for direct swab was 1.29 x 10^5 $TCID_{50}$/ml.

Specimen Stability:

The specimen stability was established using heat-inactivated SARS-CoV-2 isolate Hong Kong/VM20001061/2020. Nasal swabs spiked with the heat-inactivated SARS-CoV-2 isolate Hong Kong/VM20001061/2020 at 3X LOD were Incubated at room temperature for 0, 2, 5, and 24 hours respectively prior to testing. All samples tested produced no qualitative impact on test line signal intensity as compared to the 0-hour condition, demonstrating that the CovClear COVID-19 Rapid Antigen Test performance was not affected for up to 24 hours at room temperature.

Analytical Specificity: Cross Reactivity and Microbial Interference

The potential cross-reactivity (exclusivity) of a panel of common organisms was evaluated with SARS-CoV-2 negative samples using the CovClear COVID-19 Rapid Antigen Test. Potential microbial interference was evaluated with samples containing heat-inactivated SARS-CoV-2 isolate Hong Kong/VM20001061/2020 at approximately 3x LoD. A total of twenty-five (25) potential cross-reactant samples were evaluated for cross-reactivity at predefined concentrations in accordance with the EUA guidelines Antigen Template for Test Developers (version October 26, 2020). No cross-reactivity was observed with the CovClear COVID-19 Rapid Antigen Test.

Viral Pathogens	Bacterial Pathogens
Coronavirus OCN43 (Culture Fluid)	Mycoplasma pneumoniae
Coronavirus 229E (Heat inactivated)	Bordetella pertussis
Coronavirus NL63 (Heat inactivated)	Candida albicans
Parainfluenza Virus Type 3 (Culture Fluid)	Streptococcus pyogenes
Parainfluenza Virus Type 2 (Culture Fluid)	Streptococcus pneumoniae
Parainfluenza Virus Type 1 (Culture Fluid)	Hemophilus influenza
Human Metapneumovirus 16 (Culture Fluid)	Legionella pneumonia
Adenovirus (Culture Fluid)	Staphylococcus epidermidis
Parainfluenza Virus Type 4A (Culture Fluid)	Staphylococcus aureus
Influenza A H1N1 Virus (Culture Fluid)	Nasal Wash
Influenza B Virus (Culture Fluid)	Chlamydophila pneumoniae
Enterovirus Type 68 (Culture Fluid)	
Respiratory Syncytial Virus Type A (Culture Fluid)	
MERS-CoV (Culture Fluid, Heat Inactivated)	
Coronavirus OCN43 (Culture Fluid)	
Coronavirus 229E (Heat inactivated)	

To estimate the likelihood of cross-reactivity with SARS-CoV-2 of organisms that were not available for wet testing, in silico analysis using the Basic Local Alignment Search Tool (BLAST) managed by the National Center for Biotechnology Information (NCBI) was used

to assess the degree of protein sequence homology.

https://blast.ncbi.nlm.nih.gov/Blast.cgi?PAGE=Proteins&PROGRAM=blastp&BLAST_PROGRAMS=blastp&PAGE_TYPE=BlastSearch&BLAST_SPEC=blast2seq&DATABASE=n/a&QUERY=&SUBJECTS=

- The homology between SARS-CoV-2 nucleocapsid protein and human coronavirus HKU1 nucleocapsid protein is relatively low, at 36.7% across 86.4% of sequences, but cross- reactivity cannot be ruled out.
- The homology between SARS-CoV-2 nucleocapsid protein and Mycobacterium tuberculosis total protein (3,991 proteins) is relatively low, homology-based cross-reactivity can be ruled out.
- The homology between SARS-CoV-2 nucleocapsid protein and Pneumocystis jirovecii total protein (3,745 proteins) is relatively low, homology-based cross-reactivity can be ruled out.
- The homology between SARS-CoV-2 nucleocapsid protein and human coronavirus 229E nucleocapsid protein is relatively low, but cross- reactivity cannot be ruled out. However, a result of the cross-reactivity wet study showed that CovClear COVID-19 Antigen had no cross-reactivity against human coronavirus 229E.
- No homologous protein was detected as a result of in silico assay with the proteins of Mycoplasma pneumoniae and the nucleocapsid protein (NP) of SARS-CoV-2. So, cross-reactivity of CovClear COVID-19 Antigen against Mycoplasma pneumoniae can be ruled out.

This test has not been evaluated to determine if the CovClear COVID-19 Rapid Antigen Test is able to distinguish between SARS-CoV and SARS-CoV-2.

Endogenous Interfering Substances Effect

To assess substances with the potential to interfere with the performance of the CovClear COVID-19 Rapid Antigen, positive and negative samples were tested with the addition of potentially interfering substances. The SARS-CoV-2 target concentration in the positive samples was approximately 3x LoD. All samples tested produced no qualitative impact to test line signal intensity, demonstrating that the CovClear COVID-19 Rapid Antigen Test performance was not affected by any of the 14 potentially interfering substances listed in the table below at the concentrations tested.

Potential Interfering Substances	Concentration	Potential Interfering Substances	Concentration
Whole Blood	4%	Zicam	5% v/v
Mucin	0.5%	Homeopathic (Alkalol)	1:10 dilution
Chloraseptic (Menthol/Benzocaine)	1.5 mg/mL	Sore Throat Phenol Spray	15% v/v
NasoGEL (NeilMed)	5% v/v	Tobramycin	4 µg/mL
CVS Nasal Drops (Phenylephrine)	15% v/v	Mupirocin	10 mg/mL
Afrin (Oxymetazoline)	15% v/v	Fluticasone Propionate	5% v/v
CVS Nasal Spray (Cromolyn)	15% v/v	Tamiflu (Oseltamivir Phosphate)	5 mg/mL

High-dose Hook Effect

The CovClear COVID-19 Rapid Antigen was tested up to $1.75x10^6$ $TCID_{50}$/ml of heat-inactivated SARS- CoV-2 strain and no high-dose hook effect was observed.

Technical Support

For questions, or to report a problem, please call Empowered Diagnostics at 954-354-2768.

Test system problems may also be reported to the FDA using the MedWatch reporting system (phone: 1-800-FDA-1088; fax: 1-800-FDA-1078: or http://www.fda.gov/medwatch).