COVID-19/Influenza A+B Antigen Combo Rapid Test Cassette

English

For professional use only.
For in vitro diagnostic use only.

[INTENDED USE]

The COVID-19/Influenza A+B Antigen Combo Rapid Test Cassette is a lateral flow immunoassay intended for the qualitative detection of SARS-CoV-2, influenza A and influenza B viral nucleoprotein antigens in nasopharyngeal swab from individuals suspected of respiratory viral infection consistent with COVID-19 by their healthcare provider. Symptoms of respiratory viral infection due to SARS-CoV-2 and influenza can be similar.

The COVID-19/Influenza A+B Antigen Combo Rapid Test Cassette is intended for the detection and differentiation of SARS-CoV-2, influenza A and influenza B viral nucleoprotein antigens. Antigens are generally detectable in nasopharyngeal specimens during the acute phase of infection. Positive results indicate the presence of viral antigens, but clinical correlation with patient history and other diagnostic information is necessary to determine infection status. Positive results do not rule out bacterial infection or co-infection with other viruses.

Negative results do not rule out SARS-CoV-2, influenza A or influenza B infection and should not be used as the sole basis for treatment or patient management decisions, including infection control decisions. Negative results must be combined with clinical observations, patient history and epidemiological information, and confirmed with a molecular assay, if necessary for patient management.

The COVID-19/Influenza A+B Antigen Combo Rapid Test Cassette is intended for use by trained clinical laboratory personnel specifically instructed and trained in vitro diagnostic procedures.

[SUMMARY]

The novel coronaviruses (SARS-CoV-2) 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.

Influenza (flu) is a contagious respiratory illness caused by influenza viruses. It can cause mild to severe illness. Serious outcomes of flu infection can result in hospitalization or death. Some people, such as older people, young children, and people with certain health conditions, are at high risk of serious flu complications. There are two main types of influenza (flu) virus: Types A and B. The influenza A and B viruses that routinely spread in people (human influenza viruses) are responsible for seasonal flu epidemics each year.

[PRINCIPLE]

The COVID-19 Antigen Rapid Test is a lateral flow immunoassay based on the principle of the double-antibody sandwich technique. SARS-CoV-2 nucleocapsid protein monoclonal antibody conjugated with color micro- particles is used as detector and sprayed on conjugation pad. During the test, SARS-CoV-2 antigen in the specimen interact with SARS-CoV-2 antibody conjugated with color microparticles making antigen-antibody labeled complex. This complex migrates on the membrane via capillary action until the test line, where it will be captured by the pre-coated SARS-CoV-2 nucleocapsid protein monoclonal antibody. A colored test line (T) would be visible in the result window if SARS-CoV-2 antigens are present in the specimen. Absence of the T line suggests a negative result. The control line (C) is used for procedural control, and should always appear if the test procedure is performed properly.

The Influenza A+B Rapid Test is a lateral flow immunoassay based on the principle of the double-antibody sandwich technique. The monoclonal antibodies against influenza A and influenza B conjugated with color microparticles are used as detectors and sprayed on conjugation pad. During the test, antigen and labeled antibody complexes are formed and migrate on the membrane via capillary action. If the specimen contains influenza A antigen, the complex will be captured by the pre-coated influenza A monoclonal antibody to form a visible colored line at the A region in the result window. If the specimen contains influenza B antigen, the complex will be captured by the pre-coated influenza B monoclonal antibody to form a visible colored line at the B region in the result window. The control line (C) is used for procedural control, and should always appear if the test procedure is performed properly.

[WARNINGS AND PRECAUTIONS]

- For in vitro diagnostic use only.
- Do not use this product as the sole basis to diagnose or exclude SARS-CoV-2, influenza A or influenza B infection, or to inform infection status of COVID-19 or influenza.
- Do not use after the expiration date.
- Please read all the information in this leaflet before performing the test.
- The test cassette should remain in the sealed pouch until use.
- All specimens should be considered potentially hazardous and handled in the same manner as an infectious agent.
- The used test cassette should be discarded according to federal, state and local regulations.

[COMPOSITION]

Materials Provided

- 25 Test Cassettes: a test cassette includes the COVID-19 Antigen Test Strip and the Influenza A+B Test Strip, which are fixed inside a plastic device
- 25 Extraction Reagents: ampoule containing 0.4 mL of extraction reagent
- 25 Sterilized Swabs: single use swab for specimen collection
- 25 Extraction Tubes
- 25 Dropper Tips
- 1 Work Station
- 1 Package Insert

Materials Required but not Provided

- Timer

[STORAGE AND STABILITY]

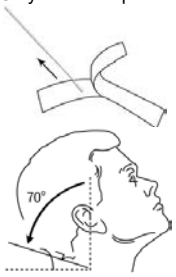
- Store as packaged in the sealed pouch at the temperature (4-30℃ or 40-86 ℉). The kit is stable within the expiration date printed on the labeling.
- Once open the pouch, the test should be used within one hour. Prolonged exposure to hot and humid environment will cause product deterioration.
- The LOT and the expiration date were printed on the labeling.

[SPECIMEN]

Specimens obtained early during symptom onset will contain the highest viral titers; specimens obtained after five days of symptoms are more likely to produce negative results when compared to an RT-PCR assay. Inadequate specimen collection, improper specimen handling and/or transport may yield a falsely negative result; therefore, training in specimen collection is highly recommended due to the importance of specimen quality for generating accurate test results.

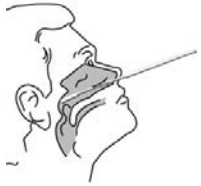
Specimen Collection

Only the swab provided in the kit is to be used for specimen collection.

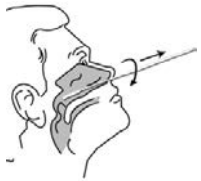


1. Remove the swab from the package.

2. Tilt patient's head back about 70°.



3. Insert the swab through the nostril parallel to the palate (not upwards) until resistance is encountered 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 the swab. Leave swab in place for several seconds to absorb secretions.



4. Slowly remove swab while rotating it.
   Specimens can be collected from both sides using the same swab, but it is not necessary to collect specimens from both sides if the minitip is saturated with fluid from the first collection. If a deviated septum or blockage creates difficulty in obtaining the specimen from one nostril, use the same swab to obtain the specimen from the other nostril.

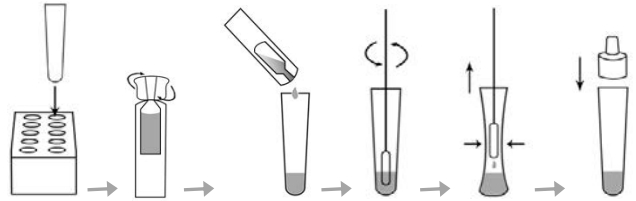
Specimen Transport and Storage

Do not return the nasopharyngeal swab to the original swab packaging. Freshly collected specimens should be processed as soon as possible, but no later than one hour after specimen collection. Specimen collected may be stored at 2-8℃ for no more than 24 hours; Store at -70℃ for a long time, but avoid repeated freeze-thaw cycles.

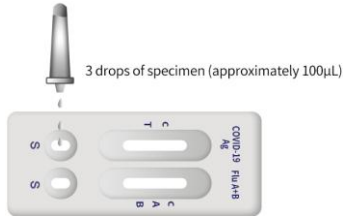
[TEST PROCEDURE]

Note: Allow the test devices, reagents and specimens to equilibrate to room temperature (15-30℃ or 59-86℉) prior to testing.

1. Put an extraction tube on the work station.
2. Unscrew the lid of an extraction reagent. Add all of the extraction reagent into an extraction tube.
3. Sampling refer to section 'Specimen Collection'.
4. Insert the swab specimen into the extraction tube which contains extraction reagent. Roll the swab at least 5 times while pressing the head against the bottom and side of the extraction tube. **Leave the swab in the extraction tube for one minute.**
5. Remove the swab while squeezing the sides of the tube to extract the liquid from the swab. The extracted solution will be used as test sample.
6. Cover the extraction tube with a dropper tip tightly.

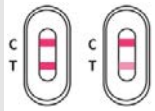
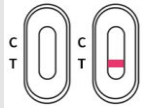


7. Remove the test cassette from the sealed pouch.
8. Reverse the specimen extraction tube, holding the specimen extraction tube upright, transfer 3 drops (approximately 100μL) to each specimen well (S) of the test cassette, then start the timer. See illustration below.
9. Wait for colored lines to appear. Interpret the test results **at 15 minutes**. Do not read results after 20 minutes.

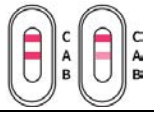
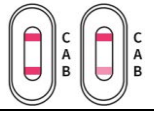
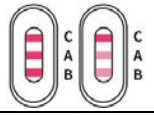
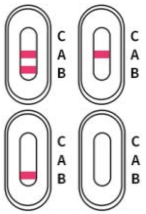


[INTERPRETATION OF RESULTS]

For COVID-19 Antigen Rapid Test

Positive		**Two lines appear.** One colored line appears at the control region (C), and another colored line appears at the test region (T), irregardless of the intensity of the test line.
Negative		One colored line appears at the control region (C), and no line appears at the test region (T).
Invalid		**Control line fails to appear.** Insufficient specimen volume or incorrect procedural techniques are the most likely reasons for control line failure. Review the procedure and repeat the test using a new test cassette. If the problem persists, discontinue using the lot immediately and contact your local distributor.

For Influenza A+B Rapid Test

Flu A Positive		One colored line appears at the control region (C), and another colored line appears at the A test region, irregardless of the intensity of the test line.
Flu B Positive		One colored line appears at the control region (C), and another colored line appears at the B test region, irregardless of the intensity of the test line.
Flu A & B Positive		One colored line appears at the control region (C), and both the A and B lines appear at the test region, irregardless of the intensity of the test line.
Negative		One colored line appears at the control region (C), and no lines appear at the test region.
Invalid		**Control line fails to appear.** Insufficient specimen volume or incorrect procedural techniques are the most likely reasons for control line failure. Review the procedure and repeat the test using a new test cassette. If the problem persists, discontinue using the lot immediately and contact your local distributor.

[QUALITY CONTROL]

A procedural control is included in the test. A colored line appearing at the control region (C) is considered an internal procedural control. It confirms sufficient specimen volume, adequate membrane wicking and correct procedural technique.

Control standards are not supplied with this kit. However, it is recommended that positive and negative controls be tested as good laboratory practice to confirm the test procedure and to verify proper test performance.

[LIMITATIONS]

- The product is limited to provide a qualitative detection. The intensity of the test line does not necessarily correlate to the concentration of the antigens in the specimens.
- Negative results are presumptive. Negative test results do not preclude infection and should not be used as the sole basis for treatment or other patient management decisions, including infection control decisions, particularly in the presence of clinical signs and symptoms consistent with COVID-19, or in those who have been in contact with the virus. It is recommended that these results be confirmed by a molecular testing method, if necessary, for patient management.
- A physician must interpret the results in conjunction with the patient's history, physical findings, and other diagnostic procedures.
- A negative result can occur if the quantity of antigens present in the specimen is below the detection threshold of the assay, or the virus has undergone minor amino acid mutation(s) in the target epitope region recognized by the monoclonal antibodies utilized in the test.

[PERFORMANCE CHARACTERISTICS]

Clinical Performance

The clinical performance of COVID-19/Influenza A+B Antigen Combo Rapid Test Cassette was established in single-blinded studies with 608 nasopharyngeal swabs collected from individual symptomatic patients (within 7 days of onset) who were suspected of COVID-19. The commercialized molecular (RT-PCR) assay for detection of SARS-CoV-2, influenza A and influenza B were used as the reference method.

Summary of the performance of COVID-19/Influenza A+B Antigen Combo Rapid Test Cassette compared to RT-PCR:

For COVID-19 Antigen Rapid Test

The RT-PCR cycle threshold (Ct) is the relevant signal value. Lower Ct value indicate higher viral load. The sensitivity was calculated for the different Ct value range (Ct value ≤33 and Ct value ≤37).

COVID-19 Antigen		RT-PCR (Ct value ≤33)		Total
		Positive	Negative	
CLUNGENE®	Positive	128	1	129
	Negative	3	451	454
Total		131	452	583

PPA (Ct≤33): 97.7% (128/131), (95%CI: 93.5%～99.2%)
NPA: 99.8% (451/452), (95%CI: 98.8%～100%)

COVID-19 Antigen		RT-PCR (Ct value ≤37)		Total
		Positive	Negative	
CLUNGENE®	Positive	144	1	145
	Negative	12	451	463
Total		156	452	608

PPA (Ct≤37): 92.3% (144/156), (95%CI: 87.0%～95.6%)
NPA: 99.8% (451/452), (95%CI: 98.8%～100%)

PPA - Positive Percent Agreement (Sensitivity)
NPA - Negative Percent Agreement (Specificity)

For Influenza A+B Rapid Test

Virus	Sensitivity (PPA)	Specificity (NPA)
Influenza A	89.0% (65/73), 95%CI: 79.8%~94.3%	99.8% (534/535), 95%CI: 99.0%~100%
Influenza B	84.7% (50/59), 95%CI: 73.5%~91.8%	99.6% (547/549), 95%CI: 98.7%~99.9%

Limit of Detection (Analytical Sensitivity)

The study used cultured viruses, which are heat inactivated and spiked into nasopharyngeal swab specimen. The Limit of Detection (LoD) was confirmed as follows:

Virus Lineage	Limit of Detection (LoD)
SARS-CoV-2*	5.7×10^2 $TCID_{50}$/mL
Influenza A (H1N1)	1.0×10^3 $TCID_{50}$/mL
Influenza A (H3N2)	1.0×10^4 $TCID_{50}$/mL
Influenza A (H1N1pdm09)	6.5×10^3 $TCID_{50}$/mL
Influenza B (Yamagata)	3.7×10^4 $TCID_{50}$/mL
Influenza B (Victoria)	1.0×10^3 $TCID_{50}$/mL

* Isolate Hong Kong/VM20001061/2020, NR-52282

Cross Reactivity (Analytical Specificity)

Cross reactivity was evaluated by testing 26 commensal and pathogenic microorganisms that may be present in the nasal cavity.

No cross-reactivity was observed with recombinant MERS-CoV NP protein when tested at the concentration of 50 μg/mL.

No cross-reactivity was seen with the following viruses when tested at the concentration of 1.0×10^6 PFU/mL: Adenovirus (type 1, 2, 3, 5, 7, 55), Human metapneumovirus, Parainfluenza virus (type 1, 2, 3, 4), Respiratory syncytial virus, Enterovirus, Rhinovirus, Human coronavirus 229E, Human coronavirus OC43, Human coronavirus NL63, Human coronavirus HKU1.

No cross-reactivity was seen with the following bacteria when tested at the concentration of 1.0×10^7 CFU/mL: Mycoplasma pneumoniae, Chlamydia pneumoniae, Legionella pneumophila, Haemophilus influenzae, Streptococcus pyogenes (group A), Streptococcus pneumoniae, Staphylococcus aureus.

Interference

The following potential interference substances were evaluated with the COVID-19/Influenza A+B Antigen Combo Rapid Test Cassette at the concentrations listed below and were found not to affect test performance.

Substance	Concentration	Substance	Concentration
Mucin	2%	Whole blood	4%
Benzocaine	5 mg/mL	Menthol	10 mg/mL
Saline nasal spray	15%	Phenylephrine	15%
Oxymetazoline	15%	Histamine dihydrochloride	10 mg/mL
Tobramycin	5 μg/mL	Mupirocin	10 mg/mL
Oseltamivir phosphate	10 mg/mL	Zanamivir	5 mg/mL
Arbidol	5 mg/mL	Ribavirin	5 mg/mL
Fluticasone propionate	5%	Dexamethasone	5 mg/mL
Triamcinolone	10 mg/mL		

High-dose Hook Effect

No high-dose hook effect was observed up to $1.0 \times 10^{5.67}$ $TCID_{50}$/mL of inactivated SARS-CoV-2, 1.0×10^5 $TCID_{50}$/mL of inactivated influenza A (H1N1), 1.0×10^6 $TCID_{50}$/mL of inactivated influenza A (H3N2), 7.5×10^5 $TCID_{50}$/mL of inactivated influenza B (Yamagata) and 1.0×10^5 $TCID_{50}$/mL of inactivated influenza B (Victoria) with the COVID-19/Influenza A+B Antigen Combo Rapid Test.

Hangzhou Clongene Biotech Co., Ltd.
No.1 Yichuang Road, Yuhang Sub-district, Yuhang District,
311121 Hangzhou, China

EC REP Shanghai International Holding Corp. GmbH (Europe)
Eiffestrasse 80, D-20537 Hamburg, Germany

Index of Symbol

Do not reuse	For in vitro diagnostic use only
Store between 4-30℃	Consult instructions for use
Lot number	Contains sufficient for <n> tests
Use by	Keep away from sunlight
Keep dry	Do not use if package is damaged
Manufacturer	Authorized representative in the European Community

Version No.: 3.0
Effective Date: December 15, 2020