Version: DR0005-A00

COVID-19 Antigen/Influenza A+B Antigen

Combo Rapid Test

Instructions For Use

Specimens: Nasal Swab **Version:** DR0005-A00

For professional and in vitro diagnostic use only.

【PRODUCT NAME】

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

【PACKING】

1 test/kit, 5 tests/kit, 20 tests/kit, 25 tests/kit, 50 tests/kit

【INTENDED USE】

COVID-19 Antigen/Influenza A+B Antigen Combo Rapid Test is a lateral flow immunoassay for the qualitative detection of SARS-CoV-2 nucleocapsid antigens and Influenza A and B virus antigens in nasal swab specimens from individuals suspected of COVID-19 and Flu A/B.

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 other bacterial or viral infections.

Negative results from patients with symptom onset beyond seven days should be confirmed with a molecular assay. Negative results do not rule out SARS-CoV-2 infection or Influenza A/B infection and should not be used as the sole basis for treatment or patient management 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 and Influenza A/B.

The product is intended to be used in any laboratory and non-laboratory environment that meets the requirements specified in the Instructions for Use and local regulations. For in vitro diagnostic use only.

【SUMMARY】

Since the first outbreak reported in December 2019, SARS-CoV-2 has spread rapidly worldwide,and the disease it causes has been named "Coronavirus Disease 2019" (COVID-19). Due to its highly contagious nature and global health crises, SARS-CoV-2 has been designated as a pandemic by the World Health Organization (WHO). SARS-CoV-2 continues to have devastating impacts on health care systems and the world economy including the U.S. To effectively end the SARS-CoV-2 pandemic, systematic screening and detection of both clinical and asymptomatic COVID-19 cases is critical. Particularly, the identification of subclinical or asymptomatic cases is important to reduce or stop the infection because these individuals may transmit the virus.

Influenza A and B are contagious infections attributed to a filterable virus. The viral infection affects mainly the nose, throat, bronchi and occasionally the lungs, causing fever, cough, sore throat, headache and pain in the back and limbs. The virus is transmitted easily from person to person via droplets and small particles produced when infected people cough or sneeze. Influenza spreads around the world in seasonal epidemics resulting in hundreds of thousands of deaths worldwide annually, reaching millions in pandemic years.

Influenza A and B are mainly diagnosed by clinical symptoms. Collection of clinical specimens for viral culture remains critical to provide information regarding circulating influenza subtypes and strains.

Since clinical symptoms of COVID-19 and Flu A/B are similar. Assay to distinct those diseases has become an urgent need for screening patients. As a point-of-care test with a 15 min testing time, COVID-19 Antigen/Influenza A+B Antigen Combo Rapid Test allows effective screening of COVID-19 and Influenza A/B infections on a large scale.

【PRINCIPLE】

COVID-19 Antigen/Influenza A+B Antigen Combo Rapid Test is based on colloidal gold immunochromatography assay.

During the test, specimens and detection buffer are applied to the test cartridges. If there are SARS-CoV-2 nucleocapsid antigens or influenza A/B virus in the specimens, they will bind to colloidal gold-labeled antibodies against SARS-CoV-2 N protein or Influenza A and B virus antigens respectively on conjugation pad forming virus antigen-antibody-colloidal gold complexes (complex A for Flu A, complex B for Flu B and complex C for COVID-19).

During lateral flow, the complexes move along nitrocellulose membrane toward one end of the absorbent paper. When passing the COVID-19 test line TC (coated with another monoclonal antibody against SARS-CoV-2 N protein), the complex C is captured by capture antibody resulting in coloring on line TC; when passing the Influenza A test line TA (coated with another monoclonal antibody against Influenza A virus N protein), the complex A is captured by capture antibody resulting in coloring on line TA; when passing the Influenza B test line TB (coated with another monoclonal antibody against Influenza B virus N protein), the complex B is captured by capture antibody resulting in coloring on line TB; when passing the line C, residual colloidal gold-labeled control molecule is captured by quality-control antibody resulting in coloring on line C.

【COMPONENT】

1. Test cartridge
2. Pre-filled extraction buffer tube
3. Nozzles to extraction tube
4. Nasal swab
5. Paper rack
6. Instructions for use

【STORAGE AND STABILITY】

1. The test cartridge should be stored at 2℃~30℃, do not freeze. The shelf life is 24 months.
2. The test cartridge should be used within 1 hour after the aluminum foil is opened, and the extraction buffer is for one time use and foil should be removed right before tests.

【WARNINGS AND PRECAUTIONS】

1. Read the instructions for use carefully before using this product.
2. This product is for professional use only.
3. This reagent is used for in vitro diagnosis only, please do not use expired products.
4. Do not use if the kit or any kit component past the indicated expiry date.
5. Wear protective clothing and disposable gloves while handling the kit reagents.
6. Do not open the sealed pouch, unless ready to conduct the assay.
7. Sample collection and handling procedures require specific training and guidance.
8. Do not use the components of any other type of test kit as a substitute for the components in this kit.
9. Discard and do not use any damaged or dropped Test Cassette or material.
10. Use of Nitrile, Latex (or equivalent) gloves is recommended when handling patient samples. Wash hands thoroughly after performing the test.
11. Do not smoke, drink, or eat in areas where specimens or kit reagents are being handled.
12. Inadequate or inappropriate sample collection, storage, and transport may yield false test results.
13. Do not touch swab tip when handling the swab sample.
14. This product is applicable to nasal swab. Using other sample types may cause inaccurate or invalid test results.
15. Please make sure that a proper amount of sample is added for testing. Too much or too little sample amount may cause inaccurate results.
16. Bring all reagents to room temperature (15~30 ℃) before use.
17. If the test line or control line is out of the test window, do not use the test cartridge. The test result is invalid and retest the sample with another one.
18. Do not reuse the used Test Cassette, Reagent Tubes, solutions, or Swabs.
19. Dispose of used products, samples, and other consumables as medical wastes under relevant regulations.

【SAMPLE COLLECTION】

1. Before running the assay, ensure the test area is sanitized. Open the kit and ensure all materials described in "Reagents and Materials Provided" are included and the kit is not expired. Obtain a timing device (clock, watch or timer) and read the Instructions for Use.
2. Remove mucus from the nose.
3. Wash or sanitize hands thoroughly.
4. Fold/assemble the sample extraction tube rack.
5. Remove one pre-filled extraction tube from the sealed pouch and close the pouch with the unused tubes. Hold the tube upright and, before opening it, tap the bottom of the tube on a clean, flat surface to ensure that any liquid on the seal is moved down into the tube.
6. Carefully remove the foil seal from the extraction tube, and place the open tube in the sample extraction tube rack. Dispose the foil seal into a waste bag. Keep the bag to later collect other used items.

7. Open the swab package. Note: Do not touch the swab's absorbent tip, so be sure to open the package on the opposite end.

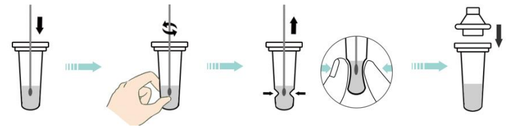
8. Hold head in a vertical position and look slightly downwards .

Nasal Swab Samples:

1. Carefully insert the entire absorbent tip of the swab in one nostril and rotate at least 5 times. Be sure that the absorbent tip of the swab scrapes against the nasal wall.

2. Remove swab from nostril and, using the same swab, repeat step 1 in the other nostril.

3. Insert the absorbent tip of the swab into the extraction buffer tube and swirl the swab at least 5 times.
4. Squeeze the tube against the submerged swab several times to facilitate extraction of the specimen. Remove the swab, place it back in its original wrapping and dispose into the waste bag.
5. Place the nozzle onto the extraction tube and ensure it is attached firmly.

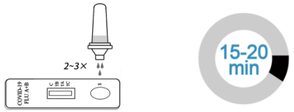


【TEST PROCEDURES】

Restore the test devices and specimens to room temperature (15-30 ℃) prior to testing.

1. Remove the cassette device from the sealed pouch just prior to testing. Lay the device on a clean, flat surface and label with specimen ID/name.

2. Invert the sample extraction tube and slowly add 2~3 drops of the extracted specimen into the sample well of the cassette device by gently squeezing the sample tube.



3. Set the timing device for 15 minutes.
4. Read the results after 15 minutes. Note: The result might be visible after a shorter time, however, it should only be interpreted between 15-20 minutes after dispensing the sample material onto the cassette device.
5. Collect all used items (swab, cassette, sample extraction tube, foil seal and nozzle, and potentially used gloves) into the waste bag. Close the bag and dispose in a biohazard trash can.
6. Thoroughly wash or sanitize hands and any used surfaces/tools for the procedure.

Alternative procedure for specimens stored in VTM:

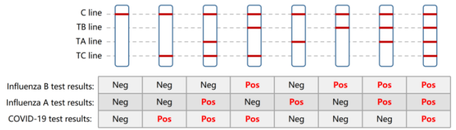
Add 70 μL of the VTM specimen directly into the sample well of the cassette device and proceed to step 3 above.

Note: This method is only recommended for samples stored in VTM not containing pH indicator dye, as the dye color might interfere with the assay.

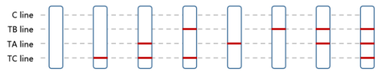
【RESULTS INTERPRETATION】

1. Negative results: coloring on C line appear only.
2. COVID-19 positive results: coloring on both TC line and C line. (Note: Faint line should be regard as coloring)
3. Flu A positive results: coloring on both TA line and C line. (Note: Faint line should be regard as coloring)
4. Flu B positive results: coloring on both TB line and C line. (Note: Faint line should be regard as coloring)
5. Invalid results: no coloring appear on C line regardless of TA, TB and TC line coloring.

Valid results:



Invalid results:



【PRODUCT PERFORMANCE】

1. The limit of detection (LoD) or analytical sensitivity

The LoD was determined as the lowest virus concentration that equal to or greater than 95% of the results were positive. (i.e., the concentration at which at least 19 out of 20 replicates tested positive). The LoD of COVID-19 Antigen/Influenza A+B Antigen Combo Rapid Test is listed below:

Viruses	Specimen type	LoD
COVID-19	Gamma-Irradiated Virus	60TCID$_{50}$/mL
	Recombinant N protein	10pg/mL
Influenza A	H1N1	3TCID$_{50}$/mL
	H3N2	5TCID$_{50}$/mL
	H5N1	250TCID$_{50}$/mL
	H7N9	300TCID$_{50}$/mL
	Recombinant N protein	1ng/mL
Influenza B	B/Yamagata（B-Y）	50TCID$_{50}$/mL
	B/Victoria（B-V）	40TCID$_{50}$/mL
	Recombinant N protein	1ng/mL

2. Clinical performance

The COVID-19 antigen test was evaluated with clinical specimens, taking commercial RT-PCR kit as the gold standard.

Nasal Swab		RT-PCR		Total
		Positive	Negative	
COVID-19 Antigen Test	Positive	97	0	97
	Negative	8	363	371
Total		105	363	468

Sensitivity=92.38% (95%CI: 85.09%-96.41%)
Specificity=100% (95%CI: 98.69%-100%)
Overall Agreement=98.29%（95%CI:96.66%-99.13%）

The Influenza A antigen test was evaluated with clinical specimens, taking commercial RT-PCR kit as the gold standard.

Nasal Swab		RT-PCR		Total
		Positive	Negative	
Influenza A Antigen Test	Positive	185	9	194
	Negative	19	602	621
Total		204	611	815

Sensitivity=90.68% (95%CI: 85.63%-94.15%)
Specificity=98.53% (95%CI: 97.12%-99.28%)
Overall Agreement=96.56%（95%CI:95.31%-97.81%）

The Influenza B antigen test was evaluated with clinical specimens, taking commercial RT-PCR kit as the gold standard.

Nasal Swab		RT-PCR		Total
		Positive	Negative	
Influenza B Antigen Test	Positive	96	6	102
	Negative	9	382	391
Total		105	388	493

Sensitivity=91.43% (95%CI: 83.93%-95.76%)
Specificity=98.45% (95%CI: 96.49%-99.37%)
Overall Agreement=96.96%（95%CI:95.44%-98.47%）

3. Cross-reactivity or analytical specificity

The analytical specificity of the COVID-19 Antigen/Influenza A+B Antigen Combo Rapid Test was evaluated by testing commensal and pathogenic microorganisms that may be present in the nasal cavity. No cross-reactivity (except SARS-coronavirus to COVID-19 test) or interference were seen with the following microorganisms when tested at the concentration presented in the table below:

Microorganism	Concentration	Cross-reactivity		
		COVID-19	Flu A	Flu B
MERS-CoV	1.17×10^6 TCID$_{50}$/mL	No	No	No
SARS-CoV	2.3×10^5 TCID$_{50}$/mL	Yes	No	No
HCoV-HKU1	1.8×10^5 TCID$_{50}$/mL	No	No	No
Influenza type A	1.98×10^6 TCID$_{50}$/mL	No	Yes	No
Influenza type B	2.32×10^6 TCID$_{50}$/mL	No	No	Yes
Human coronavirus 229E	1.77×10^6 TCID$_{50}$/mL	No	No	No
Human coronavirus OC43	1.05×10^6 TCID$_{50}$/mL	No	No	No
Human coronavirus NL63	1.17×10^6 TCID$_{50}$/mL	No	No	No
Adenovirus	7×10^{10} NIU/mL	No	No	No
Human Metapneumovirus (hMPV) Type B1	1.55×10^4 TCID$_{50}$/mL	No	No	No
Parainfluenza virus Type 1	5.01×10^5 TCID$_{50}$/mL	No	No	No
Parainfluenza virus Type 2	1.6×10^6 TCID$_{50}$/mL	No	No	No
Parainfluenza virus Type 3	1.6×10^8 TCID$_{50}$/mL	No	No	No
Parainfluenza virus Type 4b	1.15×10^7 TCID$_{50}$/mL	No	No	No
Enterovirus D68	1.0×10^6 TCID$_{50}$/mL	No	No	No
Respiratory syncytial virus	2.8×10^5 TCID$_{50}$/mL	No	No	No
Rhinovirus 1A	2.2×10^7 PFU/mL	No	No	No
Haemophilus influenzae type b	5.2×10^7 CFU/mL	No	No	No
Streptococcus pneumoniae (262)	>2×10^4 CFU/mL	No	No	No
Streptococcus pyogenes	3.6×10^7 CFU/mL	No	No	No
Candida albicans	4.50×10^8 TCID$_{50}$/mL	No	No	No
Bordetella pertussis	3.9×10^9 CFU/mL	No	No	No
Mycoplasma pneumoniae	4.4×10^7 CFU/mL	No	No	No
Chlamydia pneumoniae	1.4×10^8 IFU/mL	No	No	No
Legionella pneumoniae	7.8×10^6 CFU/mL	No	No	No
Mycobacterium tuberculosis H37Ra	>2×10^4 CFU/mL	No	No	No
Pneumocystis jirovecii (PJP)	3.45×10^8 CFU/mL	No	No	No

4. Interfering substances

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

Interfering substance	Concentration	Interference		
		COVID-19	Flu A	Flu B
Biotin	200 ng/dL	No	No	No
Whole Blood	5 %	No	No	No
Menthol	0.8 g/mL	No	No	No
Saline	15 %	No	No	No
Acetylsalicylic Acid	3 mg/dL	No	No	No
Zanamivir	282 ng/mL	No	No	No
Budesonide	0.63 μg/dL	No	No	No
Ribavirin	1 mg/mL	No	No	No
Acetaminophen	199 μM	No	No	No
Tobramycin	1.25 mg/mL	No	No	No
Oseltamivir	2.2 μg/mL	No	No	No
Diphenhydramine	77.4 μg/dL	No	No	No
Dextromethorphan	1.56 μg/dL	No	No	No
Mucin protein	2.5 mg/mL	No	No	No
OTC Nasal Drops (Phenylephrine)	15 %	No	No	No
OTC Nasal Gel (Sodium Chloride)	5 %	No	No	No
OTC Nasal Spray 3 (Fluconazole)	5 %	No	No	No
Throat Lozenge (Benzocaine,Menthol)	0.15 %	No	No	No
Antibiotic,Nasal Ointment (Mupirocin)	0.25 %	No	No	No

5. High does hook effect

The COVID-19 Antigen/Influenza A+B Antigen Combo Rapid Test was tested up to 10^{6}TCID$_{50}$/mL of inactivated SARS-CoV-2, 500μg/mL of recombinant Influenza A N protein and 500μg/mL of recombinant Influenza B N protein. There was no high-dose hook effect observed respectively.

【LIMITATIONS】

1. This product is intended for assisted diagnosis of viral infections only. A final clinical diagnosis should also consider factors like symptoms, results of other tests as well.
2. A negative result indicates that the viral load in tested sample is below the limit of detection of this product. It cannot completely exclude the possibility of viral infection of patient.
3. A positive result indicates that the tested sample has viral load higher than the limit of detection of this product. However, the color intensity of test line may not correlate with the severity of infection or disease progression of the patient.

【BIBLIOGRAPHY】

Wang C, Horby PW, Hayden FG, Gao GF. A novel coronavirus outbreak of global health concern. The Lancet. 24 January 2020.

【SYMBOL】

Symbol	Description	Symbol	Description
REF	Catalogue number	IVD	In vitro diagnostic medical device
LOT	Lot number		Consult instructions for use
	Date of manufacture		Keep dry
	Expiry date		Keep away from sunlight
	Manufacturer	2℃ 30℃	Store at 2-30℃
	Do not re-use	EC REP	European authorized representative
CE	CE Mark		

【GENERAL INFORMATION】

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