2019-nCoV Ag & FLU A/B Combo Rapid Test

(Immunochromatography)

Catalog Number:

0575C2X001(1 test/Kit) **0575C3X025(25 tests/Kit)**

0575C2X005(5 tests/Kit) **0575C2X025(25 tests/Kit)**

INTENDED USE

The 2019-nCoV Ag & FLU A/B Combo Rapid test is an in vitro immunochromatographic assay for the qualitative detection of 2019-nCoV antigen and influenza A / B antigens in nasal swab specimens collected from patients with signs and symptoms of respiratory infection. This test is intended for use as an aid in the differential diagnosis of 2019-nCoV and influenza A/ B viral infections in humans in conjunction with clinical and epidemiological risk factors.

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.

Influenza is a highly contagious acute viral infection of the respiratory tract. It is a communicable disease easily transmitted from person to person through aerosol droplets excreted when sneezing and coughing. Common symptoms include high fever, chills, headache, cough, sore throat and malaise. The type A influenza virus is more prevalent and is the primary pathogen associated with serious epidemics. The type B virus causes a disease that is generally not as severe as that caused by the type A virus.

An accurate diagnosis of 2019-nCoV and influenza based on clinical symptoms is difficult because the initial symptoms of influenza are similar to those of numerous other illnesses. Therefore, it can be confirmed only by laboratory diagnostic testing. Early differential diagnosis of 2019-nCoV and influenza type A or type B can allow for proper treatment with appropriate antiviral therapy. Early diagnosis and treatment are of particular value in a clinical setting where accurate diagnosis can assist the healthcare professional with management of 2019-nCoV and influenza patients who are at risk for complications. The Combo Rapid test is a rapid immunoassay to be used as an aid for the differential diagnosis of 2019-nCoV and influenza type A and type B.

PRINCIPLE OF THE TEST

The 2019-nCoV Ag & FLU A/B Combo Rapid test is an immunochromatographic membrane assay and contains two independent tests, the 2019-nCoV antigen test and the FLU A/B antigen test. In the test procedure, a specimen is collected and placed for one minute into the Extraction Well of the test device containing extraction solution, during which time antigen is extracted from disrupted virus particles. The test device is then raised, tapped and laid back down onto a level surface to allow the solution in the Extraction Well to migrate through the pads containing lyophilized detector antibodies conjugated to gold dye and then through the test membrane.

For the 2019-nCoV antigen test

The 2019-nCoV antigen test uses highly sensitive monoclonal antibodies to detect 2019-nCoV antigen in nasal swab specimens. These antibodies and a control protein are immobilized onto a membrane support as two distinct lines and are combined with other reagents/pads to construct a Test Strip. The 2019-nCoV antigen test has one test lines and one control line. If either Test line appears in the test result window, together with the Control line, the test result is positive for 2019-nCoV.

For the Flu A/B antigen test

The Flu A/B antigen test uses highly sensitive monoclonal antibodies to detect influenza type A and B nucleoprotein antigens in nasal swab specimens. These antibodies and a control protein are immobilized onto a membrane support as three distinct lines and are combined with other reagents/pads to construct a Test Strip.

The Flu A/B antigen test has two Test lines, one for influenza A and one for influenza B. The two Test lines allow for the separate and differential identification of influenza A and/or B from the same specimen. If either Test line appears in the test result window, together with the Control line, the test result is positive for influenza.

MATERIALS AND COMPONENTS

Materials provided with the test kits

Specifications / Ingredients	0575C2X001	0575C2X005	0575C2X025	0575C3X025
Test Cassette	1	5	10	25
Swab	1	5	10	25
Sample Buffer With Dropper	1	5	10	25
Dripper				25
Tube				25
Tube Holder				1
Instruction for use	1	1	1	1
Quick Reference Instructions	NA	1	1	1

***Note:** The components in different batches of the kit cannot be mixed.*

Materials required but not provided

1. Transfer pipette
2. Timer
3. Latex gloves

PRECAUTIONS/WARNINGS

1. For in vitro diagnostic use only.
2. Do not use kit past its expiration date.
3. Do not mix components from different kit lots.
4. Use only the swabs provided for collecting swab samples. Other swabs may not work properly.
5. Extraction Reagent is slightly caustic. Avoid contact with eyes, sensitive mucous membranes, cuts, abrasions, etc. If the reagent comes in contact with skin or eyes, flush with a large volume of water.
6. Wear disposable gloves while handling kit reagents or specimens and thoroughly wash hands afterwards.
7. All specimens should be handled as if they are capable of transmitting disease. Observe established precautions against microbiological hazards throughout all procedures and follow the standard procedures for proper disposal of specimens and test devices.
8. The Test device should remain in its original sealed pouch until ready for use.

STORAGE AND STABILITY

1. Store at 2°C - 30°C in the sealed pouch up to the expiration date printed on the package, forbidden to store under 2°C and avoid using expired products.
2. The test card is used within 15 minutes after taking out from the foil envelope. Buffer solution are re-capped in time after use.

3. The buffer should be used immediately after dropping into the dropper.

4. MFD date and EXP date: marked on the label. The product will be expired after 24 months

SPECIMEN COLLECTION AND PREPARATION

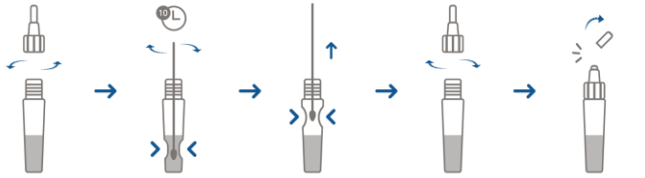
1. Inadequate or inappropriate specimen collection, storage, and transport are likely to yield false negative test results. Training in specimen collection is highly recommended because of the importance of specimen quality.
2. To collect nasal swab specimens, the swab provided in the Test kit should only be used.
3. The buffer provided in the kit should only be used. Use fresh samples for best performance. Freshly collected specimens should be tested immediately. If necessary, aspirate specimens may be stored for up to 8 hours at room temperature or up to 24 hours at 2–8°C, and swab samples for up to 4 hours at room temperature or up to 8 hours at 2–8°C. Aspirate samples can be frozen for up to 7 days.

TEST PROCEDURE

Sample Processing:

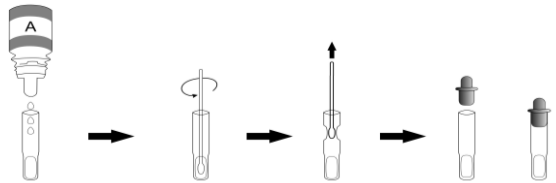
1. Open the dripper head OR Take out the tube, add about 300μL of sample buffer (to 300uL mark line or 9 drops vertically) to the tube.
2. Completely immerse the swab head of the collected sample into the buffer in the tube.
3. Rotate the sample against the inner wall of the tube approximately 10 times or squeeze the tube 10 times to elute the sample to ensure that the sample on the swab is fully eluted into the buffer.
4. Squeeze the swab head along the inner wall of the tube to keep the liquid in the tube as much as possible.
5. Discard the swab and cover the drip head to mix the liquid thoroughly.
6. Samples should be eluted and used immediately after collection; at the same time, the samples should not be inactivated, stored, or frozen and thawed.

***Note：** Recommend to use a pipette to transfer the samples to reduce deviations.*



Open the dripper head | Vigorously mix at least 10 times | Squeeze liquid from swab | Cover the dripper head | Break the dripper head

OR (for 0575C3X025)

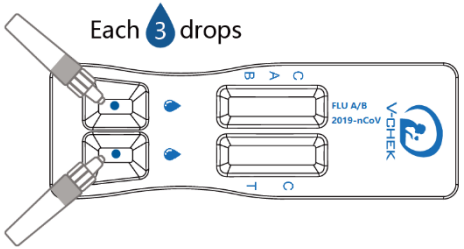


300μL (to the 300μL mark line, 9 drops)Sample Buffer | Vigorously mix at least 10 times | Squeeze liquid from swab | Cover the dripper head

Test Procedure:

Before test, please read the instruction manual.

1. Take the required reagents and test cassette to equilibrate to room temperature.
2. Unpack the aluminum foil bag, place the test cassette horizontally on the table and mark it.
3. Break the dripper head.
4. Add 80μL (3 drops) of the processed sample to each sample well, and timed. Recommended to use a pipette to take buffer/samples to reduce deviations.
5. As the test begins to work, you will see purple color move across the result window in the center of the test device.
6. Wait for 15 minutes and read the results. Do not read results after 20 minutes.



INTERPRETATION OF RESULTS

Positive Result

For the 2019-nCoV test:

A reddish-purple Control line (C position) and a reddish-purple Test line indicate that 2019-nCoV antigen has been detected. Determination of a positive result can be made as soon as a visible Test line and Control line appear.

For the Flu A/B test:

a reddish-purple Control line (C position) and a reddish-purple Test line (A or B position) indicate that Influenza A or B antigen has been detected. Lines at the A and C positions indicate the presence of Influenza type A viral antigen, and lines at the B and C positions indicate the presence of Influenza type B viral antigen in the specimen. A positive result does not rule out co-infections with other pathogens or identify any specific influenza A virus subtype. Determination of a positive result can be made as soon as both a visible Test line (either A or B) and Control line appear.

***NOTE:** The Test line (reddish purple line) may vary in shade and intensity (light or dark, weak or strong) depending on the concentration of antigen detected. The intensity of the Control line should not be compared to that of the Test line for the interpretation of the test result.*

Negative Result：

For 2019-nCoV test:

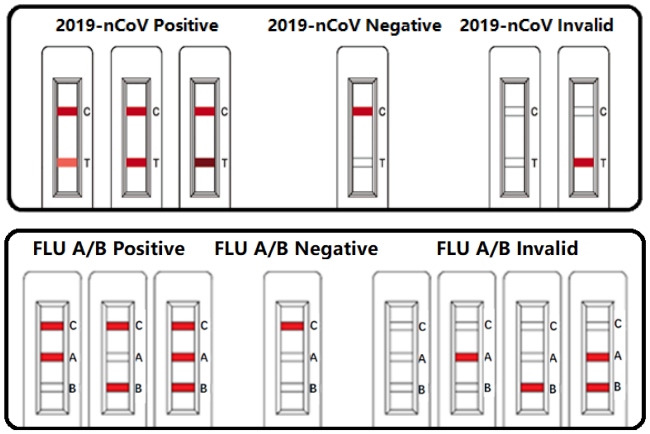
only a reddish-purple Control line (C position), with no Test line, indicates that 2019-nCoV antigen has not been detected. A negative result does not exclude 2019-nCoV viral infection. Determination of negative results should not be made before 15 minutes. If a line does not form at the Control line position in 15 minutes, the test result is invalid and the test should be repeated with a new Test device.

For Flu A/B test:

only a reddish-purple Control line (C position), with no Test line at the A or B position, indicates that Influenza A or B antigen has not been detected. A negative result does not exclude influenza viral infection. Determination of negative results should not be made before 15 minutes. If a line does not form at the Control line position in 15 minutes, the test result is invalid and the test should be repeated with a new Test device.

Invalid Result：

The test result is invalid if a colored line does not form in the control region. The sample must be re-tested, using a new test cassette.



LIMITATIONS

1. A negative test result does not exclude infection with 2019-nCoV or influenza A / B. Therefore, the results obtained with the Test should be used in conjunction with clinical findings to make an accurate diagnosis.
2. The performance of this test has not been evaluated for sample types other than those specified in the Intended Use.
3. This test cannot rule out diseases caused by other bacterial or viral pathogens.
4. The Flu A/B antigen test can distinguish between influenza A and B viruses, but it cannot differentiate influenza subtypes.
5. The Test uses highly target specific monoclonal antibodies. As in most immunoassays, it may fail to detect, or detect with less sensitivity.
6. Performance of the Test has not been established for monitoring antiviral treatment of 2019-nCoV or influenza.
7. Positive and negative predictive values are highly dependent on prevalence. False negative test results are more likely during peak activity when prevalence of disease is high. False positive test results are more likely during periods of low influenza activity when prevalence is moderate to low.
8. Individuals who received nasally administered influenza A vaccine may produce positive test results for up to three days after vaccination.
9. The performance of this assay has not been evaluated for use in patients without signs and symptoms of respiratory infection.
10. The performance of this test has not been evaluated for immunocompromised individuals.

PERFORMANCE CHARACTERISTICS

Clinical Performance:

Samples were tested with 2019-nCoV Ag & FLU A/B Combo Rapid test, and PCR.

A. Influenza A

Sensitivity:123/144 85.42%, (95% CI: 78.73, 90.26)

Specificity:373/378 98.68%, (95% CI: 96.94, 99.43)

Influenza A	Comparative RT-PCR Test Result		
	Positive (+)	Negative (-)	Total
Detected Positive	123	5	128
Detected Negative	21	373	394
Total	144	378	522

B. Influenza B

Sensitivity:99/116 85.34%, (95% CI: 77.78, 90.64)

Specificity:376/378 99.47%, (95% CI: 98.09, 99.85)

Influenza B	Comparative RT-PCR Test Result		
	Positive (+)	Negative (-)	Total
Detected Positive	99	2	101
Detected Negative	17	376	393
Total	116	378	494

C. 2019-nCoV Ag

The performance of 2019-nCoV Ag established with 260 nasopharyngeal swabs collected from symptomatic patients, who with symptoms onset within 7 days.

Sensitivity: 58/60 96.67%, (95% CI: 88.64, 99.08)

Specificity: 199/200 99.50%, (95% CI:97.22, 99.91).

2019-nCoV Ag	Comparative RT-PCR Test Result		
	Positive (+)	Negative (-)	Total
Detected Positive	58	1	59
Detected Negative	2	199	201
Total	60	200	260

Positive results broken down by days since symptom onset:

Days since symptom onset	RT-PCR Positive (+)	2019-nCoV Ag Rapid Test Kit (Immunochromatography)	PPA
1	6	6	100%
2	12	12	100%
3	20	20	100%
4	30	30	100%
5	40	40	100%
6	50	50	100%
7	60	58	96.67%

The performance of 2019-nCoV Ag with positive results stratified by the comparative method cycle threshold (Ct) counts were collected and assessed to better understand the correlation of assay performance to the cycle threshold, As presented in the table below, the positive agreement of the 2019-nCoV Ag is higher with samples of a Ct count <25.

2019-nCoV Ag	Comparative RT-PCR Method (Positive by Ct Value)	
	Positive (Ct<=25)	Positive (25<Ct<30)
Detected Positive	30	28
Total	30	30
Positive agreement	100%	93.3%

A limited number of patients who presented with symptom onset greater than seven days and also the asymptomatic patients were enrolled in the clinical study (n = 25). the sample size was relatively small, the positive agreement was 61.5% (8/13) and negative agreement was 91.6% (11/12). Therefore, negative results in patients with symptom onset greater than seven days should be treated as presumptive and confirmed with a molecular assay if needed for clinical management, and the test is for professional used.

Limit of Detection (LOD):

For the 2019-nCoV Ag test:

When the virus culture concentration was 100 $TCID_{50}$/mL and above, the positive rate was greater than or equal to 95%. At virus culture concentration of 50 $TCID_{50}$/mL and below, the positive rate is not higher than 95%, so the minimum detection limit of the 2019-

nCoV Ag test is 100 $TCID_{50}$/mL.

For the Flu A/B test

The analytical sensitivity (limit of detection or LOD) of the test was determined using quantified (TCID50/mL) cultures of three influenza A strains and two influenza B strains, serially diluted in negative nasopharyngeal matrix. Each dilution was run as 30 replicates in the test. Analytical sensitivity (LOD) is defined as the lowest concentration at which at least 95% of all replicates tested positive. The demonstrated LOD for each strain tested is shown below:

Influenza Type	Strain	TCID $_{50}$/ML
A	A/Taiwan/42/06	$1.58x10^3$
A	A/HongKong/8/68	2.37×10^4
A	A/Victoria/3/75	$1.05x10^2$
A	A/14160 (H1N1)	8×10^3
A	A/HK/403946/09	5.1×10^5
A	A/44045	2.0×10^4
A	A/924	4.8×10^3
A	A/Beijing/302/54	4.8×10^3
A	A/swine/Guangdong/2/01	7.2×10^3
A	S-OIV A/HK/415742/09	1.7×10^3
A	S-OIV A/California/4/09	2.0×10^3
B	B/1715	7.9×10^3
B	B/1704	6.3×10^2
B	B/179	2.1×10^3
B	B/668	1.4×10^4
B	B/Taiwan/2/62	1.58×10^3
B	B/ Malaysia/2506/2004	3×10^5

Cross-reactivity:

The potential cross-reactivity of the non-influenza respiratory pathogens and other microorganisms with which the majority of the population may be infected was tested using the Test at medically relevant levels, 10^6 CFU/mL for bacteria and 10^5PFU/mL for non-flu viruses. None of the organisms or viruses listed in the table below gave a positive result with the Test at the tested concentration.

A． Viruses Tested

Adenovirus	Human parainfluenza; Type 1
Human coronavirus	Human parainfluenza; Type 2
Cytomegalovirus	Human parainfluenza; Type 3
Enterovirus	Rhinovirus; Type 1A
Epstein Barr Virus	Respiratory syncytial virus; Type B
Measles	Human metapneumovirus

B． Bacteria Tested

Bordetella pertussis	Chlamydia pneumoniae
Corynebacterium sp.	Escherichia coli
Hemophilus influenzae	Lactobacillus sp.
Legionella sp.	Moraxella catarrhalis
Mycobacterium tuberculosis avirulent	Mycoplasma pneumoniae
Neisseria meningitides	Neisseria sp.
Pseudomonas aeruginosa	Staphylococcus aureus
Staphylococcus epidermidis	Streptococcus pneumoniae
Streptococcus pyogenes	Streptococcus salivarius

Interference:

The performance of 2019-nCoV Ag & FLU A/B Combo Rapid Test was evaluated with potentially interfering substances that may be present in nasal specimens. The potentially interfering substances were evaluated with influenza A (A/Taiwan/42/06), influenza B (B/ Malaysia/2506/2004) and 2019-nCoV at concentrations of 2x LOD. There was no evidence of interference caused by the substances tested at the concentrations shown below.

Substances	**Concentration**
Whole Blood	1%
Mucin	1mg/ml
Benzocaine	1mg/ml
Menthol	1mg/ml
Zanamivir	1mg/ml
Mupirocin	1mg/ml
Tobramycin	1mg/ml
Fluticasone	1mg/ml
Beclomethasone	1mg/ml
Dexamethasone	1mg/ml
Flunisolide	1mg/ml
Triamcinolone	1mg/ml
Mometasone	1mg/ml
Sodium Chloride with preservative	20%
Phenylephrine	10mg/ml
Oxymetazoline	10mg/ml

REFERENCES

1. WHO recommendations on the use of rapid testing for influenza diagnosis, July 2005.
2. Atmar, R.L. and Lindstrom, S.E. 2011. Influenza Viruses in Manual of Clinical Microbiology. 10th Edition. 1333–1334.
3. Lauer, S.A., et. al. The incubation period of Coronavirus disease 2019 (COVID-19) from publicly reported confirmed cases: estimation and application, Ann Intern Med. 2020.

INDEX OF SYMBOL

COMPONENT	Materials Included	DROPPER	Dropper with Sample Buffe
CASSETTE	Test Cassette	SWAB	Swab
TUBE	Tube	HOLDER	Tube Holder
IFU	Instructions for Use		Date of Manufacturer
	Consult Instructions For Use		Do Not Reuse
	Store at 2°C~30°C	REF	Catalogue Number
	Expiration Date		Keep away from Sunlight
	Manufacturer		Tests per Kit
LOT	Lot Number		Keep Dry
EC REP	Authorized Representative	IVD	In Vitro Diagnostic Medical Device

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Doc No.: DC-IN-0575C02 Ver 1.0
Rel.:2020/09/21