CE IVD

* Please carefully read the instructions before use
* For In Vitro Diagnostic and Professional Use only.

Influenza A/B+COVID-19/RSV Combo Ag Test

Specimen: Nasal swab specimen
Format: Multi-Panel

INTENDED USE

Influenza A/B+COVID-19/RSV Combo Ag Test is an in vitro immunochromatographic assay for the qualitative and differential detection of nucleocapsid protein antigen from influenza A (including the subtype H1N1), influenza B, respiratory syncytial virus and/or SARS-CoV-2 in nasal swab specimens from symptomatic and asymptomatic patients. It is intended to aid in the rapid diagnosis of influenza A, influenza B, respiratory syncytial virus, and/or SARS-CoV-2 infections in the healthcare setting management, general population screening, workplace screening, etc. It is intended to be used by a trained healthcare professional, member of the allied health professions, and trained lay-person at point-of-care, near-patient, and laboratory-based testing.

This test provides only a preliminary test result. Therefore, any reactive specimen with the Influenza A/B+COVID-19/RSV Combo Ag Test must be confirmed with alternative testing method(s) and clinical findings.

INTRODUCTION

Influenza is a highly contagious, acute viral infection of the respiratory tract with symptoms such as headache, chills, dry cough, body aches or fever. It is a communicable disease that is easily transmitted through aerosolized droplets containing live virus from coughing and sneezing. The causative agents of the disease are immunologically diverse single strand RNA viruses known as influenza viruses. Influenza type A viruses are typically more prevalent than influenza type B viruses and are associated with most sensitive influenza epidemics, while influenza type B infections are usually milder. Diagnosis is difficult because the initial symptoms are similar to those caused by other infectious agents. Accurate diagnosis and prompt treatment of patients can have a positive effect on public health. Rapid and accurate diagnosis of influenza viral infection can also help reduce the inappropriate use of antibiotics and gives the physician the opportunity to prescribe appropriate antiviral medications.

Respiratory syncytial virus is an RNA virus belonging to the paramyxoviridae family. The disease is spread by airborne droplets and close contact. It is more common in newborns and infants less than 6 months old. The incubation period is 3~7 days. Infants and young children have more severe symptoms, including high fever, rhinitis, pharyngitis and laryngitis, followed by bronchiolitis and pneumonia. A few sick children can be complicated with otitis media, pleurisy and myocarditis, etc. Upper respiratory tract infection is the main symptom of infection in adults and older children.

CoV is mainly transmitted through direct contact with secretions or through aerosols and droplets. Evidence suggests transmission via fecal-oral route. 7 kinds of HCoV's caused human's respiratory diseases are found by now: HCoV-229E, CoV-OC43, SARS-CoV, HCoV-NL63, HCoV-HKU1, MERS-CoV and COVID-19 which are the serious pathogens for human's respiratory diseases. Its clinical manifestation are fever, enervate and systemic symptom, with dry cough, difficult breathing etc. and it may aggravate to severe pneumonia, respiratory failure, acute respiratory distress syndrome, septic shock, multiple organ failure, severe acid-base metabolic disorders etc and even life threatening rapidly.

PRINCIPLES

The Flu A/B Antigen strip uses influenza A monoclonal antibody (T1), influenza B monoclonal antibody (T2), and goat anti-mouse IgG polyclonal antibodies (C) that are respectively immobilized on a nitrocellulose membrane. It uses colloidal gold to label influenza A monoclonal antibody and influenza B monoclonal antibody. Using nano-colloidal gold technology and applying highly specific antibody-antigen reaction and immunochromatographic analysis technology principle. When testing, the Influenza type A viruses antigen in the sample combined with the colloidal gold-labeled influenza A monoclonal antibody to form a complex, which was then combined with the influenza A monoclonal antibody coated in the test line T1 during chromatography, at this time there is one red line in the T1 area. The Influenza type B viruses antigen in the sample combined with the colloidal gold-labeled influenza B monoclonal antibody to form a complex, which was then combined with the influenza B monoclonal antibody coated in the test line T2 during chromatography, at this time there is one red line in the T2 area.When the samples do not contain Influenza type A and B viruses antigens, there is no red colored lines in the T1 and T2 areas. Regardless of the presence of Influenza type A or B viruses antigens in the sample, a red line will form in the quality control area (C). The red line appears in the quality control area (C) serves as 1.verification that sufficient volume is added. 2.That proper flow is obtained 3. And as a control for the reagents.

The COVID-19/RSV Antigen strip uses COVID-19 monoclonal antibody (T2), RSV monoclonal antibody (T1) and goat anti-mouse IgG polyclonal antibodies (C) that are respectively immobilized on a nitrocellulose membrane. It uses colloidal gold to label COVID-19 monoclonal antibody, RSV monoclonal antibody. Using nano-colloidal gold technology and applying highly specific antibody- antigen reaction and immunochromatographic analysis technology principle. When testing, the COVID-19 antigen in the sample combined with the colloidal gold-labeled COVID-19 monoclonal antibody to form a complex, which was then combined with the COVID-19 monoclonal antibody coated in the test line T2 during chromatography, at this time there is one red line in the T2 area. The RSV antigen in the sample combined with the colloidal gold-labeled RSV monoclonal antibody to form a complex, which was then combined with the RSV monoclonal antibody

coated in the test line T1 during chromatography, at this time there is one red line in the T1 area. When the samples do not contain COVID-19 and RSV antigens, there is no red colored lines in the T1 and T2 areas .Regardless of the presence of Influenza type A or B viruses antigens in the sample, a red line will form in the quality control area (C). The red line appears in the quality control area (C) serves as 1.verification that sufficient volume is added. 2.That proper flow is obtained 3. And as a control for the reagents.

MATERIALS PROVIDED

Influenza A/B+COVID-19/RSV Combo Ag Test contains the following items to perform the assay:

Model	1 Test/Box	25 Tests/Box
REF	B292-01	B292-20
Test cassette	1	25
Sample collection tube containing processing solution	1	25
Sampling swab	1	25
Instruction for use	1	1

MATERIALS REQUIRED BUT NOT PROVIDED

- Clock or Timer

WARNING AND PRECAUTIONS

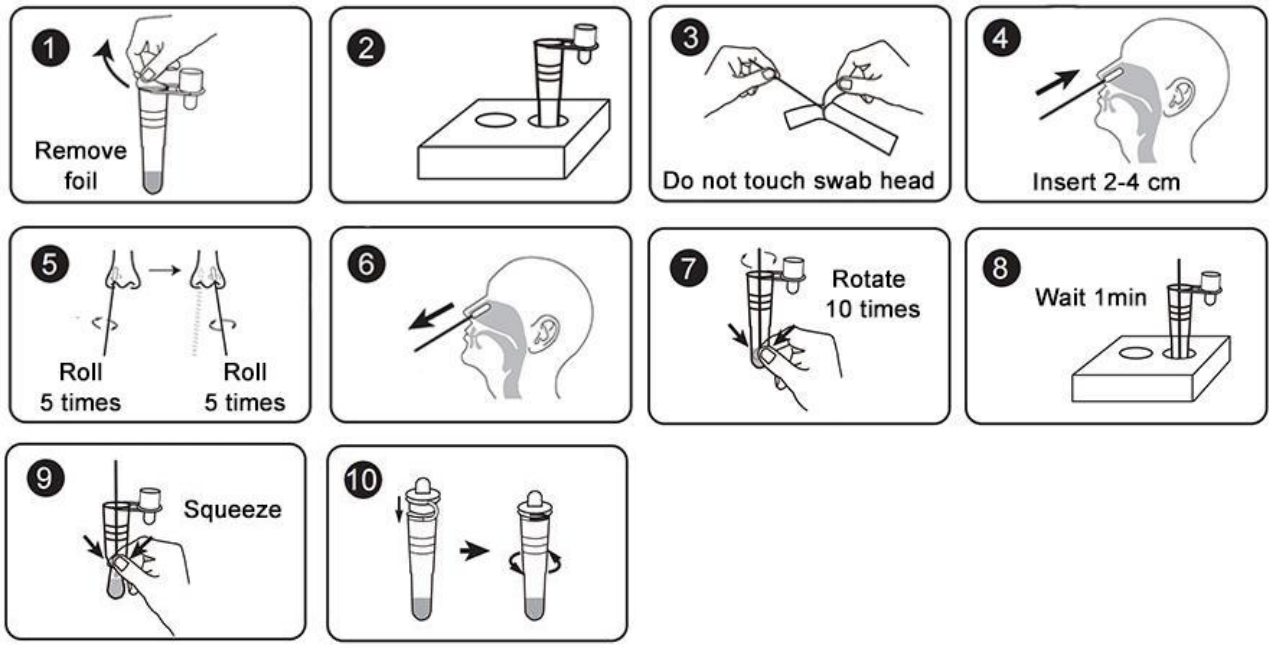
1. For in vitro diagnostic use only.
2. Do not use the test cassette beyond the expiration date.
3. The test cassette should remain in the sealed pouch until use. Do not use the test cassette if the pouch is damaged or the seal is broken.
4. Do not reuse the cassette and swab.
5. Do not mix and interchange different specimens.
6. You need to use the swab provided in the kit for sampling.
7. The testing process must follow SPECIMEN PREPARATION and TEST PROCEDURE.
8. Do not touch the swab head when handling the swab.
9. Insufficient sampling or wrong sampling process may lead to wrong results.
10. The test samples should be regarded as infectious agents and the operation should be in accordance with the infectious disease laboratory operating rules. After using this kit, the waste should be disposed according to the expected waste management system.
11. Before using this kit, you must read instructions carefully and strictly control the reaction time. If you do not follow the instructions, you will get inaccurate results.
12. Do not use turbid contaminated samples for testing.
13. Personal protective equipment is required for use of the product outside the laboratory environment.
14. The test does not include a viral inactivation step.

STORAGE AND STABILITY

Storage: store at 2~30℃.

The unsealed cassette is valid for 1 hour. It is recommended to use the testing kit immediately after opening. The expiration date is printed on the package.

SPECIMEN PREPARATION

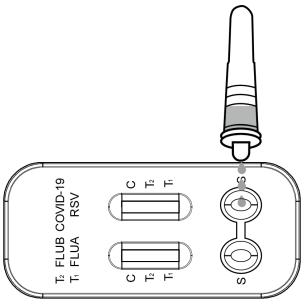


1. Remove the foil from the top of the sample collection tube.
2. Place the tube in the tube rack.
3. Remove a nasal swab from the pouch.
4. Using the sterile swab provided in the kit, carefully insert the swab into one nostril of the patient.
5. The swab tip should be inserted up to 2-4 cm until resistance is met. Roll the swab 5 times in a circular motion around the inside wall ensure that both mucus and cells are collected. Using the same swab, repeat this process for the other nostril to ensure that an adequate sample is collected from both nasal cavities.
6. Withdraw the swab from the nasal cavity.
7. The specimen is now ready for preparation using the extraction buffer provided in the test kit. Insert the swab in collection tube to the bottom, rotate and squeeze the swab 10 times while pressing the head against the bottom and side of the collection tube.
8. Leave the swab in the collection tube for 1 minute.
9. Rotate and squeeze the tube several times with fingers from outside of the tube to immerse the swab. Remove the swab.
10. Attach the dropper tip firmly onto the tube. Mix thoroughly by swirling or flicking the bottom of the tube.

Note:

1. Please use swab for specimen collection.
2. It is highly recommended to collect specimen with wearing a pair of safety gloves to avoid contamination.
3. Do not touch the tip (specimen collection area) of the swab.
4. It is recommended to treat the sample immediately after collection. The sample can be stored at 2℃~8℃ for 72 hours, and it needs to be frozen at -20℃ for long-term storage, avoiding repeated freezing and thawing.

TEST PROCEDURE



Read the instruction first prior to testing. Bring the pouched test to room temperature prior to testing. Do not open the pouch until ready to begin testing.

Remove the test from the sealed pouch. Lay it on a flat, clean and dry surface.

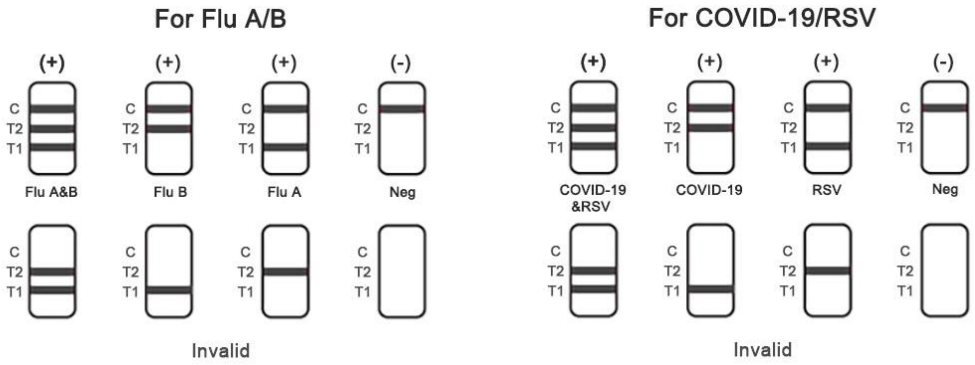
Reverse the sample collection tube, and add 3 drops of test sample by squeezing the collection solution tube into each of the sample well.

Read results at 10 minutes.

NOTE: The test is intended to be read at 10 minutes. If the test is read before 10 minutes or is read more than 30 minutes after the indicated read time, results may be inaccurate (false negative, false positive, or invalid) and the test should be repeated.

Collect all the package component and sealed in biohazard waste bag: including extraction dropper, swab, test cassette and assay diluent bottle. Discard waste bag according with local legislation.

INTERPRETATION OF RESULTS



For Flu A/B Antigen Test

1. Flu A Positive:

The presence of two lines as control line (C) and T1 test line within the result window indicates a positive result for Influenza A viral antigen.

2. Flu B Positive:

The presence of two lines as control line (C) and T2 test line within the result window indicates a positive result for Influenza B viral antigen.

3. Flu A+B Positive:
The presence of three lines as control line (C), T1 test line and T2 test line within the result window indicates a positive result for Influenza A and Influenza B viral antigen.
4. NEGATIVE:
The presence of only control band (C) within the result window indicates a negative result.
5. INVALID:
If the control band (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.

For COVID-19/RSV Antigen Test

1. RSV Positive:
The presence of two lines as control line (C) and T1 test line within the result window indicates a positive result for RSV viral antigen.
2. COVID-19 Positive:
The presence of two lines as control line (C) and T2 test line within the result window indicates a positive result for COVID-19 viral antigen.
3. COVID-19+RSV Positive:
The presence of three lines as control line (C), T1 test line and T2 test line within the result window indicates a positive result for RSV and COVID-19 viral antigen.
4. NEGATIVE:
The presence of only control band (C) within the result window indicates a negative result.
5. INVALID:
If the control band (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.

LIMITATION OF THE TEST

1. This test kit is only used for in vitro diagnosis.
2. This test kit is only used for qualitative detection and cannot indicate the level of antigens in the specimen.
3. Failure to follow the instructions for sample collection and testing will lead to erroneous results, and in this case the results are invalid.
4. If the antigen content in the sample is below the detection limit of the product, a false negative result will appear.
5. A negative test result may occur if the specimen is collected, extracted or transported improperly.
6. A negative test result does not rule out the possibility of infection.

7. A positive test result cannot exclude co-infection with other pathogens.
8. This kit is a clinical auxiliary test product. Any sample with a positive test result should be further confirmed by other methods.

PERFORMANCE CHARACTERISTICS

For Flu A/B Antigen Test:

1. Limit of Detection

The minimum Limit of Detection is 1.5×10^4 $TCID_{50}$/mL for the Influenza A virus of this kit and is 1.5×10^5 $TCID_{50}$/mL for the Influenza B virus of this kit.

2. Analytical Specificity

There is no cross reaction between the Influenza A+B Ag Test and the bacteria and viruses in the following table.

Potential Cross-reactant	Concentration	Potential Cross-reactant	Concentration
Human Adenovirus B	1.0×10^5 $TCID_{50}$/mL	Human respiratory syncytial virus A	1.0×10^5 $TCID_{50}$/mL
Human Adenovirus C	1.0×10^5 $TCID_{50}$/mL	Human respiratory syncytial virus B	1.0×10^5 $TCID_{50}$/mL
Human Adenovirus type 10	1.0×10^5 $TCID_{50}$/mL	Acinetobacter calcoaceticus	1.0×10^7 org/mL
Human Adenovirus type 18	1.0×10^2 $TCID_{50}$/mL	Bacteroides fragilis	1.0×10^7 org/mL
Human Rhinovirus 2	1.0×10^5 PFU/mL	Neisseria gonorrhoeae	1.0×10^7 org/mL
Human Rhinovirus 14	1.0×10^5 $TCID_{50}$/mL	Neisseria meningitidis	1.0×10^7 org/mL
Human Rhinovirus 16	1.0×10^5 $TCID_{50}$/mL	Pseudomonas aeruginosa	1.0×10^7 org/mL
Measles	1.0×10^5 $TCID_{50}$/mL	Staphylococcus aureus	1.0×10^7 org/mL
Human coronavirus OC43	1.0×10^5 $TCID_{50}$/mL	Streptococcus pneumoniae	1.0×10^7 cells/mL
Mumps	1.0×10^5 $TCID_{50}$/mL	Streptococcus sanguis	1.0×10^7 org/mL
Human Coxsackievirus A9	1.0×10^5 $TCID_{50}$/mL	Proteus vulgaris	1.0×10^7 org/mL
Sendai virus	1.0×10^5 $TCID_{50}$/mL	Streptococcus sp. Gp.B	1.0×10^7 org/mL
Coxsackievirus B5	1.0×10^5 $TCID_{50}$/mL	Streptococcus sp. Gp.C	1.0×10^7 org/mL
Parainfluenza virus 2	1.0×10^5 $TCID_{50}$/mL	Streptococcus sp. Gp.G	1.0×10^7 org/mL
Human herpesvirus 2	1.0×10^5 $TCID_{50}$/mL	Mycobacterium tuberculosis	1.0×10^7 cells/mL
Parainfluenza virus 3	1.0×10^2 $TCID_{50}$/mL	Mycoplasma orale	1.0×10^7 org/mL
SARS-COV-2	1.0×10^5 $TCID_{50}$/mL	Pooled human nasal wash	N/A

No cross-reactivity was observed between Influenza A and Influenza B at 1.0×10^5 $TCID_{50}$/mL.

3. Interfering Substances

Whole blood, and several over-the-counter (OTC) products and common chemicals were evaluated and did not interfere with the Influenza A+B Ag Test at the levels tested:
Whole blood (2.5%); Three OTC mouthwashes (25%); Three OTC nasal sprays (10%); 4-Acetamidophenol (10 mg/mL); Acetylsalicylic Acid (20 mg/mL); Chlorpheniramine (5 mg/mL); Dextromethorphan (10 mg/mL); Diphenhydramine (5 mg/mL); Ephedrine (20 mg/mL); Guaiacol glyceryl ether (20 mg/mL); Oxymetazoline (10 mg/mL); Phenylephrine (100 mg/mL); and Phenylpropanolamine (20 mg/mL).

For COVID-19/RSV Antigen Test :

1. Limit of Detection

The LoD of COVID-19 Ag for this kit was confirmed as 200$TCID_{50}$/mL. The LoD of RSV for this kit was confirmed as 1×10^4 $TCID_{50}$/mL.

2. Analytic Specificity

There is no cross reaction between the COVID-19 /RSV Ag Test and Cross-reactive substance in the following table.

Potential Cross-Reactant	Concentration	Potential Cross-Reactant	Concentration
Adenovirus	1.0×10^5 $TCID_{50}$/mL	Chlamydia pneumoniae	1.0×10^6 IFU/mL
Human metapneumovirus (hMPV)	1.0×10^5 $TCID_{50}$/mL	Haemophilus influenzae	1.0×10^6 cells/mL
Rhinovirus	1.0×10^5 $TCID_{50}$/mL	Legionella pnuemophila	1.0×10^6 cells/mL
Enterovirus/Coxsackievirus B4	1.0×10^5 $TCID_{50}$/mL	Mycoplasma pneumoniae	1.0×10^6 PFU/mL
Human coronavirus OC43	1.0×10^5 $TCID_{50}$/mL	Streptococcus pneumoniae	1.0×10^6 cells/mL
Human coronavirus 229E	1.0×10^5 $TCID_{50}$/mL	Streptococcus pyogenes (group A)	1.0×10^6 cells/mL
Human coronavirus NL63	1.0×10^5 $TCID_{50}$/mL	Mycobacterium tuberculosis	1.0×10^6 cells/mL
Human coronavirus HKU1	1.0×10^5 $TCID_{50}$/mL	Staphylococcus aureus	1.0×10^6 org/mL
Human parainfluenza virus 1	1.0×10^5 $TCID_{50}$/mL	Staphylococcus epidermidis	1.0×10^6 org/mL
Human parainfluenza virus 2	1.0×10^5 $TCID_{50}$/mL	Pooled human nasal wash	N/A
Human parainfluenza virus 3	1.0×10^5 $TCID_{50}$/mL	Candida albicans	1.0×10^5 $TCID_{50}$/mL
Human parainfluenza virus 4	1.0×10^5 $TCID_{50}$/mL	Negative sample from healthy people 1 (Collected in Feb. 2019)	N/A
Influenza A H3N2	1.0×10^5 $TCID_{50}$/mL	Negative sample from healthy people 2 (Collected in Feb. 2019)	N/A
Influenza A H1N1	1.0×10^5 $TCID_{50}$/mL	Negative sample from healthy people 3 (Collected in Apr. 2019)	N/A
Influenza A H5N1	1.0×10^5 $TCID_{50}$/mL	Negative sample from healthy people 4 (Collected in Jun. 2019)	N/A
Influenza A H7N9	1.0×10^5 $TCID_{50}$/mL	Negative sample from healthy people 5 (Collected in Jun. 2019)	N/A
Influenza B Yamagata	1.0×10^5 $TCID_{50}$/mL	Nasal swab sample 1 day after inoculation of COVID-19 inactivated vaccine)	N/A
Influenza B Guangdong/120/00	1.0×10^5 $TCID_{50}$/mL	Nasal swab sample 3 days after inoculation of COVID-19 recombinant subunit vaccine	N/A
Respiratory Syncytial Virus A	1.0×10^5 $TCID_{50}$/mL	Nasal swab sample 5 days after inoculation of COVID-19 adenovirus vector vaccine	N/A

Respiratory Syncytial Virus B	1.0×10^5 $TCID_{50}$/mL	Nasal swab sample 1 month after inoculation of COVID-19 inactivated vaccine	N/A
SARS-COV-2	1.0×10^5 $TCID_{50}$/mL	Nasal swab sample 3 months after inoculation of COVID-19 recombinant subunit vaccine	N/A
MERS-CoV	1.0×10^5 $TCID_{50}$/mL	Nasal swab sample 5 months after inoculation of COVID-19 adenovirus vector vaccine	N/A
Bordetella pertussis	1.0×10^6 cells/mL	/	/

No cross-reactivity was observed between SARS-COV-2 and Respiratory Syncytial Virus at 1.0×10^5 $TCID_{50}$/mL.

COVID-19 /RSV Ag Test might have cross-reactivity with SARS-CoV because they have high homology to the SARS-CoV-2.

3. Interference

The following substances and conditions were found not to interfere with the test. List of potentially interfering compounds and concentrations tested are as follows:

Substance	Active Ingredient	Concentration
Endogenous	Mucin	2% v/v
	Whole Blood	2.5% v/v
	Rheumatoid factor	200 IU/mL
	Icteric (Bilirubin)	40 mg/dL
	Hemoglobin	100 mg/L
	Triglycerides	1.5 mg/L
	Human anti-mouse antibody	1μg/mL
OTC Nasal Drops	Phenylephrine	15% v/v
OTC Nasal Gel	Sodium Chloride (i.e., NeilMed)	5% w/v
OTC Nasal Spray 1	Cromolyn	15% v/v
OTC Nasal Spray 2	Oxymetazoline	15% v/v
OTC Nasal Spray 3	Fluconazole	5% w/v
Throat Lozenge	Benzocaine, (Ethyl 4-aminobenzoate)	0.15% w/v
OTC Homeopathic Nasal Spray 1	Galphimia glauca, Veratramine	20% v/v
OTC Homeopathic Nasal Spray 2	Zincum gluconium (Zinc Gluconate)	5% w/v
OTC Homeopathic Nasal Spray 3	Alkalol	10% v/v
OTC Homeopathic Nasal Spray 4	Fluticasone Propionate	5% w/v
Sore Throat Phenol Spray	Phenol	15% w/v
Anti-viral Drug	Tamiflu (Oseltamivir Phosphate)	0.5% w/v
Antibiotic, Nasal Ointment	Mupirocin	0.25% w/v
Antibacterial, Systemic	Tobramycin	0.0004% w/v
Medications	Lopinavir	16.4 μg/L
	Ritonavir	16.4 μg/L

	Amoxicillin	5.4 mg/dL
	Chlorpheniramine	0.08 mg/dL
Biotin	D-Biotin	1.2 μg/mL
Nasal corticosteroids	Mometasone	1.28 ng/mL
	Budesonide	2.76 ng/mL

DIAGNOSTIC SENSITIVITY AND SPECIFICITY

For Flu A+B Antigen Test:

A study using total 600 nasal swab samples was conducted. The diagnostic sensitivity and specificity of the influenza A Ag test and the influenza B Ag test results are given as below:

Table 1 - Comparison of influenza A Ag test

		Results of Clinical diagnosis		Total Result
		Positive	Negative	
Results of Influenza A Ag test	Positive	118	2	120
	Negative	1	479	480
Total Results		119	481	600

Sensitivity of 99.2% (118/119), Specificity of 99.6% (479/481), A total agreement of 99.5% (597/600).

Table 2 - Comparison of influenza B Ag test

		Results of Clinical diagnosis		Total Result
		Positive	Negative	
Results of Influenza B Ag test	Positive	109	1	110
	Negative	1	489	490
Total Results		110	490	600

Sensitivity of 99.1% (109/110), Specificity of 99.8% (489/490), A total agreement of 99.7% (598/600).

For COVID-19/RSV Antigen Test:

A study using a total 260 nasal swab samples was conducted.Test results were compared with nucleic acid detection test. The diagnostic sensitivity and specificity of the test results are shown in Table 3:

Table 3 - Comparison of COVID-19 Ag Test

		Results of nucleic acid detection test		Total result
		Positive	Negative	
Results of COVID-19 Ag Test	Positive	78	0	78
	Negative	32	150	182
Total results		110	150	260

Diagnostic Sensitivity: 78/110, 70.91% (95%CI: 61.48% ~ 79.18%)

Diagnostic Specificity: 150/150, 100.00% (95%CI: 97.57% ~ 100.00%)

Total Agreement: 228/260, 87.69% (95%CI: 83.07% ~ 91.43%)

Across 110 positive samples, 40% of samples with Ct<25, 40% of samples with 25≤Ct ≤30, and 20% of samples with Ct >30.

The test results of diagnostic sensitivity of samples with Ct ≤25: 44/44,100.00% (95%CI: 91.96% to 100.00%)

A study using a total 415 nasal swab samples was conducted.Test results were compared with nucleic acid detection test. The diagnostic sensitivity and specificity of the test results are shown in Table 4:

Table 4 -Comparison of RSV Ag Test

		Results of nucleic acid detection test		Total result
		Positive	Negative	
Results of RSV Ag Test	Positive	112	2	114
	Negative	3	298	301
Total results		115	300	415

Results gave sensitivity is 97.4% (112/115), specificity is 99.3%(298/300), and a total agreement of 98.8%(410/415).

INDEX OF SYMBOLS

	Do not re-use		Manufacturer
IVD	In vitro diagnostic medical device		Use-by date
2°C 30°C	Store at 2-30°C		Consult instructions for use
CE	CE Mark	LOT	Batch code
	Do not use if package is damaged and consult instructions for use	EC REP	Authorized Representative in the European Union

	Core Technology Co., Ltd. Room 100, C Building, No.29 Life Park Rd., Changping District, Beijing 102206, P.R.China
EC REP	SUNGO Cert GmbH Harffstr. 47, 40591 Düsseldorf, Germany

No.: IFU-CORE-FluA/B+COVID/RSV-Ag-C

Ver.: 1.4

Eff. Date: Mar. 2023