HEALGEN®

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Influenza & COVID-19 Ag Combo Rapid Test Cassette (Swab)

HEALGEN®

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INTENDED USE

The Influenza & COVID-19 Ag Combo Rapid Test Cassette (Swab) 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 and/or SARS-CoV-2 in nasopharyngeal (NP) swab specimens. It is intended to aid in the rapid diagnosis of influenza A, influenza B and/or SARS-CoV-2 infections. This test provides only a preliminary test result. Therefore, any reactive specimen with the Influenza & COVID-19 Ag Combo Rapid Test Cassette (Swab) must be confirmed with alternative testing method(s) and clinical findings.

SUMMARY AND EXPLANATION

Influenza is an acute and highly contagious viral infection of the respiratory tract. The causative agents of the disease are immunologically diverse, single-strand RNA virus known as influenza viruses. There are three types of influenza viruses: A, B and C. Type A viruses are the most prevalent and are associated with most serious epidemics, while Type B infection is generally milder. Type C virus have never been associated with a large epidemic of human disease. Both type A and B viruses can circulate simultaneously, but usually one type is dominant during a given season and particular epidemic area. The disease is easily transmitted through coughing and sneezing of aerosolized droplets containing live virus. Influenza outbreaks normally occur each year during fall and winter seasons.

The novel coronaviruses belong to the β genus. COVID-19 is an acute respiratory infectious disease. Entire human population is 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, dry cough, and loss of taste and smell. Nasal congestion, runny nose, sore throat, myalgia and diarrhea are found in a few cases. This test is for detection of SARS-CoV-2 nucleocapsid protein antigen. Antigen is generally detectable in upper respiratory specimens during the acute phase of infection. Rapid diagnosis of SARS-CoV-2 infection will help healthcare professionals to treat patients and control the disease more efficiently and effectively.

Influenza & COVID-19 Ag Combo Rapid Test Cassette (Swab)

PRINCIPLE OF THE TEST

The Flu A&B Antigen Rapid Test is an immunochromatographic membrane assay that uses highly sensitive monoclonal antibodies to detect influenza type A and B nucleoprotein antigens in nasopharyngeal swab samples.The test strip is composed of the following parts: namely sample pad, reagent pad, reaction membrane, and absorbing pad. The reagent pad contains the colloidal-gold conjugated with the monoclonal antibodies against Influenza virus A and B; the reaction membrane contains the secondary antibodies either for virus A or for B. The whole strip is fixed inside a plastic device. When the sample is added into the sample well, conjugates dried in the reagent pad are dissolved and migrate along with the sample. If influenza A presents in the sample, a complex formed between the anti-influenza A conjugate and the virus will be captured by the specific anti-influenza A monoclonal antibodies coated on the A region (A). If the sample contains influenza B, a complex formed between the anti-influenza B conjugate and the virus will be captured by the specific anti-influenza B monoclonal antibodies coated on the B region (B). Results appear at 10 minutes in the form of a red line that develops on the membrane. To serve as a procedural control, a red line will always appear in the control region(C) indicating that proper volume of sample has been added and membrane wicking has occurred.

The COVID-19 Antigen Rapid Test Cassette is an immunochromatographic membrane assay that uses highly sensitive monoclonal antibodies to detect nucleocapsid protein from SARS-CoV-2 in nasopharyngeal (NP) swab. The test strip is composed of the following parts: namely sample pad, reagent pad, reaction membrane, and absorbing pad. The reagent pad contains the colloidal-gold conjugated with the monoclonal antibodies against the nucleocapsid protein of SARS-CoV-2; the reaction membrane contains the secondary antibodies for nucleocapsid protein of SARS-CoV-2. The whole strip is fixed inside a plastic device. When the sample is added into the sample well, conjugates dried in the reagent pad are dissolved and migrate along with the sample. If SARS-CoV-2 antigen presents in the sample, a complex formed between the anti-SARS-2 conjugate and the virus will be captured by the specific anti-SARS-2 monoclonal antibodies coated on the test line region (T). Absence of the T line suggests a negative result. To serve as a procedural control, a red line will always appear in the control line region (C) indicating that proper volume of sample has been added

and membrane wicking has occurred.

MATERIALS PROVIDED

1. 20 Test cassettes
2. 20 Sterile swabs
3. 20 Extraction tubes and 20 dropper tips
4. 1 Workstation
5. 2 Buffers
6. 1 Package insert

MATERIALS REQUIRED BUT NOT PROVIDED

1.Clock,timer or stopwatch

WARNINGS AND PRECAUTIONS

1.For in vitro diagnostic use only.
2.The test device should remain in the sealed pouch until use.
3.Do not use kit past its expiration date.
4.Swabs, tubes and test devices are for single use only.
5.The extraction buffer contains a solution with a preservative (0.09% sodium azide). If solution comes in contact with
the skin or eyes, flush with ample volumes of water.
6.Solutions that contain sodium azide may react explosively with lead or copper plumbing. Use large quantities of
water to flush discarded solutions down a sink.
7.Do not interchange or mix components from different kit lots.
8.When collecting a nasopharyngeal swab sample, use the Nasopharyngeal Swab supplied in the kit.
9.Wear appropriate personal protection equipment and gloves when running each test and handling patient
specimens. Change gloves between handling of specimens suspected of COVID-19.
10.Specimens must be processed as indicated in the SPECIMEN COLLECTION and SAMPLE PREPARATION
PROCEDURE sections of this Product Insert. Failure to follow the instructions for

use can result in inaccurate results.
11.To obtain accurate results, do not use visually bloody or overly viscous samples.
12.Proper laboratory safety techniques should be followed at all times when working with SARS-CoV-2 patient
samples. Patient swabs, used Test Strips and used extraction buffer vials may be potentially infectious. Proper
handling and disposal methods should be established by the laboratory in accordance with local regulatory
requirements.
13.Humidity and temperature can adversely affect results.
14.Used testing materials should be discarded in accordance with local regulations.

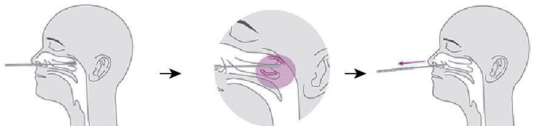
STORAGE AND STABILITY

1. The kit can be stored at room temperature or refrigerated (2-30°C).
2. Do not freeze any of the test kit components.
3. Do not use test device and reagents after expiration date.
4. Test devices that have been outside of the sealed pouch for more than 1 hour should be discarded.

SPECIMEN COLLECTION

Use the nasopharyngeal swab supplied in the kit.

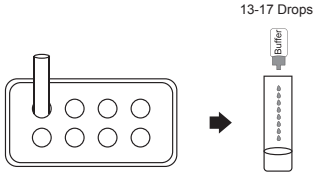
1.Carefully insert the swab into the nostril of the patient, reaching the surface of posterior nasopharynx. that presents
the most secretion under visual inspection.
2.Swab over the surface of the posterior nasopharynx. Rotate the swab several times.
3.Withdraw the swab from the nasal cavity.



SAMPLE PREPARATION PROCEDURE

1.Insert the test extraction tube into the paper stand in this product. Make sure that the tube is standing firm and reaches the bottom of the stand.

2.Add the sample extraction buffer to the extraction tube until it reaches the lower mark (about 13-17 drops, 0.5 mL).

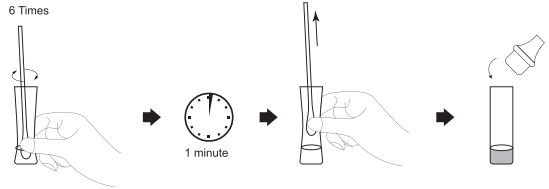


3.Insert the swab into the extraction tube which contains 0.5 ml of the extraction buffer.

4.Roll the swab at least 6 times while pressing the head against the bottom and side of the extraction tube.

5.Leave the swab in the extraction tube for 1 minute.

6.Squeeze the tube several times with fingers from outside of the tube to immerse the swab. Remove the swab. The extracted solution will be used as test sample.



SPECIMEN TRANSPORT AND STORAGE

Do not return the nasopharyngeal swab to the original paper packaging.

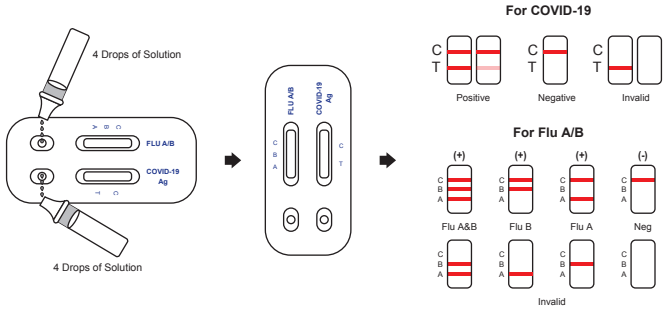
For best performance, direct nasopharyngeal swabs should be tested as soon as possible after collection. If immediate testing is not possible, and to maintain best performance and avoid possible contamination, it is highly recommended the nasopharyngeal swab is placed in a clean, unused plastic tube labeled with patient information, preserving sample integrity, and capped tightly at room temperature

(15-30°C) for up to 1 hour prior to testing. Ensure the swab fits securely within the tube and the cap is tightly closed. If greater than 1 hour delay occurs, dispose of sample. A new sample must be collected for testing.

TEST PROCEDURE

Allow the test device, test sample and buffer to equilibrate to room temperature (15-30°C) prior to testing.

1. Remove test device from the sealed pouch just prior to the testing and lay flat on work bench.
2. Insert a nozzle with filter into the sample extraction tube tightly.
3. Reverse the sample extraction tube, and add 4 drops (about 100 µl) of test sample by squeezing the extracted solution tube into the each sample well (S).
4. Wait for the colored band(s) to appear. The result should be read in 15 minutes. Do not interpret the result after 20 minutes.



INTERPRETATION OF RESULTS

For Flu A&B Antigen Rapid Test

1. POSITIVE:

1.1 Flu A Positive:

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

1.2 Flu B Positive:

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

1.3 Flu A+B Positive:

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

2. NEGATIVE:

The presence of only control band (C) within the result window indicates a negative result.

3. 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 Antigen Rapid Test

1. POSITIVE:

The presence of two lines as control line (C) and test line (T) within the result window indicates a positive result.

2. NEGATIVE:

The presence of only control line (C) within the result window indicates a negative result.

3. INVALID:

If the control line (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.

NOTE:

1.The intensity of color in the test line region (T) may vary depending on the concentration of analyses present in the specimen. Therefore, any shade of color in the test line region (T) should be considered positive. Please note that this is a qualitative test only, and cannot determine the concentration of analytes in the specimen.

2.Insufficient specimen volume, incorrect operating procedure or expired tests are

the most likely reasons for control band failure.

QUALITY CONTROL

A procedural control is included in the test. A red line appearing in the control line region (C) is the internal procedural control. It confirms sufficient specimen volume and correct procedural technique. Control standards are not supplied with this test. However, it is recommended that positive and negative controls are sourced from a local competent authority and tested as a good laboratory practice, to confirm the test procedure and verify the test performance.

LIMITATIONS

1. The Influenza & COVID-19 Ag Combo Rapid Test Cassette (Swab) is for professional in vitro diagnostic use, and should only be used for the qualitative detection of influenza A ,B and/or SARS-CoV-2 in nasopharyngeal (NP) swab specimens.

2. The etiology of respiratory infection caused by microorganisms other than influenza A , B or SARS-CoV-2 will not be established with this test.

3. The Influenza & COVID-19 Ag Combo Rapid Test Cassette (Swab) is capable of detecting both viable and non-viable influenza and SARS-CoV-2 particles. The performance of the Influenza & COVID-19 Ag Combo Rapid Test Cassette (Swab) depends on antigen load and may not correlate with cell culture performed on the same specimen.

4. If the test result is negative and clinical symptoms persist, additional testing using other clinical methods is recommended. A negative result does not at anytime rule out the presence of influenza A A , B or SARS-CoV-2 viral antigens in specimen, as they may be present below the minimum detection level of the test. As with all diagnostic tests, a confirmed diagnosis should only be made by a physician after all clinical and laboratory findings have been evaluated.

5.Inadequate or inappropriate specimen collection, storage, and transport may yield false negative test result.

6. Failure to follow the Test Procedure may adversely affect test performance and/or invalidate the test result.

7. Although this test has been shown to detect cultured avian influenza viruses, including avian influenza A subtype H5N1 virus, the performance characteristics of

this test with specimens from humans infected with H5N1 or other avian influenza viruses are unknown.

8. Performance characteristics for influenza A were established when influenza A/H3 and A/H1 were the predominant influenza A viruses in circulation. When other influenza A viruses are emerging, performance characteristics may vary.

9. Positive and negative predictive values are highly dependent on prevalence. False positive test results are more likely during periods of low influenza activity when prevalence is moderate to low. Positive test results do not rule out co-infections with other pathogens.

10.For COVID-19 Antigen Rapid Test, positive test results do not differentiate between SARS-CoV and SARS-CoV-2. Negative results should be treated as presumptive and confirmed with an FDA authorized molecular assay, if necessary, for clinical management, including infection control.

PERFORMANCE CHARACTERISTICS

For FluA&B Antigen Rapid Test:

1. Analytical Sensitivity

The minimum detection limit is 1.5 x 10^4 $TCID_{50}$ /test for the Influenza A virus antigen and is 1.5 x 10^5 $TCID_{50}$ /test for the Influenza B virus antigen.

2. Analytical Reactivity

The influenza A strain listed tested positive in the Influenza A &B Ag Rapid Test. Although the specific influenza strains causing infection in human can very, all contain the conserved nucleoproteins targeted by Influenza A&B Ag Rapid Test.

Strains	Sources	Subtypes	Concentration
Flu A/Hubei/PR8/2001	Human	H1N1	1.8×10^4 $TCID_{50}$/test
Flu A/New Kaledonia/20/99	Human	H1N1	1.8×10^4 $TCID_{50}$/test
Flu A/Yamagata/32/89	Human	H1N1	1.8×10^4 $TCID_{50}$/test
Flu A/Beijing/262/95	Human	H1N1	1.8×10^4 $TCID_{50}$/test
Flu A/Singapore/1/57	Human	H2N2	3.0×10^4 $TCID_{50}$/test
Flu A/Hubei/3/2005	Human	H3N2	3.0×10^4 $TCID_{50}$/test
Flu A/Akita/1/94	Human	H3N2	3.0×10^4 $TCID_{50}$/test
Flu A/Kita Kyusyu/159/93	Human	H3N2	3.0×10^4 $TCID_{50}$/test
Flu A/Iowa/15/30	Swine	H1N1	3.0×10^4 $TCID_{50}$/test
Flu A/Hongkong/168/93	Swine	H1N1	3.0×10^4 $TCID_{50}$/test
Flu A/Anhui/24/2004	Swine	H5N1	6.0×10^4 $TCID_{50}$/test
Flu A/Hubei/134/2000	Swine	H9N2	6.0×10^5 $TCID_{50}$/test
Flu A/Hubei/251/2001	Swine	H9N2	6.0×10^5 $TCID_{50}$/test

Flu A/Yuyao/1/2006	Chicken	H5N1	6.0×10^4 $TCID_{50}$/test
Flu A/Yuyao/2/2006	Chicken	H5N1	6.0×10^4 $TCID_{50}$/test
Flu A/Jiangsu/2/2004	Chicken	H5N1	6.0×10^4 $TCID_{50}$/test
Flu A/Hubei/216/83	Duck	H7N8	3.0×10^5 $TCID_{50}$/test
Flu A/Hubei/118/2003	Duck	H9N2	1.5×10^5 $TCID_{50}$/test
Flu A/Hubei/155/2003	Duck	H9N2	6.0×10^5 $TCID_{50}$/test
Flu A/Hubei/137/1982	Duck	H10N4	3.0×10^5 $TCID_{50}$/test
Flu A/Singapore/3/97	Duck	H5N3	6.0×10^4 $TCID_{50}$/test
Flu A/Henan/1/2004	Tree sparrow	H5N1	6.0×10^5 $TCID_{50}$/test
Flu A/Henan/2/2004	Tree sparrow	H5N1	3.0×10^5 $TCID_{50}$/test
Flu A/Henan/4/2004	Tree sparrow	H5N1	6.0×10^4 $TCID_{50}$/test
Flu A/Wisconsin/66	Turkey	H9N2	6.0×10^4 $TCID_{50}$/test
Flu A/England/1/63	Turkey	H7N3	6.0×10^4 $TCID_{50}$/test
Flu A/Singapore/1/57	Bird	H5N1	6.0×10^4 $TCID_{50}$/test
Flu A/Hunan/71/2004	Bird	H5N1	6.0×10^4 $TCID_{50}$/test
Flu A/Shanxi/50/2006	Bird	H5N1	6.0×10^4 $TCID_{50}$/test
Flu A/Shanxi/42/2006	Bird	H5N1	6.0×10^4 $TCID_{50}$/test
Flu A/Fujian/320/2004	Bird	H5N1	3.0×10^5 $TCID_{50}$/test

Influenza A&B Ag Rapid Test can detect all nine influenza B strains.

3. Clinical Study Data Summary

The Influenza A&B Ag Rapid Test performance vs. Cell Culture

Kind of samples	Type	Sensitivity(%)	Specificity(%)	Accuracy(%)
Nasal Swab	A	92.6 (25/27)	96.4 (81/84)	95.5 (106/111)
	B	90.0 (27/30)	95.8 (91/95)	94.4 (118/125)
Throat Swab	A	83.3 (20/24)	95.2 (59/62)	91.9 (79/86)
	B	82.6 (19/23)	91.8 (67/73)	89.6 (86/96)
Nasal Aspirate	A	88.9 (48/54)	93.3 (125/134)	92.0 (173/188)
	B	91.2 (52/57)	95.4 (98/103)	93.8 (150/160)
Nasal discharge/ Nasal mucus	A	80.7 (46/57)	94.9 (93/98)	89.7 (139/155)
	B	89.6 (62/69)	94.6 (87/92)	92.5 (149/161)

4. Analytical Specificity And Cross-reactivity

The Influenza A&B Ag Rapid Test was evaluated with a total of 30 bacterial and viral isolates. Bacterial isolates were evaluated at a concentration between 10^7 and 10^9 org/mL. Viral isolates were evaluated at a concentration of at least 10^4-10^8 $TCID_{50}$/mL. Adenovirus 18 and Parainfluenza virus 3 were tested at 10^2 $TCID_{50}$/mL. None of the organisms or viruses listed below gave a positive result in the Influenza A&B Ag Rapid Test.

Bacterial Panel:

Acinetobacter calcoaceticus	Bacteroides fragilis
Neisseria gonorrhoeae	Neisseria meningitidis
Pseudomonas aeruginosa	Staphylococcus aureus
Streptococcus pneumoniae	Streptococcus sanguis
Proteus vulgaris	Streptococcus sp. Gp. B
Streptococcus sp. Gp. C	Streptococcus sp. Gp. G
Mycobacterium tuberculosis	Mycoplasma orale

Viral Panel:

Human Adenovirus B	Human Rhinovirus 2
Human Adenovirus C	Human Rhinovirus 14
Adenovirus type 10	Human Rhinovirus 16
Adenovirus type 18	Measles
Human Coronavirus OC43	Mumps
Human Coxsackievirus A9	Sendai virus
Coxsackievirus B5	Parainfluenza virus 2
Human herpesvirus2	Parainfl uenza virus 3

5. 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 Rapid Test at the levels tested: whole blood (2%); three OTC mouthwashes (25%); three OTC throat drops (25%); three OTC nasal sprays (10%); 4-Acetamidophenol (10mg/mL); Acetylsalicylic Acid (20mg/mL); Chlorpheniramine (5mg/mL); Dextromethorphan (10mg/mL); Diphenhydramine (5 mg/mL); Ephedrine (20mg/mL); Guaiacol glyceryl ether (20mg/mL); Oxymetazoline (10mg/mL); Phenylephrine (100 mg/mL); and Phenylpropanolamine (20mg/mL).

For COVID-19 Antigen Rapid Test:

1.Clinical Sensitivity, Specificity and Accuracy

The COVID-19 Antigen Rapid Test Cassette (Swab) has been evaluated with specimens obtained from patients. A commercialized molecular assay was used as the reference method. The results show that the COVID-19 Antigen Rapid Test Cassette (Swab) has a high overall relative accuracy.

Table 1: The COVID-19 Antigen Rapid Test vs PCR

Method		PCR		Total Results
COVID-19 Rapid Test Cassette	Results	Positive	Negative	
	Positive	39	0	39
	Negative	6	116	122
Total Results		45	116	161

Relative Sensitivity: 86.7% (95%CI*: 73.2%-95.0%) *Confidence Intervals

Relative Specificity: 100% (95%CI*: 96.9%-100%)

Accuracy: 96.3% (95%CI*: 92.1%-98.6%)

INDEX OF SYMBOLS

	Consult instructions for use		Tests per kit	EC REP	Authorized Representative
IVD	For *in vitro* diagnostic use only		Use by		Do not reuse
2°C 30°C	Store between 2~30°C	LOT	Lot Number	REF	Catalog#

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