Rapid Response™

5-in-1 Combo CoV, FluA&B, RSV, ADV Test
(Nasopharyngeal Swab)

REF CFRA-19C, CFRA-19C1, CFRA-19C2, CFRA-19C15, CFRA-19C20

Product Insert

A rapid test for the qualitative detection of COVID-19, Flu A&B Antigen, Respiratory Syncytial Virus (RSV), Adenovirus antigen in Nasopharyngeal swab.

For professional *in vitro* diagnostic use only.

Intended Use

The Rapid Response™ 5-in-1 Combo CoV, FluA&B, RSV, ADV Test is a rapid chromatographic immunoassay for the qualitative detection of SARS-CoV-2, Influenza A&B, RSV, Adenovirus Antigen in Nasopharyngeal swab. It is intended to aid in the rapid differential diagnosis of COVID-19, Influenza A&B, RSV, Adenovirus infections.

Summary

COVID-19 Antigen Rapid Test (Nasopharyngeal Swab)

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.

FLU A&B Antigen Rapid Test (Nasopharyngeal Swab)

Influenza (commonly known as 'flu') is a highly contagious, acute viral infection of the respiratory tract. It is a communicable disease easily transmitted through the coughing and sneezing of aerosolized droplets containing live virus. Influenza outbreaks occur each year during the fall and winter months. Type A viruses are typically more prevalent than type B viruses and are associated with most serious influenza epidemics, while type B infections are usually milder.

The gold standard of laboratory diagnosis is 14-day cell culture with one of a variety of cell lines that can support the growth of influenza virus. Cell culture has limited clinical utility, as results are obtained too late in the clinical course for effective patient intervention. Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) is a newer method that is generally more sensitive than culture with improved detection rates over culture of 2-23%. However, RT-PCR is expensive, complex and must be performed in specialized laboratories.

RSV Antigen Rapid Test (Nasopharyngeal Swab)

Human respiratory syncytial virus (HRSV) is a syncytial virus that causes respiratory tract infections. It is a major cause of lower respiratory tract infections and hospital visits during infancy and childhood. A prophylactic medication, palivizumab, can be employed to prevent HRSV in preterm (under 35 weeks gestation) infants, infants with certain congenital heart defects (CHD) or bronchopulmonary dysplasia (BPD), and infants with congenital malformations of the airway. Treatment is limited to supportive care (e.g. C-PAP), including oxygen therapy. In temperate climates there is an annual epidemic during the winter months. In tropical climates, infection is most common during the rainy season.

Adenovirus Antigen Rapid Test (Nasopharyngeal Swab)

Adenoviruses are common viruses that cause a variety of illnesses in humans. Most commonly, they cause respiratory tract infections or conjunctivitis (inflammation of the lining of the eyes). Adenoviruses are very hardy and can survive for long periods outside of a host human or animal. Both animals and humans get adenovirus infections. Adenoviruses can infect different organs within the body, but most infections do not produce signs or symptoms (are asymptomatic).

Infections happen in children more often than in adults, but anyone can get them. Most kids will have at least one type of adenovirus infection by the time they're 10.

The infections usually cause only mild symptoms and get better on their own in a few days. But they can be more serious in people with weak immune systems, especially children.

Principle

The COVID-19 Antigen Rapid Test (Nasopharyngeal Swab) is a qualitative, lateral flow immunoassay for the detection of the N protein of SARS-CoV-2 in Nasopharyngeal swab. In this test, antibody specific to the N protein of SARS-CoV-2 is separately coated on the test line regions of the test cassette. During testing, the extracted specimen reacts with the antibody to N protein of SARS-CoV-2 that are coated onto particles. The mixture migrates up the membrane to react with the antibody to N protein of SARS-CoV-2 on the membrane and generate one colored line in the test regions. The presence of this colored line of the test regions indicates a positive result. To serve as a procedural control, a colored line will always appear in the control region if the test has performed properly.

The FLU A&B Antigen Rapid Test (Nasopharyngeal Swab) is a qualitative, lateral flow immunoassay for the detection of Influenza A and Influenza B nucleoproteins in Nasopharyngeal Swab. In this test, antibody specific to the Influenza A and Influenza B nucleoproteins is separately coated on the test line regions of the test cassette. During testing, the extracted specimen reacts with the antibody to Influenza A and/or Influenza B that are coated onto particles. The mixture migrates up the membrane to react with the antibody to Influenza A and/or Influenza B on the membrane and generate one or two colored lines in the test regions. The presence of this colored line in either or both of the test regions indicates a positive result. To serve as procedural control, a colored line will always appear in the control region if the test has performed properly.

The RSV Antigen Rapid Test (Nasopharyngeal Swab) is a qualitative, lateral flow immunoassay for the detection of RSV viral fusion protein antigen in nasopharyngeal swab. In this test, antibody specific to the Respiratory Syncytial Virus is separately coated on the test line regions of the test cassette. During testing, the extracted specimen reacts with the antibody to Respiratory Syncytial Virus that are coated onto particles. The mixture migrates up the membrane to react with the antibody to Respiratory Syncytial Virus on the membrane and generate one or two colored lines in the test regions. The presence of this colored line in either or both of the test regions indicates a positive result. To serve as procedural control, a colored line will always appear in the control region if the test has performed properly.

The Adenovirus Antigen Rapid Test (Nasopharyngeal Swab) is a qualitative, lateral flow immunoassay for the detection of Adenovirus antigen in nasopharyngeal swab. In this test, antibody specific to the Adenovirus is separately coated on the test line regions of the test cassette. During testing, the extracted specimen reacts with the antibody to Adenovirus that are coated onto particles. The mixture migrates up the membrane to react with the antibody to Adenovirus on the membrane and generate one or two colored lines in the test regions. The presence of this colored line in either or both of the test regions indicates a positive result. To serve as procedural control, a colored line will always appear in the control region if the test has performed properly.

Reagents

The test cassette contains anti-SARS-CoV-2 Nucleocapsid protein particles, anti-Influenza A particles, anti-Influenza B particles, anti-Respiratory Syncytial Virus, anti-Adenovirus particles and anti-SARS-CoV-2 Nucleocapsid protein, anti-Influenza A, anti-Influenza B, anti-Respiratory Syncytial Virus, anti-Adenovirus coated on the membrane.

Precautions

Please read all the information in this package insert before performing the test.

1. For professional *in vitro* diagnostic use only. Do not use after the expiration date.
2. The test should remain in the sealed pouch until ready to use.
3. All specimens should be considered potentially hazardous and handled in the same manner as an infection agent.
4. The used test should be discarded according to the local regulations.
5. Avoid using bloody samples.
6. Wear gloves when handling the samples, avoid touching the reagent membrane and sample well.

Materials

Materials provided

- Test cassettes
- Extraction reagents
- Extraction tubes
- Dropper tips
- Sterile swabs
- Product insert
- Workstation

Materials required but not provided

- Timer

Storage and Stability

Store as packaged at room temperature or refrigerated (35.6-86°F; 2-30°C). The test is stable through the expiration date printed on the sealed pouch. The test must remain in the sealed pouch until use. **DO NOT FREEZE.** Do not use beyond the expiration date.

Collection and Storage of Specimens

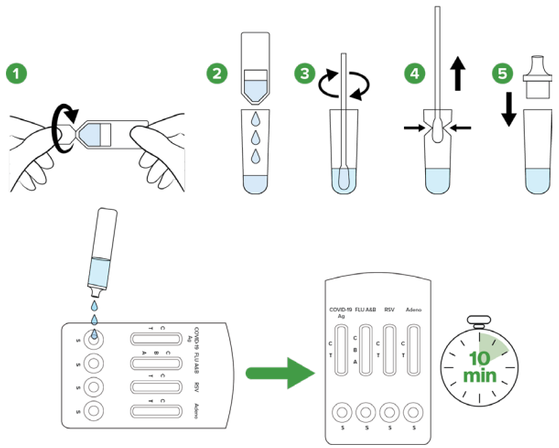
Nasopharyngeal swab

- Insert 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. 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 swab is saturated with fluid from the first collection. If a deviated septum or blockage create difficulty in obtaining the specimen from one nostril, use the same swab to obtain the specimen from the other nostril.

Test Procedure

Allow the test, specimen, extraction buffer to equilibrate to room temperature (59-86°F; 15-30°C) prior to testing.

1. Remove the test cassette from the sealed foil pouch and use it within one hour. Best results will be obtained if the assay is performed immediately after opening the foil pouch.
2. Place the extraction tube in the workstation. Turn the hand over and add all extraction buffer (approx. 500µl) to the extraction tube. See illustration 1 & 2.
3. Place the swab specimen in the extraction tube. Rotate the swab for approximately 10 seconds while pressing the head against the inside of the tube to release the antigen in the swab. See illustration 3.
4. Remove the swab while squeezing the swab head against the inside of the extraction tube as you remove it to expel as much liquid as possible from the swab. Discard the swab in accordance with your biohazard waste disposal protocol. See illustration 4.
5. Fit the dropper tip on top of the extraction tube. Place the test cassette on a clean and level surface. See illustration 5.
6. Hold the dropper vertically and transfer 3 drops of the sample solution (approx.80µL) to the sample well and then start the timer. Read the result at 10 minutes. Do not interpret the result after 20 minutes.



Results Interpretation

For FLU A&B

POSITIVE:* A colored line appears in the Control region (C) and colored line(s) appears in the Test region (T(COVID-19 Ag), A, B, T (RSV) and/or T(Adeno)).

A positive result in the COVID-19 Ag T region indicates that SARS-CoV-2 was detected in the specimen.

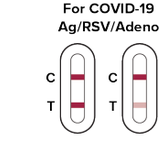
A positive result in the Influenza A region indicates that Influenza A antigen was detected in the specimen, a positive result in the Influenza B region indicates that Influenza B antigen was detected in the specimen.

A positive result in the RSV T region indicates that RSV was detected in the specimen.

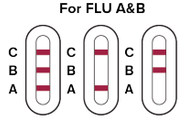
A positive result in the Adeno T region indicates that Adenovirus was detected in the specimen.

***NOTE:** The shade of the colored line(s) in the Test region(T(COVID-19), A, B, T(RSV) and/or T(Adeno)) may vary. The result should be considered positive whenever there is even a faint line.

For COVID-19 Ag/RSV/Adeno



For FLU A&B

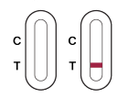


For COVID-19 Ag/RSV/Adeno

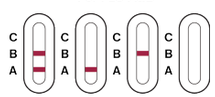
For FLU A&B

NEGATIVE: One colored line appears in the control line region (C). No line appears in the test line region (T(COVID-19), A, B, T(RSV) and/or T(Adeno)). A negative result indicates that COVID-19, Influenza A&B, RSV, Adenovirus antigen are not present in the specimen, or is present below the detectable level of the test.

For COVID-19 Ag/RSV/Adeno



For FLU A&B



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 with a new test. If the problem persists, discontinue using the test kit immediately and contact your local distributor.

Quality Control

A procedural control is included in the test. A colored line appearing in the control line region (C) is considered an internal procedural control. It confirms adequate membrane wicking. 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

1. The Rapid Response™ 5-in-1 Combo CoV, FluA&B, RSV, ADV Test is for professional *in vitro* diagnostic use only. The test should be used for the detection of SARS-CoV-2, Influenza A&B Antigen, RSV and/or Adenovirus in Nasopharyngeal swab. Neither the quantitative value nor the rate of increase in SARS-CoV-2 virus, Influenza A&B virus, Respiratory Syncytial Virus, Adenovirus concentration can be determined by this qualitative test.
2. The accuracy of the test depends on the quality of the swab sample. False negatives may result from improper sample collection or storage.
3. The Rapid Response™ 5-in-1 Combo CoV, FluA&B, RSV, ADV Test will only indicate the presence of SARS-CoV-2, Influenza A&B, RSV, Adenovirus in the specimen from both viable and non-viable SARS-CoV-2 coronavirus, Influenza A and B strains, Respiratory Syncytial Virus, Adenovirus.
4. As with all diagnostic tests, all results must be interpreted together with other clinical information available to the physician.
5. A negative result obtained from this kit should be confirmed by PCR. A negative result may be obtained if the concentration of the SARS-CoV-2, Influenza A&B virus, Respiratory Syncytial Virus, Adenovirus present in the swab is not adequate or is below the detectable level of the test.
6. Excess blood or mucus on the swab specimen may interfere with test performance and may yield a false positive result.
7. Positive result for COVID-19, Influenza A, Influenza B, Respiratory Syncytial Virus, and/or Adenovirus do not preclude an underlying co-infection with another pathogen, therefore the possibility of an underlying bacterial infection should be considered.
8. Negative results do not rule out SARS-CoV-2, Influenza A, Influenza B, RSV and/or Adenovirus infection, particularly in those who have been in contact with the virus. Follow-up testing with a molecular diagnostic should be considered to rule out infection in these individuals.
9. The use of over-the-counter and prescription nasal sprays at high concentrations can interfere with results, leading to either invalid or incorrect test results.
10. COVID-19 positive results may be due to current infection with acute non-SARS-CoV-2 coronavirus strains, such as coronavirus HKU1, NL63, OC43 or 229E.
11. Results from antigen testing should not be used as the sole basis to diagnose or exclude SARS-CoV-2, Influenza A &B, RSV infection or to inform infection status.
12. Extraction reagent has the ability to kill the virus, but it cannot inactivate 100% of the virus. The method of inactivating the virus can be referred to: what method is recommended by WHO/CDC, or it can be handled according to local regulations.

Performance Characteristics

Sensitivity, Specificity and Accuracy

The Rapid Response™ 5-in-1 Combo CoV, FluA&B, RSV, ADV Test has been evaluated with specimens obtained from the patients. PCR is used as the reference method for the Rapid Response™ 5-in-1 Combo CoV, FluA&B, RSV, ADV Test. Specimens were considered positive if PCR indicated a positive result.

Rapid Response™ 5-in-1 Combo CoV, FluA&B, RSV, ADV Test	COVID-19			Type A		
	PCR		Total	PCR		Total
	Positive	Negative		Positive	Negative	
Positive	38	0	38	68	14	82
Negative	2	324	326	10	242	252
Total	40	324	364	78	256	334
Relative Sensitivity	95.0%			87.2%		
Relative Specificity	>99.9%			94.5%		
Accuracy	99.5%			92.8%		

Rapid Response™ 5-in-1 Combo CoV,	Type B			RSV		
	PCR		Total	PCR		Total

FluA&B, RSV, ADV Test	Positive	Negative		Positive	Negative	
Positive	49	7	56	65	2	67
Negative	4	274	283	1	221	222
Total	53	281	334	66	223	289
Relative Sensitivity	92.5%			98.5%		
Relative Specificity	97.5%			99.1%		
Accuracy	96.7%			99.0%		

Rapid Response™ 5-in-1 Combo CoV, FluA&B, RSV, ADV Test	Adenovirus		
	PCR		Total
	Positive	Negative	
Positive	60	2	62
Negative	1	235	236
Total	61	237	298
Relative Sensitivity	98.4%		
Relative Specificity	99.2%		
Accuracy	99.0%		

Detection Limit of COVID-19

The LOD for the COVID-19 Antigen Rapid Test (Nasopharyngeal Swab) was established using limiting dilutions of a viral sample inactivated. The material (ZeptoMetrix, 0810587CFHI) was supplied at a concentration of 1.15 x 10^7TCID^{50}/mL. The Estimated LOD is 1000 $TCID_{50}$/mL.

Reactivity with Human Influenza Strain

Influenza A strains

Subtype of H1N1: Mal/302/54, New Jersey/8/76, NWS/33, WS/33, Guangdong-Maonan/SWL1536/2019; H3N2: Aichi/2/68, Hong Kong/8/68, Port Chalmers/1/73, Hong Kong/2671/2019; H7N9 Anhui/1/2013, all are positive.

Influenza B strains

Russia/69, Hong Kong/5/72, Lee/40, Brigit, R5, Wisconsin/1/2010, Florida/78/2015, Phuket/3073/2013, Washington/02/2019, all are positive.

Detection Limit of RSV

The minimum detection limit of RSV Antigen Rapid Test is as follows:

Subtype	
A2	1.12X10^2 $TCID_{50}$/mL
B WV/14617/85	3.67 X 10^4 PFU/mL
18537	32 PFU/mL

Detection Limit of Adenovirus

The minimum detection limit of Adenovirus Antigen Rapid Test is as follows:

Subtype	VP/mL
ADV3	6.0 x 10^3
ADV6	1.0 x 10^4
ADV7	1.0 x 10^4

VP: Viral particle. The measurement method of VP is to measure the absorbance of virus particles at 260nm (the total absorbance of virus DNA and protein is mainly DNA). One OD is equivalent to 1.1×10^{12} virus particles.

Cross Reactivity

The COVID-19 Antigen Rapid Test (Nasopharyngeal Swab) has

been tested for Influenza A virus, Influenza B virus, Adenovirus, Coxsackie virus, Parainfluenza Virus Type1, Parainfluenza Virus Type2, Parainfluenza Virus Type3, Parainfluenza Virus Type4a, Enterovirus, Mumps virus, Respiratory syncytial virus, Rhinovirus, Bordetella pertussis, Haemophilus parainfluenzae, Staphylococcus aureus, Streptococcus agalactiae, Neisseria meningitides, Streptococcus sp. group A, Streptococcus sp. Group B, Streptococcus sp. group C, Candida albicans, Human Metapneumovirus (hMPV), Legionella pneumophila, Mycobacterium tuberculosis, Mycoplasma pneumoniae, Pneumocystis jirovecii(PJP)-S cerevisiae Recombinant, Pseudomonas aeruginosa, Staphylococcus epidermis, Streptococcus pneumoniae, Streptococcus pyogenes, Streptococcus salivarius, Human coronavirus 229E, Human coronavirus OC43, Human coronavirus NL63, MERS-coronavirus positive specimens.The results showed no cross reactivity.

The FLU A&B Antigen Rapid Test (Nasopharyngeal Swab) has been tested for Adenovirus, Coxsackie virus, Cytomegalovirus, Parainfluenza Virus Type1,2,3,4a, Enterovirus, Mumps virus, Respiratory syncytial virus, Rhinovirus, Bordetella pertussis, Haemophilusparainfluenzae, Staphylococcus aureus, Streptococcus agalactiae, Neisseria meningitides, Streptococcus sp. group A, B, C. The results showed no cross reactivity.

The RSV Antigen Rapid Test (Nasopharyngeal Swab) has been tested for Adenovirus, Coxsackie virus, Cytomegalovirus, Parainfluenza Virus Type1,2,3,4a, Enterovirus, Mumps virus, Influenza A virus, Influenza B virus, Rhinovirus, Bordetella pertussis, Haemophilusparainfluenzae, Staphylococcus aureus, Streptococcus agalactiae, Neisseria meningitides, Streptococcus sp. group A, B, C. The results showed no cross reactivity.

The RSV Antigen Rapid Test (Nasopharyngeal Swab) has been tested for Adenovirus, Coxsackie virus, Cytomegalovirus, Parainfluenza Virus Type1,2,3,4a, Enterovirus, Mumps virus, Influenza A virus, Influenza B virus, Rhinovirus, Bordetella pertussis, Haemophilusparainfluenzae, Staphylococcus aureus, Streptococcus agalactiae, Neisseria meningitides, Streptococcus sp. group A, B, C. The results showed no cross reactivity.

The Adenovirus Antigen Rapid Test (Nasopharyngeal Swab) has been tested for Influenza A virus, Influenza B virus, Coxsackie virus, Cytomegalovirus, Parainfluenza Virus Type1,2,3,4a, Enterovirus, Mumps virus, Respiratory Syncytial Virus (RSV), Rhinovirus, Bordetella pertussis, Haemophilusparainfluenzae, Staphylococcus aureus, Streptococcus agalactiae, Neisseria meningitides, Streptococcus sp. group A, B, C. The results showed no cross reactivity.

Bibliography

1. Weiss SR, Leibowitz JL. Coronavirus pathogenesis. Adv Virus Res 2011;81:85-164.
2. Cui J, Li F, Shi ZL. Origin and evolution of pathogenic coronaviruses. Nat Rev Microbiol 2019;17:181-192.
3. Su S, Wong G, Shi W, et al. Epidemiology, genetic recombination, and pathogenesis of coronaviruses. TrendsMicrobiol 2016;24:490-502.
4. Williams, KM, Jackson MA, Hamilton M. (2002) Rapid Diagnostic Testing for URIs in Children; Impact on Physician Decision Making and Cost. Infec. Med. 19(3): 109-111.
5. Betts, R.F. 1995. Influenza virus, p. 1546-1567. In G.L. Mandell, R.G. Douglas, Jr. and J.E. Bennett (ed.), Principle and practice of infectious diseases, 4th ed. Churchill Livingstone, Inc., New York, N.Y.
6. WHO recommendations on the use of rapid testing for influenza diagnosis, World Health Organisation, July 2005.
7. Norihiko KUBO, Hideyuki IKEMATSU, Shigeki NABESHIMA: Evaluation of an Immunochromatography TestKit for Rapid Diagnosis of Influenz, Kansenshogaku Zasshi, 2003,77:1007 ~ 1014.
8. Michimaru HARA, Shinichi TAKAO, Shinji FUKUDA, Yukie SHIMAZU, Masaru KUWAYAMA and Kazuo MIYAZAKI: Comparison of Four Rapid Diagnostic Kits Using Immunochromatography to Detect Influenza B Viruses, Kansenshogaku Zasshi, 2005,79:803 ~ 811.
9. Rezaee, F., Linfield, D.T., Harford, T. J., & Piedimonte, G. (2017). Ongoing developments in RSV prophylaxis: a clinician's analysis. Current Opinion in Virology, 24, 70-78.
10. F M Moesker, J J A van Kampen, G Aron, M Schutten, D A M C van de Vijver, M P G Koopmans, A D M E Osterhaus, P L A Fraaij. Diagnostic performance of influenza viruses and RSV rapid antigen detection tests in children in tertiary care. Journal of Clinical Virology, 2016, 79, 12-17.
11. Yen, A. B., Demmler-Harrison, G. J. Rapid Antigen Testing to Detect Respiratory Syncytial Virus Performs Well in Neonates. The Pediatric Infectious Disease Journal, 2011, 30(3), 234-237.
12. Slinger, R., Milk, R., Gaboury, I., & Diaz-Mitoma, F. Evaluation of the QuickLab RSV Test, a New Rapid Lateral-Flow Immunoassay for Detection of Respiratory Syncytial Virus Antigen. Journal of Clinical Microbiology, 2004, 42(8), 3731-3733.
13. Urs F Greber, Justin W Flatt. Adenovirus Entry: From Infection to Immunity. Annu Rev Virol. 2019 Sep 29;6(1):177-197.
14. José Luiz Proenca-Modena, Ricardo de Souza Cardoso, Miriã Ferreira Criado, etc. Human adenovirus replication and persistence in hypertrophic adenoids and palatine tonsils in children. J Med Virol. 2019 Jul;91(7):1250-1262.

Glossary of Symbols

Consult instructions for use	Test per Kit	EC REP Authorized Representative	
35.6°F 2°C 86°F 30°C Store between 35.6°F to 86°F	Use by	Do Not Reuse	
LOT Lot Number	IVD For *in vitro* diagnostic use only	REF Catalogue #	

EC REP CE

MDSS GmbH
Schiffgraben 41
30175 Hannover, Germany

BTNX Inc.
722 Rosebank Road,
Pickering, ON L1W 4B2
Canada

Technical Support: 1-888-339-9964