COVID-19 and Influenza A+B Antigen Combo Rapid Test (Nasopharyngeal Swab) 014L419

Rapid test for the qualitative detection of COVID-19 and Influenza A and B antigens in nasopharyngeal swab specimens For professional in vitro diagnostic use only

INTENDED USE

The ulti med COVID-19 and Influenza A+B Antigen Combo Rapid Test (Nasopharyngeal Swab) is a rapid chromatographic immunoassay for the qualitative detection of SARS-CoV-2 and Influenza A and B antigens in nasopharyngeal swab specimens from individuals with suspected SARS-CoV-2/Influenza infection in conjunction with clinical presentation and the results of other laboratory tests. Results are for the detection of SARS-CoV-2 and influenza A+B antigens. An antigen is generally detectable in upper respiratory specimen during the acute phase of infection. Positive results indicate the presence of viral antigens, but clinical correlation with patient history and other information is necessary to determine infection status. Positive results do not rule out bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause of disease. Negative results do not preclude SARS-CoV-2/Influenza A+B infection and should not be used as the sole basis for treatment or patient management decisions. Negative results should be treated as presumptive and confirmed with a molecular assay, if necessary for patient management. Negative results should be considered in the context of a patient's recent exposures, history and the presence of clinical signs consistent with COVID-19/Influenza A+B. The COVID-19 and Influenza A+B Antigen Combo Rapid Test is intended for use by trained clinical laboratory personnel.

SUMMARY

The novel coronaviruses belong to the ß genus. COVID-19 is an acute respiratory infectious disease. Currently the patients infected by the novel coronavirus are the main source of infection, asymptomatic infected people can also be an infectious source. 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 (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.[1] 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.[2] 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%.[3] However; RT-PCR is expensive, complex and must be performed in specialized laboratories.

PRINCIPLE

The COVID-19 Antigen Rapid Test (Nasopharyngeal Swab) is a qualitative membrane-based immunoassay for the detection of SARS-CoV-2 Antigens in human nasopharyngeal swab Specimen. SARS-CoV-2 antibody is coated in the test line region. During testing the specimen reacts with SARS-CoV-2 antibody-coated particles in the test. The mixture then migrates upward on the membrane by capillary action and reacts with the SARS-CoV-2 antibody in the test line region. If the specimen contains SARS-CoV-2 Antigens a colored line will appear in the test line region as a result of this. If the specimen does not contain antigens to SARS-CoV-2 no colored line will appear in the test region, indicating a negative result.

To serve as a procedural control a colored line will always appear in the control line region, indicating that the proper volume of specimen has been added and membrane wicking has occurred.

The Influenza A+B Rapid Test (Nasopharyngeal Swab) is a qualitative, lateral flow immunoassay for the detection of Influenza A and Influenza B antigen in human nasopharyngeal swab specimen. In this test, antibody specific to the Influenza A and Influenza B is separately coated on the test line regions of the test. 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 a procedural control, a colored line will always appear in the control region if the test has performed properly.

REAGENTS

The test contains anti SARS-CoV-2, anti-Influenza A and anti-Influenza B as the capture reagent, anti-SARS-CoV-2, anti-Influenza A and Influenza B as the detection agent.

PRECAUTIONS

- For professional in vitro diagnostic use only.
- Do not use beyond the expiration date indicated on the package.
- Do not use when protective pouch foil is damaged.
- The test cassette should remain in the sealed pouch until use.
- Do not eat, drink or smoke in the area where the specimens and kits are handled.
- Wear protective clothing such as laboratory coats, disposable gloves and eye protection when specimens are assayed.
- Please read all the information in this package insert before performing the test. Failure to follow directions in the package insert may yield inaccurate test results.
- Humidity and temperature can adversely affect results.
- Do not reuse tests.
- Avoid cross-contamination of specimens by using a new extraction tube for each specimen obtained.
- The used testing materials should be discarded according to federal state and local regulations.
- Handle all specimens as if they contain infectious agents. Observe established precautions against microbiological hazards throughout the collection, handling, storage and the disposal of patient samples and used kit contents.
- Viral Transport Media (VTM) may affect the test result, do not store specimen in viral transport media, extracted specimen for PCR tests cannot be used for the test.
- Please ensure that an appropriate amount of samples are used for testing. Too much or too little sample size may lead to deviation of results.

STORAGE AND STABILITY

The ulti med COVID-19 and Influenza A+B Antigen Combo Rapid Test (Nasopharyngeal Swab) can be stored at room temperature or refrigerated (2-30°C). The test cassette must remain in the sealed pouch until use. The test cassette and the reagents are stable through the expiration date printed on the box.

- Do not freeze.
- Do not use beyond the expiration date.

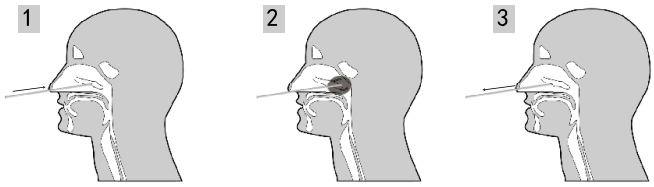
COVID-19 and Influenza A+B Antigen Combo Rapid Test (Nasopharyngeal Swab)
014L419

MATERIALS PROVIDED
- 20 Test Cassettes
- 20 Extraction Tubes
- 20 Extraction Tubes Tips
- 20 Swabs*
- 2 Extraction Buffer Bottles or 20 Disposable Extraction Buffer
- 1 Workstation
- 1 Package Insert

MATERIALS REQUIRED BUT NOT PROVIDED
- Timer

* Due to eventual delivery bottlenecks, it is possible that the swab manufacturer changes. List of enclosed possible swabs:
1) Disposable sampling swab, CE 0197, Jiangsu HanHeng Medical Technology Co., Ltd. – 16-B4, #1 North Qingyang Road, Tianning District, 213017 Changzhou, Jiangsu, China – EU-Representative: Luxus Lebenswelt GmbH, Kochstr. 1, 47877, Willich, Germany
2) Flocked swabs: FLOQSwabs® by Copan Italia Spa, Via F. Perotti, 10 - 25125 Brescia, Italy – CE Marked by Copan Italia according to MDD

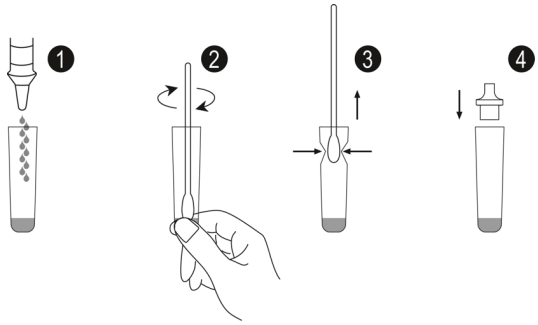
SPECIMEN COLLECTION
Only use reagents and sterile swabs provided with the ulti med COVID-19 and Influenza A+B Antigen Combo Rapid Test (Nasopharyngeal Swab).
1. Insert the sterile swab into the nostril of the patient, reaching the surface of the posterior nasopharynx.
2. Swab over the surface of the posterior nasopharynx.
3. Withdraw the sterile swab from the nasal cavity.



SPECIMEN TRANSPORT AND STORAGE
Specimen should be tested as soon as possible after collection.
If swabs are not being processed immediately, it is highly recommended to place the swab sample into a dry, sterile and tightly sealed plastic tube for storage. The swab specimen in dry and sterile condition is stable for up to 8 hours at room temperature and 24 hours at 2-8°C.
Do not store specimen in viral transport media.

SPECIMEN PREPARATION AND PROCEDURE OF THE TEST
Only the extraction buffer and tubes provided in the kit are to be used for swab specimen preparation.
Allow the test cassette, extracted specimen and extraction buffer to reach room temperature (15-30°C) prior to testing.
1. Place the extraction tube in the workstation. Open the extraction buffer bottle or disposable extraction buffer. Hold the extraction buffer bottle or the disposable extraction buffer upside down vertically. Squeeze and let the buffer drop into the extraction tube freely without touching the edge of the tube. **Add approx. 350µl (10 drops)** buffer into the extraction tube.
   See illustration 1.
2. 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 2
3. 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 3
4. Fit the extraction tube tip on top of the extraction tube.
   See illustration 4

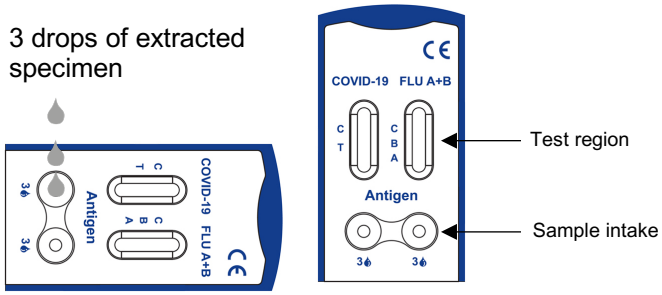
Add 10 drops of buffer by squeezing the extraction buffer bottle or add entire disposable extraction buffer (approx. 350 µl)



Reproductions may vary from original!

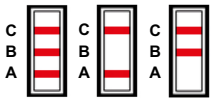
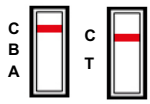
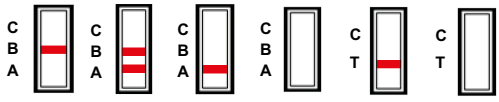
5. Remove the test cassette from the sealed foil pouch and use it within one hour. Best results will be obtained if the test is performed immediately after opening the foil pouch.
6. Label the device with patient or control identification and place it on a clean, level surface
7. Hold the extraction tube with extraction tube tip above the test cassette. Add 3 drops of the solution into each of the sample well (S) respectively and then start the timer.
8. As the test begins to work, you will see a colored line move across the Result Window in the center of the test cassette.
9. Interpret test results at **15 minutes**. Do not interpret test after more than 20 minutes.

COVID-19 and Influenza A+B Antigen Combo Rapid Test (Nasopharyngeal Swab)
014L419



Note:
1. Avoid trapping air bubbles in the specimen well.
2. Do not add any solutions to the test region.

INTERPRETATION OF RESULTS

 **COVID-19** **Positive**	**POSITIVE COVID-19*:** Two distinct colored lines appear. One colored line should be in the control region (C) and another colored line should be in the test region (T). A positive result in the test region indicates detection of COVID-19 antigens in the sample.
 **Influenza** **Positive**	**POSITIVE Influenza A and Influenza B*:** Three distinct colored lines appear. One colored line should be in the control region (C) and two colored lines should be in the Influenza A region (A) and Influenza B region (B). A positive result in the Influenza A region and Influenza B region indicates that Influenza A antigen and Influenza B antigen were detected in the sample.
	POSITIVE Influenza A*: Two distinct colored lines appear. One colored line should be in the control region (C) and another colored line should be in the Influenza A region (A). A positive result in the Influenza A region indicates that Influenza A antigen was detected in the sample.
	POSITIVE Influenza B*: Two distinct colored lines appear. One colored line should be in the control region (C) and another colored line should be in the Influenza B region (B). A positive result in the Influenza B region indicates that Influenza B antigen was detected in the sample.
Influenza  **COVID-19** **Negative**	**NEGATIVE:** One colored line appears in the control region (C). No apparent colored line appears in the test line regions (A, B, T).
 **Invalid**	**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 cassette. If the problem persists, discontinue using the test kit immediately and contact your local distributor.

* ***NOTE***: The intensity of the red color in the test line region (A, B, T) will vary based on the amount of COVID-19 antigen, Influenza A and/or B antigen present in the sample. So any shade of color in the test regions (A, B, T) should be considered positive.

INTERNAL QUALITY CONTROL
A procedural control is included in the test. A colored line appearing in the control region (C) is the internal procedural control. It confirms sufficient specimen volume and correct procedural technique. A clear background is an internal negative procedural control. If the test is working properly, the background in the result area should be white to light pink and not interfere with the ability to read the test result.

EXTERNAL QUALITY CONTROL
Controls are not included in this kit. In compliance with Good Laboratory Practice (GLP) positive/negative controls are recommended.

LIMITATIONS
1. The test procedure and the interpretation of the test result must be followed closely when testing for the presence of SARS-CoV-2 / Influenza A/ Influenza B antigens in the human nasopharyngeal specimens from suspected individuals. For optimal test performance, proper sample collection is critical. Failure to fallow the procedure may give inaccurate results.
2. The performance of the ulti med COVID-19 and Influenza A+B Antigen Combo Rapid Test (Nasopharyngeal Swab) was evaluated using the procedures provided in this product insert only. Modifications to these procedures may alter the performance of the test. Viral Transport Media (VTM) specimen and extracted specimens for PCR tests cannot be used for the tests.
3. The ulti med COVID-19 and Influenza A+B Antigen Combo Rapid Test (Nasopharyngeal Swab) is for *in vitro* diagnostic use only. This test should be used for detection of SARS-CoV-2/Influenza A/Influenza B Antigens in human nasopharyngeal specimens as an aid in the diagnosis of patients with suspected SARS-CoV-2, Influenza A or Influenza B infection in conjunction with clinical presentation and the results of other laboratory test. Neither the quantitative value nor the rate of increase in the concentration of SARS-CoV-2/Influenza A/Influenza B antigens can be determined by this qualitative test.

4. The ulti med COVID-19 and Influenza A+B Antigen Combo Rapid Test (Nasopharyngeal Swab) will only indicate the presence of SARS-CoV-2/Influenza A/Influenza B antigens in the specimen and should not be used as the sole criteria for the diagnosis of SARS-CoV-2/Influenza A/Influenza B infections.
5. The results obtained with the test should be considered with other clinical findings from other laboratory tests and evaluations.
6. If the test result is negative or non-reactive and clinical symptoms persist, it is recommended to re-sample the patient a few days later and test again or test with a molecular device to rule out infection in these individuals.
7. The test will show negative results under the following conditions: The concentration of the novel coronavirus antigens, Influenza A or Influenza B virus in the sample is lower than the minimum detection limit of the test.
8. Negative results do not rule out SARS-CoV-2 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. A negative result for Influenza A or Influenza B obtained from this kit should be confirmed by RT-PCR/culture.
10. Excess blood or mucin on the swab specimen may interfere with test performance and may yield a false positive result.
11. The accuracy of the test depends on the quality of the swab sample. False negatives may result from improper sample collection or storage.
12. Positive results of COVID-19 may be due to infection with non-SARS-CoV-2 coronavirus strains or other interference factors. A positive result for Influenza A and/or B does not preclude an underlying co-infection with another pathogen, therefore the possibility of an underlying bacterial infection should be considered.

PERFORMANCE CHARACTERISTICS

Expected values

The ulti med COVID-19 and Influenza A+B Antigen Combo Rapid Test (Nasopharyngeal Swab) has been compared with leading commercial RT-PCR tests. The correlation between these two systems is no less than 91%.

Sensitivity and Specificity and Accuracy

The ulti med COVID-19 and Influenza A+B Antigen Combo Rapid Test (Nasopharyngeal Swab) has been evaluated with specimens obtained from patients. RT-PCR is used as the reference method for the ulti med COVID-19 and Influenza A+B Antigen Combo Rapid Test (Nasopharyngeal Swab) Specimens were considered positive if RT-PCR indicated a positive result. Specimens were considered negative if RT-PCR indicated a negative result.

COVID-19 TEST:

COVID-19 and Influenza A+B Antigen Combo RapidTest		RT-PCR		
		Positive	Negative	Total
COVID-19 Antigen	Positive	80	1	81
	Negative	3	120	123
Total		83	121	204
Relative Sensitivity		96.4% (95%CI*: 89.8%~99.2%)		
Relative Specificity		99.2% (95%CI*: 95.5%~99.9%)		
Accuracy		98.0% (95%CI*: 95.1%~99.5%)		

Influenza A+B Test:

COVID-19 and Influenza A+B Antigen Combo RapidTest		Type A			Type B		
		RT-PCR		Total	RT-PCR		Total
		Positive	Negative		Positive	Negative	
Influenza A+BTest	Positive	16	1	17	11	0	11
	Negative	1	62	63	1	68	69
Total		17	63	80	12	68	80
Relative Sensitivity		94.1% (95%CI*: 71.3%~99.9%)			91.7% (95%CI*: 61.5%~99.8%)		
Relative Specificity		98.4% (95%CI*: 91.5%~>99.9%)			100.0% (95%CI*: 95.7%~100.0%)		
Accuracy		97.5% (95%CI*: 91.3%~99.7%)			98.8% (95%CI*: 93.2%~>99.9%)		

*Confidence Intervals

Specificity Testing with Various Viral Strains

The ulti med COVID-19 and Influenza A+B Antigen Combo Rapid Test (Nasopharyngeal Swab) was tested with the following viral strains. No discernable line at either of the test-line regions was observed at these listed concentrations.

COVID-19 Test:

Description	**Test Level**
Adenovirus type 3	3.16 x 10^4 TCID50/ml
Adenovirus type 7	1.58 x 10^5 TCID50/ml
Human coronavirus OC43	2.45 x 10^6 LD50/ml
Influenza A H1N1	3.16 x 10^5 TCID50/ml
Influenza A H3N2	1 x 10^5 TCID50/ml
Influenza B	3.16 x 10^6 TCID50/ml
Human Rhinovirus 2	2.81 x 10^4 TCID50/ml
Human Rhinovirus 14	1.58 x 10^6 TCID50/ml
Human Rhinovirus 16	8.89 x 10^6 TCID50/ml
Measles	1.58 x 10^4 TCID50/ml
Mumps	1.58 x 10^4 TCID50/ml
Parainfluenza virus 2	1.58 x 10^7 TCID50/ml
Parainfluenza virus 3	1.58 x 10^8 TCID50/ml
Respiratory syncytial virus	8.89 x 10^4 TCID50/ml

COVID-19 and Influenza A+B Antigen Combo Rapid Test (Nasopharyngeal Swab) 014L419

Influenza A+B Test:

Description	Test Level
Adenovirus type 3	3.16 x 10^4 TCID50/ml
Adenovirus type 7	1.58 x 10^5 TCID50/ml
Human coronavirus OC43	2.45 x 10^6 LD50/ml
Human Rhinovirus 2	2.81 x 10^4 TCID50/ml
Human Rhinovirus 14	1.58 x 10^6 TCID50/ml
Human Rhinovirus 16	8.89 x 10^6 TCID50/ml
Measles	1.58 x 10^4 TCID50/ml
Mumps	1.58 x 10^4 TCID50/ml
Parainfluenza virus 2	1.58 x 10^7 TCID50/ml
Parainfluenza virus 3	1.58 x 10^8 TCID50/ml
Respiratory syncytial virus	8.89 x 10^4 TCID50/ml

TCID50 = Tissue Culture Infectious Dose is the dilution of virus that under the conditions of the assay can be expected to infect 50% of the culture vessels inoculated.
LD50 = Lethal Dose is the dilution of virus that under the conditions of the assay can be expected to kill 50% of the suckling mice inoculated.

Precision
Intra-Assay & Inter-Assay
Within-run and Between-run precision has been determined by using seven specimens of COVID-19 and Influenza A+B standard control. Three different lots of COVID-19 and Influenza A+B Antigen Combo Rapid Test (Nasopharyngeal Swab) have been tested using negative, SARS-CoV-2 Antigen Weak, SARS-CoV-2 Antigen Strong, Influenza A Weak, Influenza B Weak, Influenza A Strong and Influenza B Strong. Ten replicates of each level were tested each day for 3 consecutive days. The specimens were correctly identified >99% of the time.

Cross-Reactivity
The following organisms were tested at 1.0x10^8org/ml and all found to be negative when tested with the COVID-19 and Influenza A+B Antigen Combo Rapid Test (Nasopharyngeal Swab):

Arcanobacterium
Candida albicans
Corynebacterium
Enterococcus faecalis
Escherichia coli
Moraxella catarrhalis
Neisseria lactamica
Neisseria subilava
Pseudomonas aeruginosa
Staphylococcus aureus subspaureus
Staphylococcus epidermidis
Streptococcus pneumoniae
Streptococcus pygenes
Streptococcus salivarius
Streptococcus sp group F

BIBLIOGRAPHY

1. 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.
2. 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.
3. WHO recommendations on the use of rapid testing for influenza diagnosis, World Health Organisation, July 2005.
4. Westgard JO, Barry PL,Hunt MR, Groth T. A multi-rule Shewhart for quality control in clinical chemistry 1981;27;493-501

	Manufacturer		Contents sufficient for <n> tests
IVD	For in vitro diagnostic use only	LOT	Lot. no.
	For single use only		Expiration date
	Read instructions for use		Store at
	Keep away from direct sunlight	REF	Ordering number
	Keep dry		

This operating manual conforms to the latest technology / revision. Subject to change without prior notice!

ulti med Products (Deutschland) GmbH
Reeshoop 1 • 22926 Ahrensburg
Telefon: 04102 - 80090
Fax: 04102 - 50082
e-mail: info@ultimed.org
www.ultimed.org

CE

November 2020 AL / FF-GV
Rev. C