SARS-CoV-2 & Influenza A/B Ag Combo Rapid Test Package Insert

Flowflex™

REF L031-120B5	REF L031-120C5	English

A rapid test for the qualitative and differential detection of SARS-CoV-2, Influenza virus type A and type B nucleoprotein antigens in nasal swab or nasopharyngeal swab.
For professional in vitro diagnostic use only.

INTENDED USE

The SARS-CoV-2 & Influenza A/B Ag Combo Rapid Test is a lateral flow chromatographic immunoassay for the qualitative and differential detection of SARS-CoV-2, Influenza virus type A and type B nucleoprotein antigens in nasal swab and nasopharyngeal swab specimens directly from individuals who are suspected of influenza or SARS-CoV-2 by their healthcare provider. Results are for the identification of SARS-CoV-2 and Influenza A/B nucleocapsid antigens. These antigens are generally detectable in upper respiratory specimens during the acute phase of infection. Positive results indicate the presence of viral antigens, but clinical correlation with patient history and other diagnostic information is necessary to determine infection status. Negative results do not preclude SARS-CoV-2 or influenza virus infections and should not be used as the sole basis for treatment or other patient management decisions.
The SARS-CoV-2 & Influenza A/B Ag Combo Rapid Test is intended for use by trained clinical laboratory personnel and individuals trained in point of care settings.

SUMMARY

The novel coronaviruses belong to the β genus. COVID-19 is an acute respiratory infectious disease. People are generally susceptible. Currently, the patients infected by the novel coronavirus are the main source of infection; asymptomatic infected people can also be an infectious source. Based on the current epidemiological investigation, the incubation period is 1 to 14 days, mostly 3 to 7 days. The main manifestations include fever, fatigue, and dry cough. Nasal congestion, runny nose, sore throat, myalgia, and diarrhea are found in a few cases.
Influenza is an acute respiratory disease caused by influenza viruses (type A, type B and type C), which is highly infectious and has a short window period. Influenza A and B viruses circulate and cause seasonal epidemics of disease. Influenza A virus poses a greater risk as compared to the influenza B virus. Based on the current epidemiological investigation, the incubation period is generally 1 to 7 days, most of which are 2 to 4 days. Influenza patients usually have symptoms of high fever, headache, muscle pain and fatigue, accompanied by respiratory symptoms, such as sore throat, cough, and sputum. The disease is self-limiting, but infants, the elderly, and patients with underlying cardiopulmonary diseases are prone to severe complications such as pneumonia that can lead to death.

PRINCIPLE

The SARS-CoV-2 & Influenza A/B Ag Combo Rapid Test are immobilized with mouse monoclonal anti-SARS-CoV-2 antibodies, anti-Influenza A and anti-Influenza B antibodies. The selected antibodies can specifically recognize SARS-CoV-2, influenza A and B virus nucleoprotein antigen. Anti-SARS-CoV-2, anti-Influenza A and anti-Influenza B antibodies are conjugated with colored particles and pre-treated on the label pad and other anti-SARS-CoV-2, anti-Influenza A and anti-Influenza B antibodies are pre-coated on the membrane. When specimens are processed and added to the test cassette, if SARS-CoV-2, Influenza A or Influenza B antigen is present in the specimen, the antigen will react with the antibody on the label pad. Then the mixture migrates upward on the membrane by capillary action, and the SARS-CoV-2 or Influenza antigen will react with another antibody pre-coated on the membrane. Test results are interpreted visually at 15-30 minutes based on the presence or absence of visually colored lines.
To serve as a procedure control, a colored line will always appear in the control line region indicating that proper volume of specimen has been added and membrane wicking has occurred.

REAGENTS

The test cassette contains anti-SARS-CoV-2 antibodies, anti-Influenza A antibodies and anti-Influenza B antibodies.

PRECAUTIONS

- For professional *in vitro* diagnostic use only. Do not use after the expiration date.
- This package insert must be read completely before performing the test. Failure to follow directions in the insert may cause inaccurate test results.
- Do not use the test if the pouch is damaged.
- Handle all specimens as if they contain infectious agents. Observe established precautions against biological hazards throughout testing and follow the standard procedures for proper disposal of specimens.
- Wear protective clothing such as laboratory coats, face mask, disposable gloves, and eye protection when specimens are being tested.
- The used test should be discarded according to local regulations.
- Humidity and temperature can adversely affect results.
- Do not eat, drink, or smoke in the area where the specimens or kits are handled.
- Do not use nasal sprays for at least 30 minutes before collecting a nasal swab specimen.

STORAGE AND STABILITY

- The test kit should be stored at temperatures between 2 - 30 °C.
- The test is stable until the expiration date printed on the sealed pouch.
- The test must remain in the sealed pouch until use.
- DO NOT FREEZE.
- Do not use after the expiration date.

MATERIALS

Materials Provided

- Test Cassettes
- Disposable Swabs*
- Extraction Buffer Tubes
- Package Insert

** The Disposable Swab is a medical device which produced by another manufacturer. Either Nasal Swabs, or Nasopharyngeal Swabs are supplied in the kit depending on the package you ordered.*

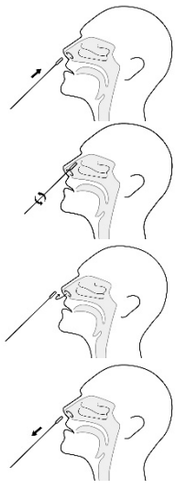
Materials Required But Not Provided

- Personal Protective Equipment
- Timer

SPECIMEN COLLECTION AND PREPARATION

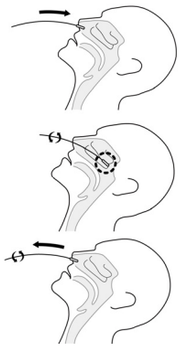
- The SARS-CoV-2 & Influenza A/B Ag Combo Rapid Test can be performed using *Nasal swabs or Nasopharyngeal swabs* specimens.
- Testing should be performed immediately after specimen collection, or at most within one (1) hour after specimen collection, if stored at room temperature (15 - 30°C).
- **To collect a Nasal Swab sample:**

1. Carefully insert the Disposable Nasal Swab, provided with your kit, into one nostril. Using gentle rotation, insert the swab into the nostril to less than 2.5 cm (1 inch) from the edge of the nostril.
2. Rotate the swab 5 times against the mucosa inside the nostril to ensure sufficient specimen collection.
3. Using the same swab, repeat the process in the other nostril to ensure that an adequate amount of sample is collected from both nostrils.
4. Withdraw the swab from the nasal cavity. The specimen is now ready for preparation using the extraction buffer tubes.



- **To collect a Nasopharyngeal Swab sample:**

1. Tilt patient's head back 70 degrees. Gently and slowly insert a Disposable Nasopharyngeal Swab, provided with your kit, through the nostril parallel to the palate until resistance is encountered.
2. Gently rub and roll the swab, leaving it in place for several seconds to absorb secretions. If a deviated septum or blockage creates difficulty in obtaining the specimen from one nostril, use the same swab to obtain the specimen from the other nostril.
3. Slowly remove the swab while rotating it. The specimen is now ready for preparation using the extraction buffer tubes.

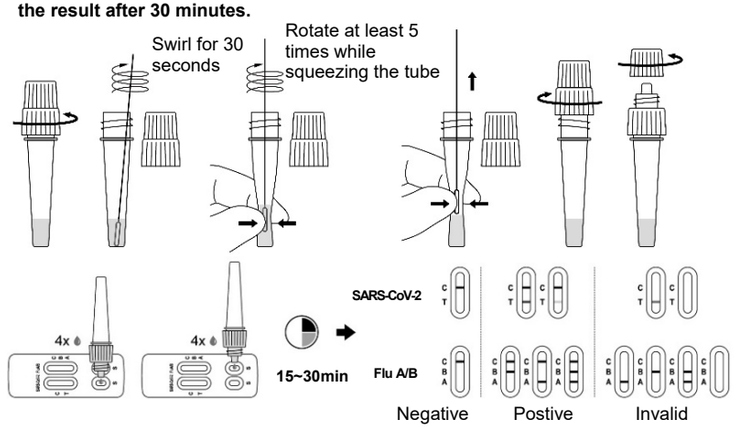


DIRECTIONS FOR USE

Allow the test and extraction buffer to reach room temperature (15-30 °C) prior to testing.

1. Use an extraction buffer tube for each specimen to be tested and label each tube appropriately.
2. Unscrew the dropper cap from the extraction buffer tube without squeezing.
3. Insert the swab into the tube and swirl it for 30 seconds. Then rotate the swab at least 5 times while **squeezing the sides of the tube**. Take care to avoid splashing contents out of the tube.
4. Remove the swab **while squeezing the sides of the tube** to extract the liquid from the swab.
5. Screw the dropper cap firmly onto the extraction buffer tube containing the sample. Mix thoroughly by swirling or flicking the bottom of the tube.
6. Remove the test cassette from the foil pouch and use it as soon as possible.
7. Place the test cassette on a flat and clean surface.
8. Add the processed specimen to the sample well**s** of the test cassette.
   a. Unscrew the small cap from the dropper tip.
   b. Invert the extraction buffer tube with the dropper tip pointing downwards and hold it vertically.
   c. Gently squeeze the tube, dispensing 4 drops of the processed specimen **into each sample well.**

   Please note: This cassette has 2 sample wells, and both sample wells need to receive 4 drops of the processed specimen.
9. Wait for the colored line(s) to appear. The results should be read at 15 minutes. **Do not read the result after 30 minutes.**



INTERPRETATION OF RESULTS

(Please refer to the illustration above)

NEGATIVE: Only the colored control lines appear in the control region (C). No colored lines appear in the test line regions (T/A/B). This means that no SARS-CoV-2 and/or Influenza A/B antigen were detected.

COVID 19 POSITIVE:* Two distinct colored lines appear in the SARS-CoV-2 side. One line in the control line region (C) and the other line in the test line region (T). This means that the presence of SARS-CoV-2 antigen was detected.

Flu A POSITIVE:* Two distinct colored lines appear in the Flu A/B side. One line in the control line region (C) and the other line in the test line region (A). This means that the presence of Influenza A antigen was detected.

Flu B POSITIVE:* Two distinct colored lines appear in the Flu A/B side. One line in the control line region (C) and the other line in the test line region (B). This means that the presence of Influenza B antigen was detected.

Flu A/B POSITIVE:* Three distinct colored lines appear in the Flu A/B side. One line in the control line region (C) and the other two lines in the test line region (A and B). This means that the presence of Influenza A/B antigen was detected.

***NOTE:** The intensity of the color in the test line (T/A/B) may vary depending on the level of antigen present in the specimen. Therefore, any shade of color in the test line regions (T/A/B) should be considered positive.

INVALID RESULT: A control line fails to appear in either the SARS-CoV-2, or the Flu A/B side of the cassette. Insufficient specimen volume or incorrect operation are the most likely reasons for a control line's failure to appear. 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.

QUALITY CONTROL

Internal procedural controls are included in the test. A colored line appearing in the control line region (C) is an internal procedural control. It confirms sufficient specimen volume was applied and correct procedural technique was followed.

LIMITATIONS

1. The SARS-CoV-2 & Influenza A/B Ag Combo Rapid Test should be used for the qualitative detection of SARS-CoV-2, Influenza virus type A and type B nucleoprotein antigens in nasal swab and nasopharyngeal swab only. The intensity of the test line does not necessarily correlate to SARS-CoV-2 or Influenza A/B viral titer in the specimen.
2. Specimens should be tested as quickly as possible after specimen collection or at most within one (1) hour after specimen collection, if stored at room temperature (15 - 30°C).
3. Use of viral transport media may result in decreased test sensitivity.
4. A false-negative test result may happen if the level of antigen in a sample is below the detection limit of the test or if the sample was improperly collected.
5. Test results should be correlated with other clinical data available to the physician.
6. A positive test result does not rule out co-infections with other pathogens.
7. A positive test result of SARS-CoV-2 does not differentiate between SARS-CoV and SARS-CoV-2.
8. A negative test result is not intended to rule out other viral or bacterial infections.

PERFORMANCE CHARACTERISTICS

Clinical Sensitivity, Specificity and Accuracy

Nasal Swab Specimens

The clinical performance of SARS-CoV-2 & Influenza A/B Ag Combo Rapid Test for nasal swab specimen was established with 580 nasal swabs collected from individual symptomatic patients who were suspected of COVID-19 or Influenza A/B. The results show that the relative sensitivity and the relative specificity are as follows:

Method		RT-PCR (Nasopharyngeal Swab Specimens)		
		Negative	Positive	Total
SARS-CoV-2 Test Results (Nasal Swab Specimens)	Negative	429	4	433
	Positive	1	146	147
	Total	430	150	580

Relative sensitivity: 97.33% (93.11%-99.19%)* Relative specificity: 99.77% (98.56%-99.99%)*
Accuracy: 99.14% (97.94%-99.69%)* *95% Confidence Intervals

Method		Comparator (Nasopharyngeal Swab Specimens)		
		Negative	Positive	Total
Flu A Test Results (Nasal Swab Specimens)	Negative	503	2	505
	Positive	2	73	75
	Total	505	75	580

Relative sensitivity: 97.33% (90.23%-99.83%)* Relative specificity: 99.60% (98.47%-99.99%)*
Accuracy: 99.31% (98.17%-99.80%)* *95% Confidence Intervals

Method		Comparator (Nasopharyngeal Swab Specimens)		
		Negative	Positive	Total
Flu B Test Results (Nasal Swab Specimens)	Negative	504	3	507
	Positive	1	72	73
	Total	505	75	580

Relative sensitivity: 96.00% (88.42%-99.10%)* Relative specificity: 99.80% (98.77%-99.99%)*
Accuracy: 99.31% (98.17%-99.80%)* *95% Confidence Intervals

Nasopharyngeal Swab Specimens

The clinical performance of SARS-CoV-2 & Influenza A/B Ag Combo Rapid Test for nasopharyngeal swab specimen was established with 395 nasopharyngeal swabs collected from individual symptomatic patients who were suspected of COVID-19 or Influenza A/B. The results show that the relative sensitivity and the relative specificity are as follows:

Method		RT-PCR (Nasopharyngeal Swab Specimens)		
		Negative	Positive	Total
SARS-CoV-2 Test Results (Nasopharyngeal Swab Specimens)	Negative	256	3	259
	Positive	1	135	136
	Total	257	138	395

Relative sensitivity: 97.83% (93.52%-99.54%)* Relative specificity: 99.61% (97.60%-99.99%)*
Accuracy: 98.99% (97.33%-99.70%)* *95% Confidence Intervals

Method		Comparator (Nasopharyngeal Swab Specimens)		
		Negative	Positive	Total
Flu A Test Results (Nasopharyngeal Swab Specimens)	Negative	333	1	334
	Positive	2	59	61
	Total	335	60	395

Relative sensitivity: 98.33% (90.30%-99.99%)* Relative specificity: 99.40% (97.70%-99.98%)*
Accuracy: 99.24% (97.68%-99.85%)* *95% Confidence Intervals

Method		Comparator (Nasopharyngeal Swab Specimens)		
		Negative	Positive	Total
Flu B Test Results (Nasopharyngeal Swab Specimens)	Negative	334	1	335
	Positive	1	59	60
	Total	335	60	395

Relative sensitivity: 98.33% (90.30%-99.99%)* Relative specificity: 99.70% (98.15%-99.99%)*
Accuracy: 99.49% (98.05%-99.99%)* *95% Confidence Intervals

Limit of Detection (LOD)

A SARS-CoV-2 viral sample was spiked with negative human nasal and nasopharyngeal sample pool into a series of concentrations. Each level was tested for 30 replicates. The results show that the LOD of SARS-CoV-2 Antigen test is $1.6*10^2$ $TCID_{50}$/mL.

The Influenza A and Influenza B virus sample was spiked with negative human nasal and nasopharyngeal sample pool into a series of concentrations. Each level was tested for 30 replicates. The results show that the LOD of the Influenza A/B Antigen test is $6.88*10^2$ $TCID_{50}$/mL on Influenza A virus and $1.88*10^2$ $TCID_{50}$/mL on Influenza B virus.

Cross-Reactivity and Interference

No cross-reactivity or interference was observed with the following microorganisms: Adenovirus, Enterovirus, Coronavirus-229E, Coronavirus-NL63, Coronavirus-OC43, Human metapneumovirus, MERS-coronavirus, Parainfluenza virus 1, Parainfluenza virus 2, Parainfluenza virus 3, Parainfluenza virus 4, Respiratory syncytial virus, Rhinovirus, Human coronavirus- HKU1, Bordetella pertussis, Chlamydia trachomatis, Haemophilus influenza, Legionella pneumophila, Mycobacterium tuberculosis, Mycoplasma pneumonia, Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pneumonia, Streptococcus pyogenes, Pneumocystis jirovecii-S. cerevisiae, Pseudomonas aeruginosa, Chlamydia pneumonia, Candida albicans.

The interfering substances including Whole Blood, Dafenlin Oxymetazoline Hydrochloride Spray, Mometasone Furoate Nasal Spray, Fluticasone Propionate andPhysiological Seawater Nasal Cleaner with a certain concentration have no interference on the test of SARS-CoV-2 & Influenza A/B Ag Combo Rapid Test.

Precision and Reproducibility

Intra-Assay

Within-run precision was determined using 60 replicates of specimens: negative specimen and SARS-CoV-2/Influenza A/Influenza B antigen positive specimen. The specimens were correctly identified 100% of the time.

Inter-Assay

Between-run precision was determined using 60 independent assays on the same specimen: negative specimen and SARS-CoV-2/influenza A/Influenza B antigen positive specimen. Three different lots of the SARS-CoV-2 & Influenza A/B Ag Combo Rapid Test were tested using these specimens. The specimens were correctly identified 100% of the time.

BIBLIOGRAPHY

1. Clémence Magnard, Martine Valette, Michèle Aymard, Bruno Lina. Comparison of Two Nested PCR, Cell Culture, and Antigen Detection for the Diagnosis of Upper Respiratory Tract Infections due to Influenza Viruses. Journal of Medical Virology, 59:215–220 (1999)
2. Shuo Su, Gary Wong, Weifeng Shi, et al. Epidemiology, Genetic recombination, and pathogenesis of coronaviruses. Trends in Microbiology, June 2016, vol. 24, No. 6: 490-502
3. Susan R. Weiss, Julian L. Leibowitz, Coronavirus Pathogenesis, Advances in Virus Research, Volume 81: 85-164

Index of Symbols

	Manufacturer	Σ	Contains sufficient for <*n*> tests		Temperature limit
IVD	*In vitro* diagnostic medical device		Use-by date		Do not re-use
	Consult instructions for use	LOT	Batch code	REF	Catalogue number
EC REP	Authorized representative in the European Community	MD	Medical device		Date of manufacture

Index of Contents

Extraction Buffer Tubes	Extraction Buffer Tubes
Disposable Swabs	Disposable Swabs
Nasal Swabs	Nasal Swabs
Nasopharyngeal Swabs	Nasopharyngeal Swabs

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