SARS-CoV-2 & Flu A/B & RSV & Adenovirus Antigen Combo Rapid Test Package Insert

Flowflex™

REF L031-12335	English

A rapid test for the qualitative and differential detection of SARS-CoV-2, Influenza virus type A and type B nucleoprotein antigens (Flu A/B), respiratory syncytial virus（RSV）and respiratory adenovirus antigens in nasal swab or nasopharyngeal swab.

For professional in vitro diagnostic use only.

INTENDED USE

The SARS-CoV-2 & Flu A/B & RSV & Adenovirus Antigen 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 (Flu A/B), RSV and respiratory adenovirus antigens in nasal swab or nasopharyngeal swab specimens directly from individuals who are suspected of SARS-CoV-2 or Flu A/B or RSV or adenovirus infection by their healthcare provider. Results are for the identification of SARS-CoV-2 and Flu A/B nucleocapsid antigens and RSV and respiratory adenovirus 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 Flu A/B or RSV or adenovirus infections and should not be used as the sole basis for treatment or other patient management decisions.

The SARS-CoV-2 & Flu A/B & RSV & Adenovirus Antigen 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（Flu） is an acute respiratory disease caused by Flu viruses (type A, type B and type C), which is highly infectious and has a short window period. Flu A and B viruses circulate and cause seasonal epidemics of disease. Flu A virus poses a greater risk as compared to the Flu 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. Flu 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.

Respiratory syncytial virus, or RSV, is a common respiratory virus that usually causes mild, cold-like symptoms. Most people recover in a week or two, but RSV can be serious, especially for infants and older adults. By age 2, nearly every child will have been infected with the virus. In adults and older, healthy children, RSV symptoms are mild. However, RSV can cause severe infection in some people, including infants under 6 months of age, premature infants, infants born with heart or lung diseases, children and adults with weakened immune systems, children who have difficulty swallowing, older adults, and adults with heart and lung disease. Each year, RSV sends more than 57,000 children to the hospital.

Adenoviruses are extremely common viruses that infect humans at any time of year. Adenovirus infections are often asymptomatic but can cause mild to severe illness. The illnesses can range from the common cold to pneumonia, croup, and bronchitis. People with weakened immune systems, or chronic respiratory or cardiac disease are at high risk for developing severe illness from an adenovirus infection.

Adenoviruses are usually spread from an infected person to others through close personal contact, such as touching or shaking hands; coughing and sneezing; touching an object or surface with adenoviruses on it, then touching your mouth, nose, or eyes before washing your hands.

PRINCIPLE

Anti-SARS-CoV-2, anti-Flu A, anti-Flu B, anti-RSV and anti-adenovirus antibodies are conjugated with colored particles and pre-treated on the label pad and other anti-SARS-CoV-2, anti-Flu A and anti-Flu B, anti-RSV, anti-adenovirus antibodies are pre-coated on the membrane. When specimens are processed and added to the test cassette, if SARS-CoV-2 or Flu A/B antigen or RSV or adenovirus 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 SARS-CoV-2 or Flu A/B or RSV or adenovirus 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-Flu A antibodies, anti-Flu B antibodies, anti-RSV antibodies, and anti-adenovirus antibodies.

PRECAUTIONS

- For professional *in vitro* diagnostic use only. Do not use after the expiration date.
- Do not eat, drink or smoke in the area where the specimens or kits are handled.
- 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, disposable gloves, mask and eye protection when specimens are being tested.
- The used test should be discarded according to local regulations. The used test should be considered potentially infectious and be discarded according to local regulations.
- Humidity and temperature can adversely affect results.
- This package insert must be read completely before performing the test. Failure to follow directions in insert may cause inaccurate test results.
- The test line for a high viral load sample may become visible within 15 minutes, or as soon as the sample passes the test line region.
- The test line for a low viral load sample may become visible within 30 minutes.
- Do not use nasal sprays for at least 30 minutes before collecting a nasal swab specimen

STORAGE AND STABILITY

- The kit can 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
- Extraction Buffer Tubes
- Package Insert
- Disposable Swabs*
- Specimen Collection Guide

* *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 & Flu A/B & RSV & Adenovirus Antigen Combo Rapid Test can be performed using nasal swab or nasopharyngeal swab specimens.

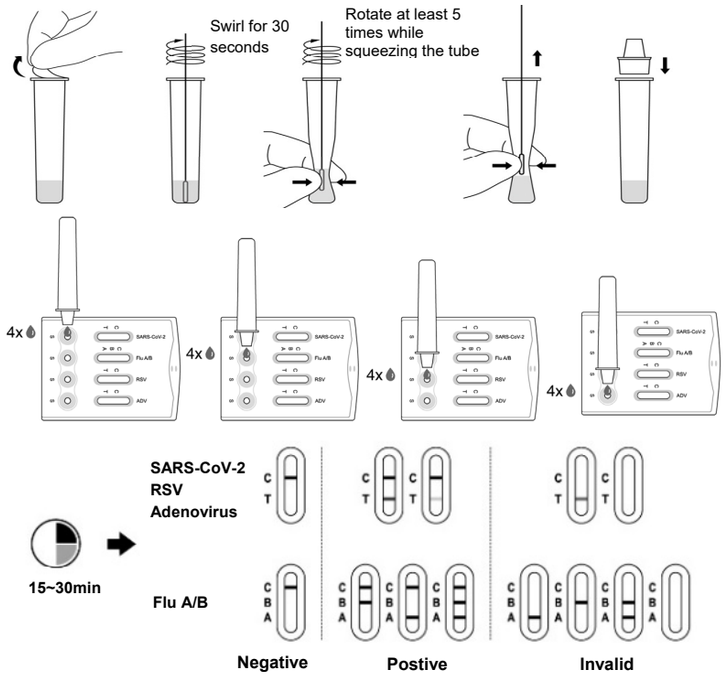
Testing should be performed immediately after specimen collection, or at most within one (1) hour after specimen collection, if stored at room temperature (15-30°C).

Please refer to the Specimen Collection Guide provided with the kit for specimen collection details.

DIRECTIONS FOR USE

Allow the test and extraction buffer tubes 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. Remove the aluminum foil from the top of extraction buffer tube.
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. Attach the dropper tip 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 of the test cassette.
   a. Invert the extraction buffer tube with the dropper tip pointing downwards and hold it vertically.
   b. Gently squeeze the tube, dispensing 4 drops of the processed specimen into the sample well.
9. Wait for the colored line(s) to appear. The result should be read at 15-30 minutes. **Do not read the result after 30 minutes.**



INTERPRETATION OF RESULTS

(Please refer to the illustration above)

NEGATIVE: Only one colored control line appears in the control region (C). No apparent colored line appears in the test line region (T/A/B). This means that no antigen was detected.

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

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

INVALID: Control line fails to appear. Insufficient specimen volume or incorrect operation 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.

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 and correct procedural technique.

LIMITATIONS

1. It is for *in vitro* diagnostic use only. The test should be used in nasal, nasopharyngeal swab specimens only. The intensity of the test line does not necessarily correlate to viral titer in the specimen.
2. Specimens should be tested as quickly as possible after specimen collection and at most within the hour following collection.
3. Use of viral transport media may result in decreased test sensitivity.
4. A false-negative test may result if the level of antigen in a sample is below the detection limit of the test or if the sample was collected incorrectly.
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.
9. A negative result, from a patient with SARS-CoV-2 symptom onset beyond seven days, should be treated as presumptive and confirmed with a molecular assay, if necessary, for clinical management. (If the differentiation of specific SARS viruses and strains is needed, additional testing is required.)

PERFORMANCE CHARACTERISTICS

Clinical Sensitivity, Specificity and Accuracy

Nasal Swab Specimens

The performance of SARS-CoV-2 & Flu A/B & RSV & Adenovirus Antigen Combo Rapid Test was established with nasal swabs from a population of individuals. The results show that the relative sensitivity and the relative specificity are as follows:

Candidate method		RT-PCR		
		Negative	Positive	Total
SARS-CoV-2 Test Results	Negative	403	4	407
	Positive	2	99	101
	Total	405	103	508

Relative Sensitivity: 96.12% (90.12%-98.80%)* Relative Specificity: 99.51% (98.10%-99.99%)*
Accuracy: 98.82% (97.38%-99.52%)* *95% Confidence Intervals

Candidate method		Comparator		
		Negative	Positive	Total
Flu A Test Results	Negative	461	0	461
	Positive	2	45	47
	Total	463	45	508

Relative Sensitivity: 100.00% (90.62%-100.00%)* Relative Specificity: 99.57% (98.33%-99.99%)*
Accuracy: 99.61% (98.48%-99.99%)* *95% Confidence Intervals

Candidate method		Comparator		
		Negative	Positive	Total
Flu B Test Results	Negative	457	1	458
	Positive	2	48	50
	Total	459	49	508

Relative Sensitivity: 97.96% (88.31%-99.99%)* Relative Specificity: 99.56% (98.32%-99.99%)*
Accuracy: 99.41% (98.19%-99.88%)* *95% Confidence Intervals

Candidate method		Comparator		
		Negative	Positive	Total
RSV Test Results	Negative	470	0	470
	Positive	3	35	38
	Total	473	35	508

Relative Sensitivity: 100.00% (88.24%-100.00%)* Relative Specificity: 99.37% (98.06%-99.88%)*
Accuracy: 99.41% (98.19%-99.88%)* *95% Confidence Intervals

Candidate method		Comparator		
		Negative	Positive	Total
Adenovirus Test Results	Negative	465	1	466
	Positive	3	39	42
	Total	468	40	508

Relative Sensitivity: 97.50% (85.96%-99.99%)* Relative Specificity: 99.36% (98.04%-99.87%)*
Accuracy: 99.21% (97.92%-99.77%)* *95% Confidence Intervals

Nasopharyngeal Swab Specimens

The performance of SARS-CoV-2 & Flu A/B & RSV & Adenovirus Antigen Combo Rapid Test was established with nasopharyngeal swabs from a population of individuals. The results show that the relative sensitivity and the relative specificity are as follows:

Candidate method		RT-PCR		
		Negative	Positive	Total
SARS-CoV-2 Test Results	Negative	401	4	405
	Positive	2	97	99
	Total	403	101	504

Relative Sensitivity: 96.04% (89.93%-98.77%)* Relative Specificity: 99.50% (98.09%-99.99%)*
Accuracy: 98.81% (97.36%-99.52%)* *95% Confidence Intervals

Candidate method		Comparator		
		Negative	Positive	Total
Flu A Test Results	Negative	471	0	471
	Positive	3	30	33
	Total	474	30	504

Relative Sensitivity: 100.00% (86.53%-100.00%)* Relative Specificity: 99.37% (98.07%-99.88%)*
Accuracy: 99.40% (98.18%-99.88%)* *95% Confidence Intervals

Candidate method		Comparator		
		Negative	Positive	Total
Flu B Test Results	Negative	471	1	472
	Positive	2	30	32
	Total	473	31	504

Relative Sensitivity: 96.77% (82.42%-99.99%)* Relative Specificity: 99.58% (98.37%-99.99%)*
Accuracy: 99.40% (98.18%-99.88%)* *95% Confidence Intervals

Candidate method		Comparator		
		Negative	Positive	Total
RSV Test Results	Negative	471	0	471
	Positive	3	30	33
	Total	474	30	504

Relative Sensitivity: 100.00% (86.53%-100.00%)* Relative Specificity: 99.37% (98.07%-99.88%)*
Accuracy: 99.40% (98.18%-99.88%)* *95% Confidence Intervals

Candidate method		Comparator		
		Negative	Positive	Total
Adenovirus Test Results	Negative	469	1	470
	Positive	3	31	34
	Total	472	32	504

Relative Sensitivity: 96.88% (82.89%-99.99%)* Relative Specificity: 99.36% (98.06%-99.87%)*
Accuracy: 99.21% (97.90%-99.77%)* *95% Confidence Intervals

Limit of Detection (LOD)

The LOD of SARS-CoV-2 & Flu A/B & RSV & Adenovirus Antigen Combo Rapid Test was established using limiting dilutions of an inactivated viral sample. The results show that the LOD of SARS-CoV-2 Antigen test is $1.60*10^2$ $TCID_{50}$/mL, the LOD of Flu A is $6.88*10^2$ $TCID_{50}$/mL, the LOD of Flu B is $1.88*10^2$ $TCID_{50}$/mL, the LOD of RSV is $1.58*10^2$ $TCID_{50}$/mL, the LOD of adenovirus is $4.35*10^4$ $TCID_{50}$/mL.

Cross-Reactivity and Interference

No cross-reactivity or interference was observed with the following microorganisms: Enterovirus, Coronavirus-229E, Coronavirus-NL63, Coronavirus-OC43, Human metapneumovirus, MERS-coronavirus, Parainfluenza virus 1, Parainfluenza virus 2, Parainfluenza virus 3, Parainfluenza virus 4, 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 (Biotin, Mucin, Whole Blood, Oxymetazoline, Homeopathic, Menthol Benzocaine, Fluticasone propionate, Phenylephrine, Phenol, Menthol, Cromolyn, Sodium Hyaluronate, Dyclonine Hydrochloride, Galphimia glauca, Luffa operculata, Sabadilla, Mupirocin, Oseltamivir Phosphate, Tobramycin, Mometasone Furoate, NaCl) with a certain concentration have no interference.

Precision and Reproducibility

Intra-Assay

Within-run precision was determined using 60 replicates of specimens: negative specimens and positive specimens. The specimens were correctly identified >99% of the time.

Inter-Assay

Between-run precision was determined using 60 independent assays on the same specimen: negative specimen and positive specimen. Three different lots of the products were tested using these specimens. The specimens were correctly identified >99% of the time.

BIBLIOGRAPHY

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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

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