Flowflex COVID-19 Antigen Rapid Test Package Insert Instructions

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Flowflex

Flowflex COVID-19 Antigen Rapid Test Package Insert

A rapid test for the qualitative detection of SARS-CoV-2 nucleocapsid antigen in anterior nasal swab specimens. For prescription use only. For in vitro diagnostic use only. For use under an Emergency Use Authorization (EUA) only.

INTENDED USE

The Flowflex COVID-19 Antigen Rapid Test is a rapid, lateral flow chromatographic immunoassay intended for the qualitative detection of the SARS-CoV-2 nucleocapsid protein antigen in direct anterior nasal swab specimens from individuals, who are suspected of COVID-19 by their healthcare provider within the first 7 days of symptom onset when tested at least twice over three days with at least 48 hours between tests, and from individuals without symptoms or other epidemiological reasons to suspect COVID-19

when tested at least three times over five days with at least 48 hours between tests. Testing is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. § 263a, that meet the requirements to perform moderate, high or waived complexity tests. This test is authorized for use at the Point of Care (POC), i.e., in inpatient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation.

The Flowflex COVID-19 Antigen Rapid Test does not differentiate between SARS-CoV and SARS-CoV-2. Results are for the identification of SARS-CoV-2 nucleocapsid protein antigen, which is generally detectable in anterior nasal (nares) swab specimens during the acute phase of infection. Positive results indicate the presence of viral antigens, but clinical correlation with past medical history and other diagnostic information is necessary to determine patient 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 the disease. Laboratories within the United States and its territories are required to report all results to the appropriate public health authorities. All negative results are presumptive and confirmation with a molecular assay, if necessary for patient management, may be performed.

Negative results do not rule out SARS-CoV-2 infection and should not be used as the sole basis for treatment or patient management decisions, including infection control measures such as isolating from others and wearing masks. Negative results should be considered in the context of an individual’s recent exposures, history and the presence of clinical signs and symptoms consistent with COVID-19.

The Flowflex COVID-19 Antigen Rapid Test is intended for use by healthcare professionals or individuals trained in point-of-care settings. The Flowflex COVID-19 Antigen Rapid Test is only for use under the Food and Drug Administration’s Emergency Use Authorization. This product has not been FDA-cleared or approved.

SUMMARY AND EXPLANATION

The novel coronavirus, SARS-CoV2, also known as COVID-19 virus, belongs to the enveloped, single-stranded RNA virus of the β genus. The virus can cause 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. Based on the current epidemiological investigation, the incubation period is 1 to 14 days, mostly 3 to 7 days.

The symptoms include fever, fatigue, and dry cough. Nasal congestion, runny nose, sore throat, myalgia and diarrhea are found in a few cases. The Flowflex COVID-19 Antigen Rapid Test is a fast lateral flow immunoassay for the qualitative detection and diagnosis of SARS-CoV-2 directly from anterior nasal swab specimens.

PRINCIPLE

The Flowflex COVID-19 Antigen Rapid Test is a membrane-based chromatographic immunoassay for the qualitative detection of the nucleocapsid protein antigen from SARS-CoV-2 in human anterior nasal swab specimens. When specimens are processed and added to the test cassette, SARS-CoV-2 antigens, if present in the specimen, will react with the colored anti-SARS-CoV-2 antibody-coated particles, which have been pre-coated on the test strip.

The antigen-antibody complex then migrates toward the membrane by capillary action. This complex is then captured by anti-SARS-CoV-2 monoclonal antibodies immobilized at the test line region, and a colored line appears 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 red or pink line will always appear in the control line region after the proper volume of specimen has been added, and membrane wicking has occurred.

WARNINGS, PRECAUTIONS, AND SAFETY INFORMATION

- Read the all instructions provided in Flowflex COVID-19 Antigen Rapid Test Package Insert carefully before performing a test. Failure to follow the instructions may result in inaccurate test results.
- In the USA, this product has not been FDA-cleared or approved, but has been authorized by FDA under an Emergency Use Authorization for use by authorized laboratories; use by laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet the requirements to perform moderate, high, or waived complexity tests.
- The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization emergency use of an in vitro diagnostic detection and/or diagnosis of COVID-19 under section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization is revoked sooner.
- Federal Law restricts this device to sale by or on the order of a licensed practitioner (U.S. only).
- Serial testing should be performed in individuals with negative results at least twice over three days (with 48 hours between tests) for symptomatic individuals and three times over five days (with at least 48 hours between tests) for asymptomatic individuals.
- Treat all specimens as potentially infectious. Follow universal precautions when handling samples, this kit, and its contents.
- Immediately use after opening the test cassette in the pouch. Once opened, the test should be used within one hour.
- Do no store specimens in viral transport media for specimen storage.
- All components of this kit should be discarded as Biohazard waste according to Federal, State, and local

regulatory requirements.

- Solutions used to make the positive control swab are non-infectious. However, patients' samples, controls, and cassettes should be handled as though they could transmit disease. Observe established precautions against microbial hazards during use and disposal.
- Wear appropriate personal protective equipment and gloves when running each test and handling patient specimens. Change gloves between the handling of specimens suspected of COVID-19.
- This product has been authorized only for the detection of proteins from SARS-CoV-2, not for any other viruses or pathogens.
- Swabs in the kit are approved for use with Flowflex COVID-19 Antigen Rapid Test. Do not use other swabs.
- Do not use on anyone under 2 years of age.
- Leave the test cassette sealed in its pouch until just before use. Do not use if any of the test kit contents or packaging is damaged.
- Do not use the test past its expiration date.
- Test components are single-use. Do not reuse.
- Make sure there is sufficient light when reading and interpreting test results.
- Do not use nasal sprays for at least 30 minutes before collecting a nasal sample.
- Remove any piercings from the nose before starting the test. Do not use on anyone who is prone to nosebleeds or has had facial injuries or head injuries/surgery in the past six months.
- Do not touch the swab tip.
- Do not read test results before 15 minutes or after 30 minutes. Results read before 15 minutes or after 30 minutes may lead to a false positive, false negative, or invalid result.
- Keep testing kit and kit components away from children and pets before and after use. Avoid contact with your (e.g., skin, eyes, nose, or mouth).
- Do not ingest any kit components.
- The reagent solution in the tube contains harmful chemicals (see table below). If the solution contacts your (e.g., skin, eyes, nose, or mouth), flush with large amounts of water. If irritation persists, seek medical advice. **https://www.poisonhelp.org** or 1-800-222-1222

Hazardous Ingredients for the Reagent Solution		
Chemical Name	Harms (GHS) code for each ingredient	Concentration
TX-100	H302 Acute oral toxicity H315 Skin irritation H318 Serious eye damage H400 Short-term (acute) aquatic hazard H410 Long-term (chronic) aquatic hazard	1%
Sodium Azide	H300 Acute oral toxicity H310 Acute dermal toxicity H373 Oral, Brain toxicity H400 Short-term (acute) aquatic hazard H410 Long-term (chronic) aquatic hazard	0.02%

If INHALED
Move to fresh air. If not breathing, give artificial respiration. Do not use mouth-to-mouth resuscitation if the victim ingested or inhaled the substance; give artificial respiration with the aid of a pocket mask equipped with a one-

way valve or other proper respiratory medical device. Immediate medical attention is required.

If Contact SKIN
Immediately remove all contaminated clothing. Flush the skin with plenty of water for at least 15 minutes. Immediate medical attention is required.

If Contact with EYES
Immediately flush the eyes with plenty of water for at least 15 minutes. Ensure adequate flushing by separating the eyelids with fingers. Immediate medical attention is required.

If INGESTED
Rinse the mouth with water. Do not induce vomiting. Risk of aspiration! Keep airways free. Pulmonary failure is possible after the aspiration of vomit. Immediately contact a physician or Poison Control Center.

- For more information on EUAs please visit: **https://www.fda.gov/**emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization
- For the most up-to-date information on COVID-19, please visit: **www.cdc.gov/COVID19**

STORAGE AND STABILITY

- The kit can be stored at temperatures between 36-86°F (2-30°C) when not in use.
- The test is stable until the expiration date is printed on the sealed pouch.
- The test must remain in the sealed pouch until use. Once the pouch has been opened, the test device should be used within 60 minutes. Use beyond 60 minutes may not produce accurate results.
- DO NOT FREEZE.

MATERIALS

Materials Provided

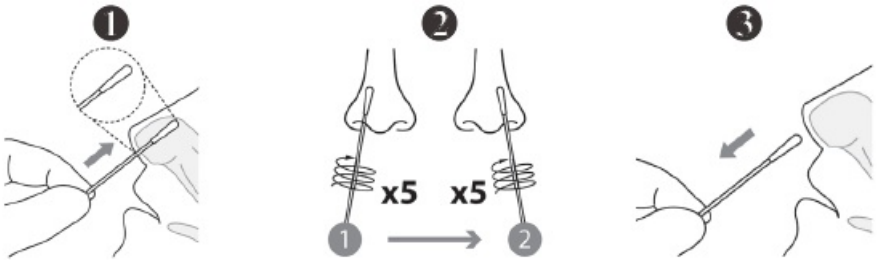
- Test Cassettes
- Extraction Buffer Tubes
- Positive Control Swab
- Negative Control Swab
- Disposable Nasal Swabs
- Package Insert
- Tube holder

  Note: This test comes in a 25-test quantity.

Materials Required But Not Provided
Test specimens immediately after collection for optimal test performance. Inadequate specimen collection or improper sample handling may yield erroneous results. For more information on anterior nasal swab specimen collection, please refer to Interim Guidelines for Collecting, Handling and Testing Clinical Specimens from persons for COVID-19 at: **https://www.cdc.gov/coronavirus/2019-nCoV/lab/**guidelines-clinical-specimens.html

- The Flowflex COVID-19 Antigen Rapid Test is performed using anterior nasal swab specimens.
- Wash or sanitize your hands. Make sure they are dry before starting the test.

- Open the test cassette pouch and lay the cassette on a clean, flat surface.
- To collect an anterior nasal swab sample:



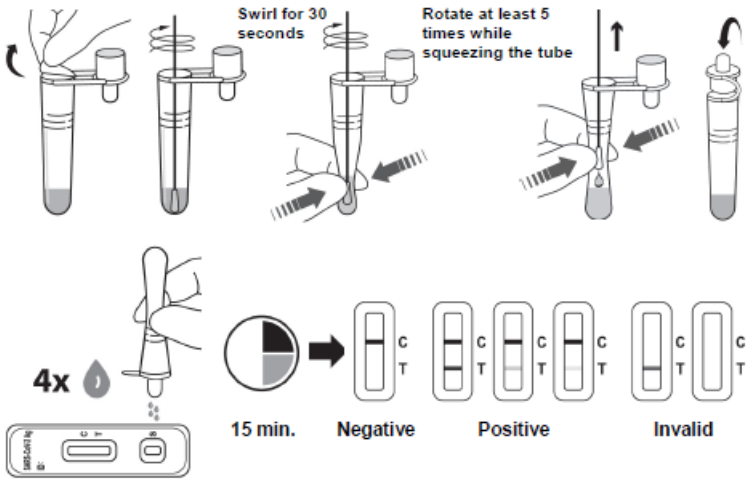
1. Gently insert the entire absorbent tip of the swab into 1 nostril (½ to ¾ of an inch). With children, the maximum depth of insertion into the nostril may be less than ¾ of an inch and you may need to have a second person to hold the child's head while swabbing.
   Note: A false negative result may occur if the nasal swab specimen is not properly collected.
2. Firmly rub the swab in a circular motion around the inside wall of the nostril 5 times. Take approximately 15 seconds to collect the specimen. Be sure to collect any nasal drainage that may be present on the swab. Repeat this in the other nostril using the same swab.
3. Remove the swab from the nostril and place it into the extraction buffer tube.

SPECIMEN TRANSPORT AND STORAGE

Do not return the nasal swab in its original paper packaging. Samples should be tested immediately after collection. If immediate testing is not possible, swabs should be placed in the extraction solution tube and tested within 60 minutes of collection. If the sample cannot be tested within 60 minutes of collection, it should be discarded, and another sample should be taken at least 60 minutes after the initial sample was taken.

DIRECTIONS FOR USE

1. Remove the foil from the top of the extraction buffer tube. Place the tube in the tube holder.
2. Immediately place the swab into the tube and swirl for 30 seconds.
3. Rotate the swab 5 times while squeezing the tube.
4. Remove the swab while squeezing the tube to extract as much liquid as possible. Dispose of the swab in the biohazard box.
5. Attach the dropper tip firmly onto the tube. Mix thoroughly by swirling or flicking the bottom of the tube.
   Note: A false negative result may occur if the swab was not swirled at least 30 seconds or rotated 5 times.
6. Place the cassette on a clean, flat surface. Gently squeeze the tube and dispense 4 drops of solution into the Sample Well. Dispose of the tube in the biohazard box.
   Note: A false negative or invalid result may occur if less than 4 drops of fluid are added to the Sample Well.
7. Set the timer for 15 minutes. The result should be read at 15 minutes. Do not read after 30 minutes. Dispose of the test cassette in the biohazard box.
   Note: A false negative or false positive result may occur if the test result is read before 15 minutes or after 30 minutes.



INTERPRETATION OF RESULTS

(Please refer to the illustration above) Repeat testing is needed to improve test accuracy. Please follow the table below when interpreting test results for COVID-19.

Status on first day of Testing	First Result Day 1	Second Result Day 3	Third Result Day 5	Interpretation
With Symptoms	Positive	N/A	N/A	Positive for COVID-19
	Negative	Positive	N/A	Positive for COVID-19
	Negative	Negative	N/A	Negative for COVID-19
Without Symptoms	Positive	N/A	N/A	Positive for COVID-19
	Negative	Positive	N/A	Positive for COVID-19
	Negative	Negative	Positive	Positive for COVID-19
	Negative	Negative	Negative	Negative for COVID-19

Results should be considered in the context of an individual's recent exposures, history, and the presence of clinical signs and symptoms consistent with COVID-19.
COVID-19 Negative (-): If the Control (C) line is visible, but the Test (T) line is not visible, the test is negative. To increase the chance that the negative result for COVID-19 is accurate, you should:

- Test again in 48 hours if the individual has symptoms on the first day of testing.
- Test 2 more times at least 48 hours apart if the individual does not have symptoms on the first day of testing. A negative test result indicates that the virus that causes COVID-19 was not detected in the sample. A negative result does not rule out COVID-19.
- There is a higher chance of false negative results with antigen tests compared to laboratory-based tests such as PCR tests. If the test is negative but COVID-19-like symptoms, e.g., fever, cough, and/or shortness of breath continue, follow-up testing for SARS-CoV-2 with a molecular test or testing for another respiratory disease should be considered.
- If applicable, seek follow-up care with the primary health care provider. All negative results should be treated as presumptive and confirmation with a molecular assay may be necessary if there is a high likelihood of SARS-CoV-2 infection, such as in an individual with close contact with COVID-19 or with suspected exposure to

COVID-19 or in communities with a high prevalence of infection.

- Negative results do not rule out SARS-CoV-2 infection and should not be used as the sole basis for treatment or patient management decisions, including infection control decisions.
- COVID-19 Positive (+): If the Control (C) line and the Test (T) line are visible, the test is positive. Any faint visible red or pink test (T) line with the control line (C) should be read as positive. Repeat testing does not need to be performed if patients have a positive result at any time.
- A positive test result means that the virus that causes COVID-19 was detected in the sample, and it is very likely the individual has COVID-19 and is contagious. Please contact the patient's doctor/primary care physician (if applicable) and the local health authority immediately and instruct your patient to adhere to the local guidelines regarding self-isolation.
- There is a very small chance that this test can give a positive result that is incorrect (a false positive). Positive results do not rule out bacterial infection or co-infection with other viruses.
- The agent detected may not be the definite cause of the disease. Individuals who test positive with the Flowflex COVID-19 Antigen Rapid Test should self-isolate and seek follow-up care with their physician or healthcare provider as additional confirmatory testing with a molecular test for positive results may also be necessary, if there is a low likelihood of COVID-19, such as in individuals without known exposures to COVID-19 or residing in communities with a low prevalence of infection.
- INVALID: If at 15 minutes, if the control (C) line is not visible, the test is invalid. Re-test with a new swab and new test cassette. If the problem persists, call (800) 838-9502 for assistance.

QUALITY CONTROL

Internal Quality Control
Internal procedural controls are included in the test. A red or pink line appearing in the control line region (C) is internal procedural control. The appearance of the procedural control line indicates that the proper volume of specimen has been added and capillary flow occurred. If the procedural control line does not develop in 15 minutes, the test result is considered invalid, and retesting with a new cassette is recommended.

External Quality Control
Positive and Negative control swabs are supplied with each kit. A positive control swab is a non-infectious recombinant SARS-CoV-2 protein with buffer and stabilizer solution dried onto a swab. A negative control swab is a buffer and stabilizer solution dried onto a swab. These control swabs should be used to ensure that the test cassette and the test procedure is performed correctly. Follow the section "DIRECTIONS FOR USE" steps 1 to 7 to perform the control test. Note: If the controls do not perform as expected, repeat the test or contact Customer Support before testing patient specimens.

LIMITATIONS

1. The Flowflex COVID-19 Antigen Rapid Test is for in vitro diagnostic use only. The test should be used for the detection of SARS-CoV-2 antigens in anterior nasal swab specimens only. The intensity of the test line does not necessarily correlate to SARS-CoV-2 viral titer in the specimen.
2. A false-negative result may occur if the level of antigen in a sample is below the detection limit of the test.
3. Incorrect test results may occur if the sample was collected or handled incorrectly.
4. A false negative result may occur if the swab is not swirled at least 30 seconds or rotated five times
5. A false negative or invalid result may occur if less than 4 drops of fluid are added to the Sample Well.
6. A false negative or false positive result may occur if the test result is read before 15 minutes or after 30 minutes This test detects both viable (live) and non-viable, SARS-CoV, and SARS-CoV-2.

7. Test performance depends on the amount of virus (antigen) in the sample and may or may not correlate with viral culture results performed on the same sample.
8. The Flowflex COVID-19 Antigen Rapid Test does not differentiate between SARS-CoV and SARS-CoV-2.
9. Test results must be evaluated in conjunction with other clinical data available to the physician.
10. A positive or negative test result does not rule out co-infections with other pathogens such as other viral or bacterial infections.
11. There is a higher chance of false negative results with antigen tests than with laboratory-based molecular tests due to the sensitivity of the test technology. This means that there is a higher chance this test will give a false negative result in an individual with COVID-19 as compared to a molecular test, especially in samples with low viral load.
12. All COVID-19 antigen test negative results are presumptive, and confirmation with a molecular assay may be necessary.
13. A negative result is not intended to rule out other viral or bacterial infections.
14. If the patient continues to have symptoms of COVID-19, and both the patient's first and second tests are negative, the patient may not have COVID-19, however additional follow-up may be needed.
15. If the test is positive, then proteins from the virus that causes COVID-19 have been found in the sample and the individual likely has COVID-19.
16. This test is read visually and has not been validated for use by those with impaired vision or color-impaired vision.
17. The performance of this test was established based on the evaluation of a limited number of clinical specimens
18. collected between March 2021 and May 2021. The clinical performance has not been established in all circulating variants but is anticipated to be reflective of the prevalent variants in circulation at the time and location of the clinical evaluation.
19. Performance at the time of testing may vary depending on the variants circulating, including newly emerging strains of SARS-CoV-2 and their prevalence, which change over time.

PERFORMANCE CHARACTERISTICS

A prospective clinical study was conducted between January 2021 and May 2022 as a component of the Rapid Acceleration of Diagnostics (RADx) initiative from the National Institutes of Health (NIH). A total of 7,361 individuals were enrolled via a decentralized clinical study design, with a broad geographical representation of the United States.

Per inclusion criteria, all individuals were asymptomatic upon enrollment in the study and at least 14 days prior to it and did not have a SARS-CoV-2 infection in the three months prior to enrollment. Participants were assigned to one of three EUA-authorized SARSCoV-2 OTC rapid antigen tests to conduct serial testing (every 48 hours) for 15 days. If an antigen test was positive, the serial-antigen testing result is considered positive.

At each rapid antigen testing time point, study subjects also collected a nasal swab for comparator testing using a home collection kit (using a 15-minute normalization window between swabs). SARS-CoV-2 infection status was determined by a composite comparator method on the day of the first antigen test, using at least two highly sensitive EUA RT-PCRs. If the results of the first two molecular test were discordant a third highly sensitive EUA RT-PCR test was performed, and the final test result was based upon the majority rule.

Study participants reported symptom status throughout the study using the MyDataHelps app. Two-day serial antigen testing is defined as performing two antigen tests 36 – 48 hours apart. Three-day serial antigen testing is defined as performing three antigen tests over five days with at least 48 hours between each test.

Out of the 7,361 participants enrolled in the study, 5,609 were eligible for analysis. Among eligible participants, 154 tested positive for SARS-CoV-2 infection based on RT-PCR, of which 97 (62%) were asymptomatic on the first day of their infection, whereas 57 (39%) reported symptoms on the first day of infection.

Pre-symptomatic subjects were included in the positive percent agreement (PPA) of asymptomatic individuals, if they were asymptomatic on the first day of antigen testing, regardless of whether they developed symptoms at any time after the first day of testing.

The performance of the antigen test with serial testing in individuals is described in the table below. Data establishing PPA of COVID-19 antigen serial testing compared to the molecular comparator single-day testing throughout the course of infection with serial testing. Data is from all antigen tests in the study combined.

DAYS AFTER FIRST PCR POSITIVE TEST RESULT	**ASYMPTOMATIC ON FIRST DAY OF TESTING**			**SYMPTOMATIC ON FIRST DAY OF TESTING**		
	Ag Positive / PCR Positive (Antigen Test Performance % PPA)					
	1 Test	2 Tests	3 Tests	1 Test	2 Tests	3 Tests
0	9/97 (9.3%)	35/89 (39.3%)	44/78 (56.4%)	34/57 (59.6%)	47/51 (92.2%)	44/47 (93.6%)
2	17/34 (50.0%)	23/34 (67.6%)	25/32 (78.1%)	58/62 (93.5%)	59/60 (98.3%)	43/42 (100%)
4	16/21 (76.2%)	15/20 (75.0%)	13/15 (86.7%)	55/58 (94.8%)	53/54 (98.1%)	39/40 (97.5%)
6	20/28 (71.4%)	24/27 (77.8%)	16/18 (88.9%)	27/34 (79.4%)	26/33 (78.8%)	22/27 (81.5%)
8	13/23 (56.5%)	13/22 (59.1%)	4/11 (36.4%)	12/17 (70.6%)	12/17 (70.6%)	7/11 (63.6%)
10	5/9 (55.6%)	5/8 (62.5%)	/	4/9 (44.4%)	3/7 (42.9%)	/

Test = one (1) test performed on the noted days after the first PCR positive test result. Day 0 is the first day of documented infection with SARS-CoV-2.

1. Tests = two (2) tests performed an average of 48 hours apart. The first test was performed on the indicated day and the second test was performed 48 hours later.
2. Tests = three (3) tests performance an average of 48 hours apart. The first test was performed on the indicated day, the second test was performed 48 hours later, and a final test was performed 48 hours after the second test.
3. Clinical Sensitivity, Specificity, and Accuracy
4. The performance of Flowflex COVID-19 Antigen Rapid Test was established in an all-comers clinical study conducted between March 2021 and May 2021 with 108 nasal swabs self-collected or pair-collected by another study participant from symptomatic subjects (within 7 days of onset) suspected of COVID-19.
5. The study was conducted in a simulated home setting environment at two study sites in the U.S. All study participants performed the test unassisted and interpreted the result, using only the product labeling.
6. The Flowflex COVID-19 Antigen Rapid Test results were compared to an FDA EUA RT-PCR COVID-19 assay to determine test performance in the tables below:Table 1. Performance of the Flowflex COVID-19 Antigen

Rapid Test in Symptomatic subjects

Flow*flex* COVID-19 Antigen Rapid Test	**RT-PCR method**		
	Positive	**Negative**	**Total**
Positive	28	0	28
Negative	2	78	80
Total	30	78	108
Positive Percent Agreement (PPA)	93% (95%CI: 78% – 99%)		
Negative Percent Agreement (NPA)	100% (95%CI: 95% – 100%)		

Table 2. Cumulative PPA results by days since symptom onset

Days Since Symptom Onset	**# Specimens Tested**	**# Cumulative Positive Flow*flex* COVID-19 Antigen Rapid Test**	**Cumulative Positive RT-PCR**	**Cumulative PPA**
0 to 1 day	29	6	7	86%
0 to 2 days	64	15	16	94%
0 to 3 days	90	20	21	95%
0 to 4 days	96	21	22	95%
0 to 5 days	100	23	24	96%
0 to 6 days	106	26	28	93%
0 to 7 days	108	28	30	93%

Symptomatic Subject Age Distribution
A total of 108 symptomatic subjects participated in the study. Ages of symptomatic subjects ranged from 2 years to 93 years. The table below shows age distribution and the positive results broken down by age of the symptomatic subject:
Table 3. Age distribution of subjects and specimen positivity

Age Group	Flow*flex* COVID-19 Antigen Rapid Test (N=108)		
	Total	**Total Positive**	**Prevalence**
2-13 years	8	1	13%
14- 24 years	12	4	33%
25- 64 years	67	21	31%
≥ 65 years	21	2	10%
Total	108	28	26%

	Analytical Sensitivity: Limit of Detection (LoD)	

Analytical Sensitivity: Limit of Detection (LoD)

The Limit of Detection (LoD) of the Flowflex COVID-19 Antigen Rapid Test was determined using limiting dilutions of the heat-inactivated SARS-CoV-2 virus (USA-WA1/2020). Nasal swabs from healthy donors were collected and eluted with PBS. The swab eluates were combined and mixed thoroughly to create a negative clinical matrix pool to be used as the diluent. Inactivated SARS-

The coV-2 virus was diluted in this negative clinical matrix pool to generate virus dilutions for testing. The contrived nasal swab samples were prepared by absorbing 50 µL of each virus dilution onto the swab. The contrived swab samples were processed and tested according to the package insert.

SARS-CoV-2 Concentration in nasal matrix	**Number of Positives/Total**	**% Detected**
2.5 x 10^3 TCID50/mL	60/60	100%

LoD was determined as the lowest virus concentration that was detected ≥ 95% of the time.
Based on this testing, the LoD in the nasal matrix was confirmed to be 2.5 x 103 TCID50/mL. Based upon the testing procedure for this study, the LoD of 2.5 x 103 TCID50/mL equates to 1.3 x 102 TCID50/swab.

The performance of this test device in the detection of the Omicron variant of SARS-CoV-2 was evaluated in a dilution series of clinical specimens which were positive for the Omicron variant. This testing was conducted by the National Institutes of Health (NIH) as a component of the Rapid Acceleration of Diagnostics (RADx) initiative. The clinical specimens used to prepare these dilution series were not identical to the previous specimen pools prepared and tested by RADx to assess performance with the omicron variant.

Results from this dilution series cannot be compared to other specimen pools and do not indicate that a test will have different clinical performance compared to other EUA-authorized tests. Compared to a EUA-authorized RT-PCR method, the Flowflex COVID-19 Antigen Rapid Test detected 100% of live virus Omicron samples at a Ct-value of 25.6 (n=5). Testing was also compared to two additional EUA-authorized OTC antigen tests (Assay #1 and Assay #2).

Omicron dilutions at lower viral concentrations (Ct-values greater than 25.6) were not detected by the Flowflex COVID-19 Antigen Rapid Test in this study.

Omicron BA.2 Pool 1 Dilutions	Avg (N=9)	Assay #1 Percent Positive N=5	ACON Flow*flex* Percent Positive N=5	Assay #2 Percent Positive N=5
Dilution 1	19.4	100	100	100
Dilution 2	20.6	100	100	100
Dilution 3	21.6	100	100	100
Dilution 4	22.4	100	100	100
Dilution 5	23.3	100	100	100
Dilution 6	24.5	0	100	100
Dilution 7	25.6	0	100	100
Dilution 8	26.5	0	0	0
Dilution 9	27.7	0	0	0
Dilution 10	28.5	0	0	0
Dilution 11	29.4	0	0	0
Dilution 12	30.3	0	0	0

Analytical Specificity: Cross -Reactivity and Microbial Interference
Cross-reactivity was evaluated by testing a panel of related pathogens and microorganisms that are likely to be present in the nasal cavity. Each organism and virus were tested in the absence or presence of heat-inactivated SARS-CoV-2 virus (USA-WA1/2020) at a low concentration.

No cross-reactivity or interference was observed with the following organisms when tested at the concentration presented in the table below.

Potential Cross Reactant		Test Concentration	Cross-Reactivity Results	Interference Results
Virus	Adenovirus	1.14 x 10^6 TCID50/mL	No cross-reactivity	No Interference
	Enterovirus	9.50 x 10^5 TCID50/mL	No cross-reactivity	No Interference
	Human coronavirus 229E	1.04 x 10^5 TCID50/mL	No cross-reactivity	No Interference
	Human coronavirus OC43	2.63 x 10^5 TCID50/mL	No cross-reactivity	No Interference
	Human coronavirus NL63	1.0 x 10^5 TCID50/mL	No cross-reactivity	No Interference
	Human Metapneumovirus	1.25 x 10^5 TCID50/mL	No cross-reactivity	No Interference
	MERS-coronavirus	7.90 x 10^5 TCID50/mL	No cross-reactivity	No Interference
	Influenza A	1.04 x 10^5 TCID50/mL	No cross-reactivity	No Interference
	Influenza B	1.04 x 10^5 TCID50/mL	No cross-reactivity	No Interference
	Parainfluenza virus 1	1.25 x 10^5 TCID50/mL	No cross-reactivity	No Interference
	Parainfluenza virus 2	3.78 x 10^5 TCID50/mL	No cross-reactivity	No Interference
	Parainfluenza virus 3	1.0 x 10^5 TCID50/mL	No cross-reactivity	No Interference
	Parainfluenza virus 4	2.88 x 10^6 TCID50/mL	No cross-reactivity	No Interference
	Respiratory syncytial virus	3.15 x 10^5 TCID50/mL	No cross-reactivity	No Interference
	Rhinovirus	3.15 x 10^5 TCID50/mL	No cross-reactivity	No Interference
Bacteria	*Bordetella pertussis*	2.83 x 109 CFU/mL	No cross-reactivity	No Interference
	Chlamydia pneumonia	3.5 x 107 IFU/mL	No cross-reactivity	No Interference
	Chlamydia trachomatis	3.13 x 108 CFU/mL	No cross-reactivity	No Interference

	Haemophilus influenzae	1.36 x 108 CFU/mL	No cross-reactivity	No Interference
	Legionella pneumophila	4.08 x 109 CFU/mL	No cross-reactivity	No Interference
	Mycobacterium tuberculosis	1.72 x 107 CFU/mL	No cross-reactivity	No Interference
	Mycoplasma pneumoniae	7.90 x 107 CFU/mL	No cross-reactivity	No Interference
	Staphylococcus aureus	1.38 x 107 CFU/mL	No cross-reactivity	No Interference
	Staphylococcus epidermidis	2.32 x 109 CFU/mL	No cross-reactivity	No Interference
	Streptococcus pneumoniae	1.04 x 108 CFU/mL	No cross-reactivity	No Interference
	Streptococcus pyogenes	4.10 x 106 CFU/mL	No cross-reactivity	No Interference
	Pneumocystis jirovecii-S. cerevisiae	8.63 x 107 CFU/mL	No cross-reactivity	No Interference
	Pseudomonas aeruginosa	1.87 x 108 CFU/mL	No cross-reactivity	No Interference
Yeast	*Candida albicans*	1.57 x 108 CFU/mL	No cross-reactivity	No Interference

To estimate the likelihood of cross-reactivity with SARS-CoV-2 of organisms that were not available for wet testing, in-silico analysis was used to assess the degree of protein sequence homology. The comparison between the SARS-CoV-2 nucleocapsid protein and human coronavirus HKU1 revealed a low homology of 36.7% across 82.8% of the SARS-CoV-2 nucleocapsid sequence. The result suggests that cross-reactivity with human coronavirus HKU1 cannot be completely ruled out.

Compared the sequence homology between the SARS-CoV-2 nucleocapsid protein and the structural proteins of SARS coronavirus (SARS-CoV) and with given the substantial homology rate (91.5%), there is a high probability of cross-reactivity between the nucleocapsid proteins of SARS-CoV-2 and SARS-CoV. The Flowflex COVID-19 Antigen Rapid Test does not differentiate between SARS-CoV and SARS-CoV-2.

Endogenous Interfering Substances The following substances, naturally present in respiratory specimens or that may be artificially introduced into the nasal cavity or nasopharynx, were evaluated. In addition to the materials that are found in the nasal cavity, substances that are commonly found on the hands were also tested. Each substance was tested in the absence or presence of the SARS-CoV-2 virus (USA-WA1/2020) at a low concentration. The performance of the Flowflex COVID-19 Antigen Rapid Test was not affected by any of the potentially interfering substances listed in the table below at the concentrations tested.

Interfering Substance	Source/Item	Test Concentration	Cross-Reactivity Results	Interference Results
Biotin	Sigma/ B4501	3500 ng/mL	No cross-reactivity	No interference
Chloraseptic Throat Lozenge (Menthol/Benzocaine)	Chloraseptic	1.5 mg/mL	No cross-reactivity	No interference
Cough Lozenge (Menthol)	Ricola	1.5 mg/mL	No cross-reactivity	No interference
Dyclonine Hydrochloride	Sigma/PHR1849	1.5mg/mL	No cross-reactivity	No interference
Fluticasone propionate	Flonase	5% v/v	No cross-reactivity	No interference
Mucin	Sigma/M3895	0.5% w/v	No cross-reactivity	No interference
Mupirocin	Sigma/M7694	10 mg/mL	No cross-reactivity	No interference
Nasal Drops (Phenylephrine)	Equate (Walmart)	15% v/v	No cross-reactivity	No interference
Nasal Spray (Cromolyn)	NasalCrom	15% v/v	No cross-reactivity	No interference
Nasal Spray (Homeopathic)	ALKALOL	1:10 Dilution	No cross-reactivity	No interference
Nasal Spray (Oxymetazoline HCl)	Afrin	15% v/v	No cross-reactivity	No interference
Naso GEL (NeilMed)	NeilMed	5% v/v	No cross-reactivity	No interference
Sore Throat Phenol Spray	Equate (Walmart)	15% v/v	No cross-reactivity	No interference
Tamiflu (Oseltamivir Phosphate)	Tamiflu	5 mg/mL	No cross-reactivity	No interference
Tobramycin	Sigma/LRAC4285	4 µg/mL	No cross-reactivity	No interference
Whole Blood	In-house	4% v/v	No cross-reactivity	No interference
Zicam	Zicam	5% v/v	No cross-reactivity	No interference
Potential Interfering Household Items	**Source /Item**	**Test Concentration**	**Cross-Reactivity Results**	**Interference Results**
Body & Hand Lotion	Aveeno	0.5% w/v	No cross-reactivity	No interference
Body Lotion, with 1.2% dimethicone	Aveeno	0.5% w/v	No cross-reactivity	No interference
Hand Lotion	Bath & Body	5% w/v	No cross-reactivity	No interference
Hand Sanitizer with Aloe, 62% ethyl alcohol	Hand in Hand	5% v/v	No cross-reactivity	No interference
Hand Sanitizer cream lotion	Dove	15% v/v	No cross-reactivity	No interference
Hand Sanitizer, 80% ethanol, fast drying	Allied Photo Chemical	15% w/v	No cross-reactivity	No interference
Hand soap liquid gel	SoftSoap	10% w/v	No cross-reactivity	No interference

High Dose Hook Effect

No high dose hook effect was observed when tested with up to a concentration of 1.0 x 106 TCID50/mL of heat-inactivated SARS-CoV-2 virus (USA-WA1/2020) with the Flowflex COVID-19 Antigen Rapid Test.

BIBLIOGRAPHY

1. 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
2. Susan R. Weiss, Julian L. Leibowitz, Coronavirus Pathogenesis, Advances in Virus Research, Volume 81: 85-164

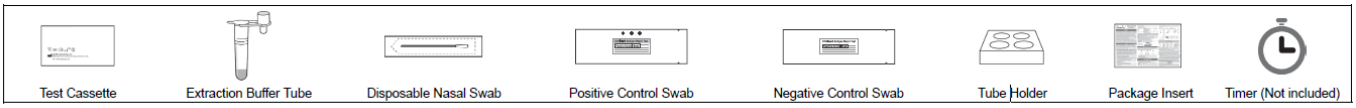
Index of Symbols

	Manufacturer		Date of manufacture
Σ	Contains sufficient for <*n*> tests	REF	Catalogue number
IVD	*In vitro* diagnostic medical device		Use-by date
	Consult instructions for use	LOT	Batch code
	Temperature limit		Do not reuse

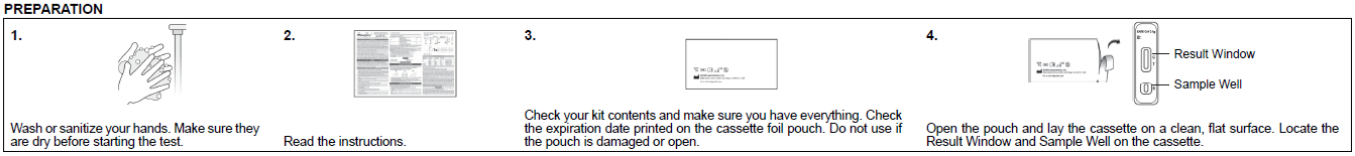
A rapid, lateral flow chromatographic immunoassay intended for the qualitative detection of the SARS-CoV-2 nucleocapsid protein antigen in direct anterior nasal swab specimens from individuals who are suspected of COVID-19 by their healthcare providers within 7 days of symptom onset when tested at least twice over three days with at least 48 hours between tests, and from individuals without symptoms or other epidemiological reasons to suspect COVID-19, when tested at least three times over five days with at least 48 hours between tests.

Testing is limited to authorized laboratories. This test is authorized for use at the Point of Care (POC). For prescription use only. For in vitro diagnostic use only. For use under an Emergency Use Authorization (EUA) only. See the Package Insert for complete use instructions, warnings, precautions, and limitations.

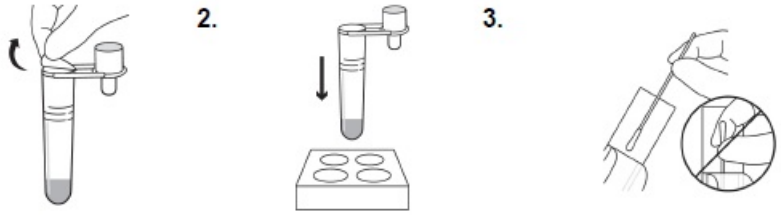
KIT CONTENTS



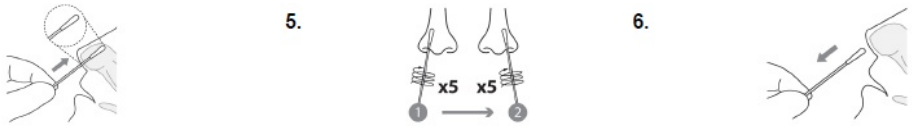
PREPARATION



TEST PROCEDURE



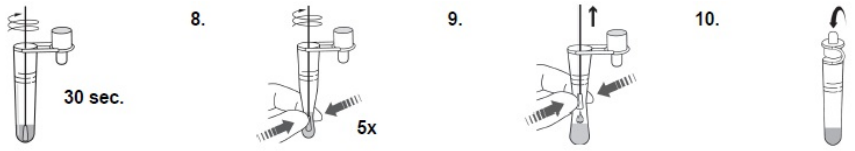
1. Remove the foil from the top of the extraction buffer tube.
2. Place the tube in the tube holder provided in the kit box.
3. Open the swab packaging at the stick end, not the swab tip. Do not touch the swab tip.



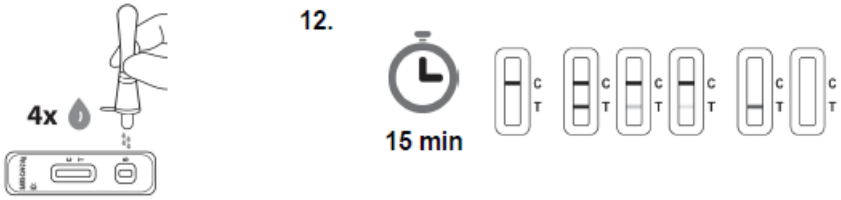
4. Gently insert the entire absorbent tip of the swab into 1 nostril (½ to ¾ of an inch). With children, the maximum depth of insertion into the nostril may be less than ¾ of an inch, and you may need to have a second person to hold the child's head while swabbing. Note: A false negative result may occur if the nasal swab specimen is not

properly collected.

5. Firmly rub the swab in a circular motion around the inside wall of the nostril 5 times. Take approximately 15 seconds to collect the specimen. Be sure to collect any nasal drainage that may be present on the swab. Repeat this in the other nostril.
6. Remove the swab from the nostril and immediately place it into the extraction buffer tube. Note Test samples immediately after collection, and no more than one hour after the swab is added to the reagent solution if stored at room temperature.



7. Immediately place the swab into the tube and swirl for 30 seconds. Note: A false negative result may occur if the swab is not swirled at least 30 seconds.
8. Rotate the swab 5 times while squeezing the tube.
   Note: A false negative result may occur if the swab is not rotated five times.
9. Remove the swab while squeezing the tube. Dispose of the swab in the biohazard box.
10. Attach the dropper tip firmly onto the tube. Mix thoroughly by swirling or flicking the bottom of the tube.
11. Gently squeeze the tube and dispense 4 drops of solution into the Sample Well. Dispose of the tube in the biohazard box. Note: A false negative or invalid result may occur if less than 4 drops of fluid are added to the Sample Well.



12. Set the timer for 15 minutes. The result should be read at 15 minutes. Do not read after 30 minutes. Dispose of the test cassette in the biohazard box. Note: A false negative or false positive result may occur if the test result is read before 15 minutes or after 30 minutes.

WARNINGS, PRECAUTIONS, AND SAFETY INFORMATION

- Read all instructions carefully before performing the test. Failure to follow the instructions may result in inaccurate test results.
- In the USA, this product has not been FDA-cleared or approved but has been authorized by FDA under an Emergency Use Authorization for use by authorized laboratories.
- This product has been authorized only for the detection of proteins from SARS-CoV-2, not for any other viruses or pathogens.
- The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for the detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization is revoked sooner.
- Serial testing should be performed in individuals with negative results at least twice over three days (with 48 hours between tests) for symptomatic individuals and three times over five days (with at least 48 hours between tests) for asymptomatic individuals. You may need to purchase additional tests to perform this serial (repeat) testing.

QUALITY CONTROL

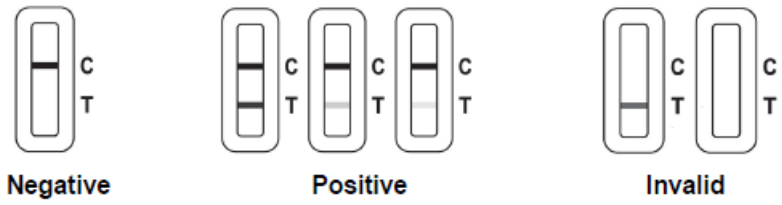
Internal procedural controls are included in the test. A red or pink line appearing in the control line region (C) is internal procedural control. The appearance of the procedural control line indicates that the proper volume of specimen has been added and capillary flow occurred. If the procedural control line does not develop in 15 minutes, the test result is considered invalid, and retesting with a new cassette is recommended.

External Quality Control
Positive and Negative control swabs are supplied with each kit. A positive control swab is a non-infectious recombinant SARS-CoV-2 protein with buffer and stabilizer solution dried onto a swab. A negative control swab is a buffer and stabilizer solution dried onto a swab. These control swabs should be used to ensure that the test cassette and the test procedure is performed correctly. Follow the section “TEST PROCEDURE” steps 1-3 and 7-12 to perform the control test. Note: If the controls do not perform as expected, repeat the test or contact Customer Support before testing patient specimens.

RESULT INTERPRETATION
Repeat testing is needed to improve test accuracy. Please follow the table below when interpreting test results for COVID-19.

Status on first day of Testing	First Result Day 1	Second Result Day 3	Third Result Day 5	Interpretation
With Symptoms	Positive	N/A	N/A	Positive for COVID-19
	Negative	Positive	N/A	Positive for COVID-19
	Negative	Negative	N/A	Negative for COVID-19
Without Symptoms	Positive	N/A	N/A	Positive for COVID-19
	Negative	Positive	N/A	Positive for COVID-19
	Negative	Negative	Positive	Positive for COVID-19
	Negative	Negative	Negative	Negative for COVID-19

Results should be considered in the context of an individual’s recent exposures, history, and the presence of clinical signs and symptoms consistent with COVID-19.



COVID-19 Negative (-): If the Control (C) line is visible, but the Test (T) line is not visible, the test is negative. To increase the chance that the negative result for COVID-19 is accurate, you should:

- Test again in 48 hours if the individual has symptoms on the first day of testing.
- Test 2 more times at least 48 hours apart if the individual does not have symptoms on the first day of testing.

A negative test result indicates that the virus that causes COVID-19 was not detected in the sample. A negative result does not rule out COVID-19. There is a higher chance of false negative results with antigen tests compared to laboratory-based tests such as PCR tests. If the test is negative but COVID-19-like symptoms, e.g., fever, cough, and/or shortness of breath continue, follow-up testing for SARS-CoV-2 with a molecular test or testing for

another respiratory disease should be considered. If applicable, seek follow-up care with the primary health care provider.

All negative results should be treated as presumptive and confirmation with a molecular assay may be necessary if there is a high likelihood of SARS-CoV-2 infection, such as in an individual with close contact with COVID-19 or with suspected exposure to COVID-19 or in communities with a high prevalence of infection.

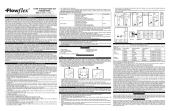
Negative results do not rule out SARS-CoV-2 infection and should not be used as the sole basis for treatment or patient management decisions, including infection control decisions. COVID-19 Positive (+): If the Control (C) line and the Test (T) line are visible, the test is positive. Any faint visible red or pink test (T) line with the control line (C) should be read as positive. Repeat testing does not need to be performed if patients have a positive result at any time.

A positive test result means that the virus that causes COVID-19 was detected in the sample, and it is very likely the individual has COVID-19 and is contagious. Please contact the patient's doctor/primary care physician (if applicable) and the local health authority immediately and instruct your patient to adhere to the local guidelines regarding self-isolation. There is a very small chance that this test can give a positive result that is incorrect (a false positive).

Positive results do not rule out bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause of the disease. Individuals who test positive with the Flowflex COVID-19 Antigen Rapid Test should self-isolate and seek follow-up care with their physician or healthcare provider as additional confirmatory testing with a molecular test for positive results may also be necessary, if there is a low likelihood of COVID-19, such as in individuals without known exposures to COVID-19 or residing in communities with a low prevalence of infection.

Invalid: If at 15 minutes, the control (C) line is not visible, the test is invalid. Re-test with a new swab and new test cassette. If the problem persists, call (800) 838-9502 for assistance.ACON Laboratories, Inc. San Diego, CA 92121, USA **aconlabs.com** Customer Support: 1-800-838-9502

Documents / Resources

	**Flowflex COVID-19 Antigen Rapid Test Package Insert** [pdf] Instructions COVID-19 Antigen Rapid Test Package Insert, Rapid Test Package Insert, COVID-19 Antigen P ackage Insert, Package Insert

References

- **Home - ACON LABS INC.**
- **Coronavirus Disease 2019 (COVID-19) | CDC**
- **Interim Guidelines for Clinical Specimens for COVID-19 | CDC**
- **Poison help**