COVID-19 Antigen Rapid Test Device
Product Insert
REF COV-19C25

INTENDED USE

The Rapid Response™ COVID-19 Antigen Rapid Test Device is an in vitro immunochromatographic assay for the direct and qualitative detection of SARS-CoV-2 viral nucleoprotein antigens from nasal and nasopharyngeal secretions from individuals suspected of COVID-19 within 6 days of symptom onset and from individuals without symptoms or other epidemiological reasons to suspect COVID-19 infection, when tested twice over two (or three) days with at least 24 hours (and no more than 36 hours) between tests. This test is authorized for use at the Point of Care i.e., in patient care setting.

Results are for the identification of SARS-CoV-2 viral nucleoprotein antigen. Antigens are generally detectable in nasopharyngeal and nasal secretions 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. 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. Laboratories are required to report all positive results to the appropriate public health authorities.

Negative results should be treated as presumptive, and 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. Negative results should be considered in the context of a patient's recent exposures, history, and the presence of clinical signs and symptoms consistent with COVID-19, and confirmed with a molecular assay, if necessary, for patient management.

The Rapid Response™ COVID-19 Antigen Rapid Test Device is intended for use by trained laboratory personnel or health care professionals.

PRINCIPLE

The Rapid Response™ COVID-19 Antigen Rapid Test Device detects SARS-CoV-2 viral antigens through visual interpretation of colour development. Anti-SARS-CoV-2 antibodies are immobilized on the test region of the nitrocellulose membrane. Anti-SARS-CoV-2 antibodies conjugated to coloured particles are immobilized on the conjugated pad. A sample is added to the extraction buffer which is optimized to release the SARS-CoV-2 antigens from specimen.
During testing, the extracted antigens bind to anti-SARS-CoV-2 antibodies conjugated to coloured particles. As the specimen migrates along the strip by capillary action and interacts with reagents on the membrane, the complex will be captured by the anti-SARS-CoV-2 antibodies at the test region. Excess coloured particles are captured at the internal control zone.
The presence of a coloured band in the test region indicates a positive result for the SARS-CoV-2 viral antigens, while its absence indicates a negative result. A coloured band at the control region serves as a procedural control, indicating that the proper volume of specimen has been added and membrane wicking is working.

MATERIALS

Materials Provided

- Individually packed test devices
- Extraction tube
- Individually packed swabs
- Package insert
- Extraction buffer
- Nozzle with filter
- Tube stand

Materials Required but Not provided

Clock, timer, or stopwatch

Materials provided upon request

COVID-19 Antigen Controls: Positive and Negative

PRECAUTIONS

- For *in vitro* Diagnostic Use Only.
- Read the Product Insert prior to use. Directions should be read and followed carefully.
- Do not use kit or components beyond the expiration date.
- The device contains material of animal origin and should be handled as a potential biohazard. Do not use if pouch is damaged or open.
- Test devices are packaged in foil pouches that exclude moisture during storage. Inspect each foil pouch before opening. Do not use devices that have holes in the foil or where the pouch has not been completely sealed. Erroneous result may occur if test reagents or components are improperly stored.
- Do not use the Extraction Buffer if it is discoloured or turbid. Discolouration or turbidity may be a sign of microbial contamination.
- All patient specimens should be handled and discarded as if they are biologically hazardous. All specimens must be mixed thoroughly before testing to ensure a representative sample prior to testing.
- Failure to bring specimens and reagents to room temperature before testing may decrease assay sensitivity. Inaccurate or inappropriate specimen collection, storage, and transport may yield false negative test results.
- Avoid skin contact with buffer.
- If infection with SARS-CoV-2 is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions and sent to state or local health departments for testing.
- Viral isolation in cell culture and initial characterization of viral agents recovered in cultures of SARS-CoV-2 specimens are NOT recommended, except in a BSL3 laboratory using BSL3 work practices.

STORAGE AND STABILITY

- Store the Rapid Response™ COVID-19 Antigen Rapid Test at 2~30°C when not in use.
- **DO NOT FREEZE.**
- Kit contents are stable until the expiration dates marked on their outer packaging and containers.

SPECIMEN COLLECTION AND STORAGE

Nasal swab (N swab):

1) Remove the swab from its packing.
2) Tilt patient's head back 70°. Insert the swab through the anterior nares in contact with nasal septum at least 0.5 inches inside the nostril until mild resistance is encountered at the middle turbinate.
3) Using a circular motion, the nasal orifice should be swabbed for a minimum of five seconds.
4) Compress the nostril with the fingers to trap the swab tip and rotate the tip for a minimum of five seconds.
5) Remove and repeat for the other nostril with the same swab.
6) Process the swab as soon as possible after collecting the specimen.

Nasopharyngeal swab (NP swab):

1) Remove the swab from its packing.
2) Gently insert the sterile swab into the nostril parallel to the palate, not upwards. The distance should be equivalent to that from the ear to the nostril of the patient, indicating contact with the nasopharynx, or until resistance is encountered. Gently rub and roll the swab, leave in place several seconds to saturate tip with secretions. Slowly remove the swab while rotating it.
3) Process the swab as soon as possible after collecting the specimen.

Note:

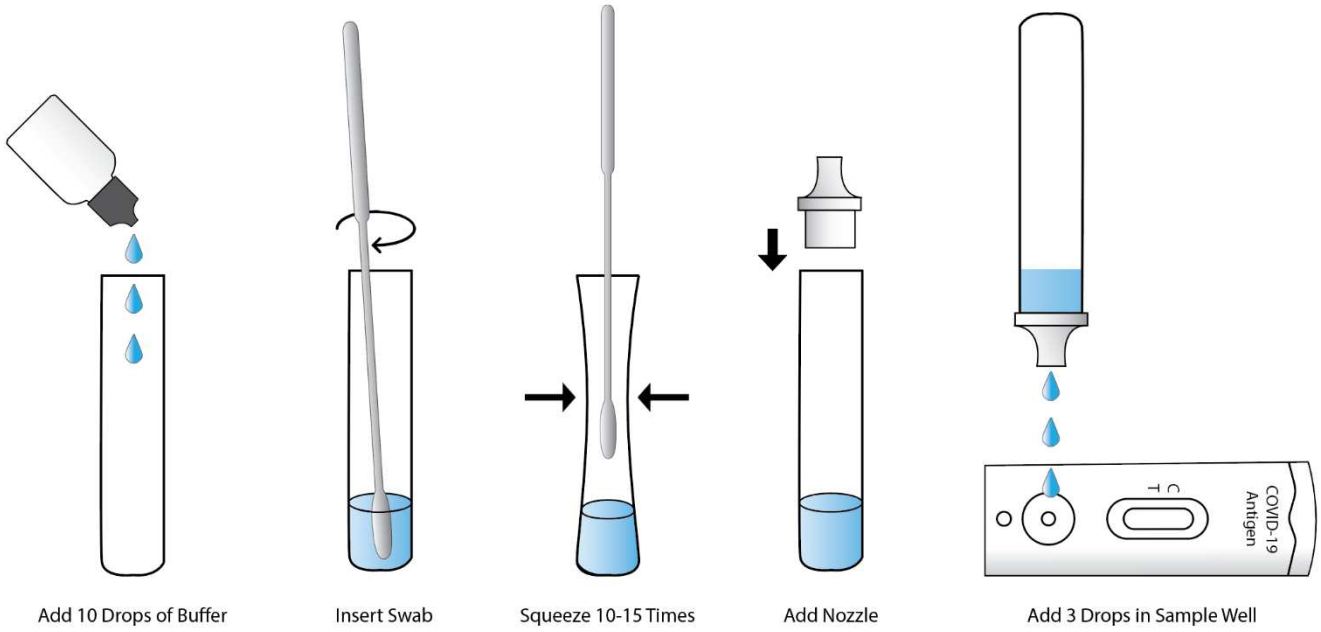
1. Use only synthetic fiber swabs with plastic shafts. Do not use calcium alginate swabs or swabs with wooden shafts, as they may contain substances that inactivate some viruses and inhibit further testing.
2. Swab specimens should be tested as soon as possible after collection. Use freshly collected specimens for best test performance.
3. If not tested immediately, swab specimens may be stored at 2-8°C for 21 hours after collection.
4. Do not use specimens that are obviously contaminate with blood, as it may interfere with the flow of

sample and with the interpretation of test results.

TEST PROCEDURE

Bring devices, reagents, and specimens and/or controls to room temperature (15~30°C) before use.

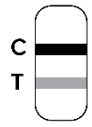
1. Label a clean extraction tube with patient or control identification and place it into the tube stand.



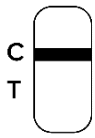
Add 10 Drops of Buffer | Insert Swab | Squeeze 10-15 Times | Add Nozzle | Add 3 Drops in Sample Well

2. Gently mix extraction buffer. Without touching the buffer bottle to the extraction tube, add 10 drops into the extraction tube.
3. Insert the swab with the collected specimen into the extraction tube. Swirl the swab, mixing well. Squeeze the swab 10-15 times by compressing the walls of the tube against the swab.
4. **Let the solution stand for 2 minutes.**
5. Remove the swab while pressing the swab head firmly against the inner wall of the tube to release as much liquid as possible. Dispose of the used swab in accordance with the appropriate biohazard waste disposal protocol.
6. For each specimen, open the foil pouch just before testing and remove the test device and put it on a clean, level surface. For best results, the assay should be performed within one hour. Label the test device with patient or control identification.
7. Attach nozzle to sample extraction tube. Invert the tube and add 3 drops of the extracted solution into the sample well of the test device by gently squeezing the tube.
8. Start the timer. Wait for coloured line(s) to appear. Read results at 15 minutes.

RESULT INTERPRETATION



POSITIVE: Two coloured bands appear on the membrane. One band appears in the control region (C) and another band appears in the test region (T).



NEGATIVE: Only one coloured band appears, in the control region (C). No apparent coloured band appears in the test region (T).

INVALID: Control band fails to appear. Results from any test which has not produced a control band at the specified read time must be discarded. Please review the procedure and repeat with a new test. If the problem persists, discontinue using the kit immediately and contact your local distributor.

NOTE:

1. The colour intensity in the test region (T) may vary depending on the concentration of analytes present in the specimen. Therefore, any shade of colour in the test region should be considered positive. Note that this is a qualitative test only and cannot determine the concentration of analytes in the specimen.
2. Insufficient specimen volume, incorrect operating procedure or expired tests are the most likely reasons for control band failure.

QUALITY CONTROL

Internal Procedural Controls

The Rapid Response™ COVID-19 Antigen Rapid Test Device has built-in (procedural) controls. Each test device has an internal standard zone to ensure proper sample flow. The user should confirm that the coloured band located at the "C" region is present before reading the result.

External Positive and Negative Controls

Good laboratory practice suggests that positive and negative external controls are run routinely to ensure that the test is correctly performed. External positive and negative controls should be used in accordance with applicable accrediting organizations. However, BTNX recommends that labs receiving this test execute a control test for each lot of kits that they receive.

COVID-19 Antigen Controls:

Positive and Negative controls are provided upon request with the kit. These controls should be used according to the nasopharyngeal swab test procedure provided in this package insert.

LIMITATIONS OF THE TEST

1. The Rapid Response™ COVID-19 Antigen Rapid Test Device is for professional *in vitro* diagnostic use and should only be used for the qualitative detection of SARS-CoV-2 antigen. The intensity of colour in a positive band should not be evaluated as "quantitative or semi-quantitative".
2. Both viable and nonviable SARS-CoV-2 viruses are detectable with the Rapid Response™ COVID-19 Antigen Rapid Test Device.
3. As with all diagnostic tests, a definitive clinical diagnosis should not be based on the results of a single test but should only be made by the physician after all clinical and laboratory findings have been evaluated.
4. Failure to follow the test procedure and result interpretation may adversely affect test performance and/or invalidate the test result.
5. Results obtained with this assay, particularly in the case of weak test lines that are difficult to interpret, should be used in conjunction with other clinical information available to the physician.
6. Negative results do not preclude SARS-CoV-2 infection and should be confirmed via molecular assay.
7. The performance of the device has not been assessed on specimens from individuals who have been infected with emerging variants of SARS-CoV-2 of public health concern.
8. The performance of this device has not been assessed in a population vaccinated against COVID-19.
9. This assay is not intended for home testing (or self-testing).
10. Clinical studies in asymptomatic patients undergoing serial testing are ongoing to establish the clinical performance.
11. The performance of this test has not yet been clinically validated for use in patients without signs and symptoms of respiratory infection or for serial screening applications, and performance may differ in these populations.

PERFORMANCE CHARACTERISTICS

Analytical Sensitivity (Limit of Detection):

The limit of detection was determined with a quantified SARS-CoV-2 virus and has been evaluated at $2x10^{2.4}$ $TCID_{50}$/mL.

Clinical Evaluation:
Clinical studies in asymptomatic patients undergoing serial testing are ongoing to establish the clinical performance. The performance of this test has not yet been clinically validated for use in patients without signs and symptoms of respiratory infection or for serial screening applications, and performance may differ in these populations.

Study 1: With Nasal Swab as a sample type:
Clinical performance characteristics for Rapid Response™ COVID-19 Antigen Rapid Test Device were evaluated in a multi-site prospective, single-blind, controlled clinical trial in the USA from October 2020 to December 2020. The study was performed by Point-of-Care operators with no laboratory experience. These clinical trials were aimed to evaluate the performance of the Rapid Response™ COVID-19 Antigen Rapid Test Device with a Nasal Swab by comparing with an FDA EUA approved RT-PCR comparator.
The performance of the Rapid Response™ COVID-19 Antigen Rapid Test Device was established with direct anterior nasal swabs collected from individual symptomatic patients (within 7 days from symptom onset) who were suspected of COVID-19. Two samples from each patient were collected – one for PCR and another for the Rapid Antigen test. 51 positive specimens and 128 negative specimens were confirmed by RT-PCR.

Table 1: Rapid Response™ COVID-19 Antigen Rapid Test Clinical Evaluation with Nasal Swabs:

		RT-PCR		Total
		Positive	Negative	
Rapid Response™ COVID-19 Antigen Rapid Test Device	Positive	46	0	46
	Negative	5	128	133
Total		51	128	179

Diagnostic Sensitivity: 90.2% (78.6% ~ 96.2%)*
Diagnostic Specificity: 100.0% (96.5% ~ 100.0%)*
Overall Agreement: 97.2% (93.2% ~ 98.9%)*
*95% Confidence Interval

Study 2:
Clinical trials for the Rapid Response™ COVID-19 Antigen Rapid Test Device were performed at two Point-of-care sites in the USA from August 2020 to October 2020. These clinical trials were aimed to evaluate the performance of the Rapid Response™ COVID-19 Antigen Rapid Test Device by comparing with an RT-PCR comparator.
The performance of the Rapid Response™ COVID-19 Antigen Rapid Test Device was established with 82 direct nasopharyngeal swabs collected and enrolled from individual symptomatic patients who were suspected of COVID-19. Samples were freshly collected from 2 sites where the operators were minimally trained. 46 positive specimens and 36 negative specimens were confirmed by RT-PCR.
The performance of the Rapid Response™ COVID-19 Antigen Rapid Test Device based on the results from these two sites is summarized below.

Table 2: Site 1 for Nasopharyngeal Swab Specimen vs. RT-PCR

		RT-PCR		**Total**
		Positive	Negative	
Rapid Response™ COVID-19 Antigen Rapid Test Device	Positive	23	0	23
	Negative	1	21	22
		24	21	45

Diagnostic Sensitivity: 95.8% (79.8% ~ 99.3%)*
Diagnostic Specificity: 100.0% (84.5% ~ 100.0%)*

Overall Agreement: 97.8% (88.4% ~ 99.6%)*
*95% Confidence Interval

Table 3: Site 2 for Nasopharyngeal Swab Specimen vs. RT-PCR

		RT-PCR		Total
		Positive	Negative	
Rapid Response™ COVID-19 Antigen Rapid Test Device	Positive	21	0	21
	Negative	1	15	16
		22	15	37

Diagnostic Sensitivity: 95.5% (78.2% ~ 99.2%)*
Diagnostic Specificity: 100.0% (79.6% ~ 100.0%)*
Overall Agreement: 97.3% (86.2% ~ 99.5%)*
*95% Confidence Interval

Table 4: Site 1 & 2 Combined for Nasopharyngeal Swab Specimen vs. RT-PCR

		RT-PCR		Total
		Positive	Negative	
Rapid Response™ COVID-19 Antigen Rapid Test Device	Positive	44	0	44
	Negative	2	36	38
		46	36	82

Diagnostic Sensitivity: 95.6 % (85.5% ~ 98.8%)*
Diagnostic Specificity: 100.0 % (90.4% ~ 100.0%)*
Overall Agreement: 97.6 % (91.5% ~ 99.3%)*
*95% Confidence Interval

Cross Reactivity:
Cross reactivity with the following organisms has been studied. Samples positive for the following organisms were found negative when tested with the Rapid Response™ COVID-19 Antigen Rapid Test Device.

HCoV-HKU1	Influenza A (H5N1)	Coxsackie virus A16
HCoV-OC43	Influenza A (H7N9)	Norovirus
HCoV-NL63	Influenza A (H7N7)	Mump virus
HCoV-229E	Influenza B Victoria lineage	*Legionella pneumophila*
Measles virus	Influenza B Yamagata lineage	*Mycoplasma pneumoniae*
Streptococcus pneumoniae	Respiratory syncytial virus	*Chlamydia pneumoniae*
Epstein-Barr virus	Adenovirus	*Streptococcus pyogenes*
Bordetella Para pertussis	Parainfluenza 1/2/3 virus	*Streptococcus agalactiae*
Influenza A (H1N1) pdm09	Human metapneumovirus	Group C *Streptococcus*
Influenza A (H3N2)	Rhinovirus	*Staphylococcus aureus*

Microbial Interference Study:
Potential microbial interference was evaluated to demonstrate that false negatives will not occur when SARS-CoV-2 is present in a specimen with other microorganisms. Low concentration of SARS-CoV-2 (3 X LOD) was spiked into the higher concentrations of interfering organism and it was found that there is no microbial interference for following organisms.

HCoV-HKU1	Influenza A (H5N1)	Coxsackie virus A16
HCoV-OC43	Influenza A (H7N9)	Haemophilus influenzae
HCoV-NL63	Influenza A (H7N7)	Candida albicans

HCoV-229E	Influenza B Victoria lineage	Mycobacterium tuberculosis
Measles virus	Influenza B Yamagata lineage	Norovirus
Streptococcus pneumoniae	Respiratory syncytial virus	Mump virus
Epstein-Barr virus	Adenovirus	Legionella pneumophila
Bordetella Para pertussis	Parainfluenza 1/2/3 virus	Mycoplasma pneumoniae
Influenza A (H1N1) pdm09	Human metapneumovirus	Chlamydia pneumoniae
Influenza A (H3N2)	Rhinovirus	Streptococcus pyogenes
Group C Streptococcus	Staphylococcus aureus	Streptococcus agalactiae
Pooled human nasal wash – representative of normal respiratory microbial flora		

Interfering Substances
The following substances, naturally present in respiratory specimens or that may be artificially introduced into the respiratory tract, were evaluated at the concentrations listed below. None of them were found to affect test performance of the Rapid Response™ COVID-19 Antigen Rapid Test Device.

Substance	**Concentration**	**Substance**	**Concentration**
3 OTC nasal sprays	10%	Guaiacol glyceryl ether	20 mg/ml
3 OTC mouthwashes	10%	Mucin	1%
3 OTC throat drops	10%	Mupirocin	250 µg/ml
4-acetamidophenol	10 mg/ml	Oxymetazoline	10 mg/ml
Acetylsalicylic acid	20 mg/ml	Phenylephrine	10 mg/ml
Albuterol	20 mg/ml	Phenylpropanolamine	20 mg/ml
Chlorpheniramine	5 mg/ml	Relenza ® (zanamivir)	20 mg/ml
Dexamethasone	5 mg/ml	Rimantadine	500 ng/ml
Dextromethorphan	10 mg/ml	Tamiflu ® (oseltamivir)	100 mg/ml
Diphenhydramine	5 mg/ml	Tobramycin	40 mg/ml
Doxylamine succinate	1 mg/ml	Triamcinolone	14 mg/ml
Flunisolide	3 mg/ml		

High Dose Hook Effect
No high dose hook effect was observed when tested with up to a concentration of 1 x $10^{6.4}$ $TCID_{50}$/mL of heat inactivated SARS-CoV-2 virus with the Rapid Response™ COVID-19 Rapid Test

GLOSSARY OF SYMBOLS

	Consult instructions for use		Test per Kit		Catalogue number
	Store between 2°C to 30°C		Use by date		Do Not Reuse
	In vitro diagnostic medical device		Lot Number		Authorized Representative

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EC REP

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