ACCESSBIO

CareStart™

# COVID-19 Antigen

*Rapid Diagnostic Test for the Detection of SARS-CoV-2 Antigen*

**Package Insert**

**(Instructions for Use)**

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**For use under the Emergency Use Authorization (EUA) only**
**For *in vitro* diagnostic use only**
**For prescription use only**

## Intended Use

The *CareStart*™ COVID-19 Antigen test is a lateral flow immunochromatographic assay intended for the qualitative detection of the nucleocapsid protein antigen from SARS-CoV-2 in nasopharyngeal swab specimens directly collected, or collected in BD universal transport media, from individuals suspected of COVID-19 by their healthcare provider within five days of symptom onset. 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 patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation.

Results are for the identification of the SARS-CoV-2 nucleocapsid protein antigen. The antigen is generally detectable in nasopharyngeal swab specimens during the acute phase of infection. Positive results indicate the presence of viral antigens, but the clinical correlation with patient history and other diagnostic information is necessary to determine infection status. Positive results do not rule out a bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause of disease. Laboratories within the United States and its territories are required to report all results to the appropriate public health authorities.

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 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.

The *CareStart*™ COVID-19 Antigen is intended for use by medical professionals or trained operators who are proficient in performing tests and trained clinical laboratory personnel or individuals trained in point of care settings. The *CareStart*™ COVID-19 Antigen is only for use under the Food and Drug Administration's Emergency Use Authorization.

## Summary and Explanation of the Test

Since the first outbreak reported in December 2019, SARS-CoV-2 has spread rapidly worldwide, and the disease it causes has been named "Coronavirus Disease 2019" (COVID-19). Due to its highly contagious nature and global health crises, SARS-CoV-2 has been designated as a pandemic by the World Health Organization (WHO). SARS-CoV-2 continues to have devastating

impacts on healthcare systems and the world economy including the U.S. To effectively end the SARS-CoV-2 pandemic, systematic screening and detection of both clinical and asymptomatic COVID-19 cases is critical. Particularly, the identification of subclinical or asymptomatic cases is important to reduce or stop the infection because these individuals may transmit the virus. As a point-of-care test with a 10 min testing time, *CareStart*™ COVID-19 Antigen test allows effective screening of COVID-19 infection on a large scale.

**Principles of the Test**

The *CareStart*™ COVID-19 Antigen test is a lateral flow immunochromatographic assay for the detection of extracted nucleocapsid protein antigens specific to SARS-CoV-2 in nasopharyngeal swab specimens either directly collected or collected in BD universal transport media from individuals who are suspected of COVID-19 by their healthcare provider within the first five days of symptom onset.

Nasopharyngeal swabs require a sample preparation step in which the sample is eluted into the extraction buffer solution. Extracted swab sample is added to the sample well of the test device to initiate the test. When the swab sample migrates in the test strip, SARS-CoV-2 viral antigens bind to anti-SARS-CoV-2 nucleocapsid protein antibodies conjugated to indicator and capture particles in the test strip forming an immune complex. The immune complex is then captured by the test line on the nitrocellulose membrane as it migrates through the strip.

Test results are interpreted at 10 minutes. The presence of two colored lines in the control line region “C” and test line region “T” indicates COVID-19 positive. The presence of one colored lines in the control line region “C” indicates COVID-19 negative. No appearance of a colored line in the control region “C” indicates an invalid test.

**Reagents and Materials Provided**

| Contents Name | Quantity (in a kit) | Description |
|---|---|---|
| Test device | 20 each | Foil pouched test device containing one test strip which is encased in plastic device cassette. |
| Extraction vial / cap | 20 vials and caps | The extraction vial contains 400 µl extraction buffer solution. |
| Nasopharyngeal swab | 20 each | swabs for nasopharyngeal specimen collection. |
| Positive control swab | 1 each | Recombinant SARS-CoV-2 nucleocapsid protein antigen is dried on the foam-tipped head. |
| Negative control swab | 1 each | Blank Universal Viral Transport media (BD UVT) is dried on the foam-tipped head. |
| Package insert | 1 each | Instructions for use |
| Quick Reference Instructions (QRI) | 1 each | Quick reference instructions |

The following materials are needed but not provided:

- Pair of gloves
- Timer
- Biohazard or sharps container
- Micropipette

## Warnings and Precautions

- For prescription and *in vitro* diagnostic use only.
- This test has not been FDA cleared or approved.
- This test has not been FDA cleared or approved; the test has been authorized by FDA under an Emergency Use Authorization (EUA) for use by laboratories certified under the CLIA 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 patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation.
- This test is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostic tests for 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 authorization is terminated or revoked sooner.
- This test has been authorized only for the detection of proteins from SARS-CoV-2, not for any other viruses or pathogens.
- As with all diagnostic tests, all results must be interpreted together with other clinical information available to the physician.
- Immediately use after opening the test device in the pouch.
- In order to obtain accurate results, the test must follow this package insert.
- Excess blood or mucus on the swab specimen may interfere with test performance and may yield a false-positive result. Avoid touching any bleeding areas of the nasopharynx when collecting specimens.
- Do not interpret the test result before 10 minutes and after 15 minutes starting the test.
- Inadequate or inappropriate sample collection, storage, and transport can result in incorrect results.If specimen storage is necessary, swabs can be placed into extraction buffer for up to four hours. Specimens should not be stored dry.
- Do not use if the test device package is damaged.
- Do not use the kit contents beyond the expiration date.
- Do not eat, drink, or smoke in the area where the specimens and kit contents are handled.
- Use appropriate precautions in the collection, handling, storage, and disposal of patient samples and used kit contents.
- Dispose of used contents as biohazardous wastes in accordance with federal, state, and local requirements.
- Nitrile or latex gloves should be worn when performing this test.
- If the extraction buffer contacts the skin or eye, flush with copious amounts of water.
- Handle all specimens as though they contain infectious agents.
- Observe established precautions against microbiological hazards throughout the procedure and follow the standard procedures for proper disposal of specimens.
- Reagents contain sodium azide, which is harmful if inhaled, swallowed, or exposed to skin. Contact with acids produces a very toxic gas. If there is contact with skin, wash immediately with plenty of water. Sodium azide may react with lead and copper plumbing to form highly explosive metal azides. On disposal, flush with a large volume of water to prevent azide build-up.
- Do not interchange kit contents from different lots.
- Do not re-use any contents in the kit as they are single-use only.
- For additional information on hazard symbols, safety, handling and disposal of the components within this kit, please refer to the Safety Data Sheet (SDS) located at accessbio.net.

**Storage and Stability**

- Store the test kit as packaged between 1 ~ 30°C.
- The reagents and materials in the *CareStart*™ COVID-19 Antigen are stable until the expiration date printed on the outer packaging. Do not use beyond the expiration date.
- The test device must remain in the sealed pouch until use.
- Do not freeze any contents of the kit.

**Quality Control**

**Internal Quality Control:** The *CareStart*™ COVID-19 Antigen contains a built-in internal procedural control that is included in the test device. A red-colored line appearing in the control region "C" is designed as an internal procedural control. The appearance of the procedural control line indicates that sufficient flow has occurred, and the functional integrity of the test device has been maintained. If the procedural control line does not develop in 10 minutes, the test result is considered invalid and retesting with a new device is recommended. If the internal procedural control line is still absent in the retest, please contact the Technical Support at +1-888-898-1270 (Available Hours: Mon. to Fri.: 8 a.m. – 5 p.m.) or TShelp@accessbio.net (24/7 available).

**External Control:** External control is used to demonstrate that the test device and test procedure perform properly. It is recommended that positive and negative external control swabs are run once with every new lot, shipment, and each new user. External positive and negative control swabs are provided in the kit. The external control should be tested using the nasopharyngeal swab test procedure provided in this package insert or the quick reference instruction card. If the external control results are invalid, please contact the Technical Support at +1-888-898-1270 (Available Hours: Mon. to Fri.: 8 a.m. – 5 p.m.) or TShelp@accessbio.net (24/7 available) before testing patient specimens.

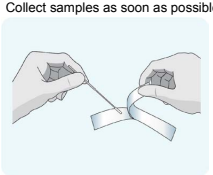
**Specimen Collection and Handling**

Acceptable specimen type for testing with the *CareStart*™ COVID-19 Antigen is a direct nasopharyngeal swab specimen or a swab in BD universal transport media. It is essential that correct specimen collection and preparation methods be followed. Inadequate specimen collection, improper specimen handling and/or transport may yield false results; therefore, specimen collection requires specific training and guidance due to the importance of specimen quality to obtain accurate test results. Specimens may be frozen at -80C and used up to 5 days and are stable for 4 hours in extraction buffer. Refer to the CDC Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens from Persons for Coronavirus Disease 2019 (COVID-19) https://www.cdc.gov/coronavirus/2019-nCoV/lab/guidelines-clinical-specimens.html

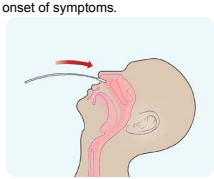
## Nasopharyngeal Swab Sample Collection Procedure

**Procedural Notes**

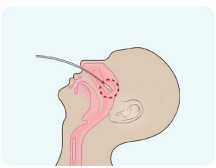
- Process the test sample immediately after collection.
- Use only provided or recommended nasopharyngeal swab for specimen collection.
- Collect the specimen wearing safety gloves to avoid contamination.
- Do not touch the tip (specimen collection area) of the swab.
- Collect samples as soon as possible after the onset of symptoms.



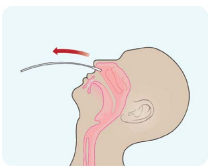
1. Remove a nasopharyngeal swab from the pouch.



2. Place the swab into one of the patient's nostrils until it reaches the posterior nasopharynx; keep insert until resistance is encountered or the distance is equivalent to that from the ear to the nostril of the patient.



3. Slowly rotate 3-5 times the swab over the surface of the posterior nasopharynx.



4. Slowly remove the swab from the nostril while rotating it.

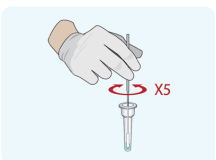
## Test Procedures

### Procedural Notes

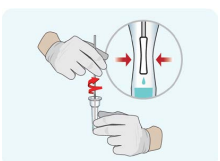
- Allow test devices, reagents, specimens, and/or controls to equilibrate to room temperature (15~30˚C) prior to testing.
- Remove the *CareStart*™ COVID-19 Antigen test device and extraction vial from its foil pouch immediately before testing.
- The *CareStart*™ COVID-19 Antigen kit IS INTENDED to be used only with a direct nasopharyngeal swab specimen or a swab in BD universal transport media.
- The *CareStart*™ COVID-19 Antigen kit IS NOT INTENDED for testing other liquid samples such as nasal wash or aspirate samples as results can be compromised by over dilution.

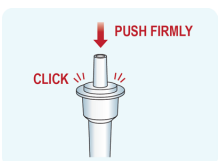
**Direct Nasopharyngeal Swab Test Procedure**


1. Peel off aluminum foil seal from the top of the extraction vial containing the extraction buffer




2. Place the swab into the extraction vial. Rotate the swab vigorously at least 5 times.



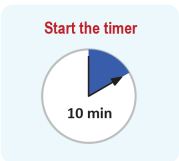


3. Remove the swab by rotating against the extraction vial while squeezing the sides of the vial to release the liquid from the swab. Properly discard the swab.


4. Close the vial with the provided cap and push firmly onto the vial.


5. Mix thoroughly by flicking the bottom of the tube.

6. Invert the extraction vial and hold the sample vertically above the sample well. Squeeze the vial gently. Allow three (3) drops of sample to fall into the sample well. 2 drops of the sample are required minimum volume to initiate the test run and invalid results will be obtained if 1 drop of sample is added to the cassette. Leakage of the sample is possible when 6 drops or more of the sample are added.




7. Read and interpret the test result at 10 minutes. The test result should not be read and interpreted after 15 minutes.

**Nasopharyngeal Swab in Viral Transport Media (VTM) Test Procedure**

**NOTE:** Only BD universal transport media have been validated with the assay.

1. Mix the specimen stored in VTM by vortexing.
2. Collect 400 µl of swab specimen with a calibrated micropipette from the VTM tube.

**NOTE:** Avoid mucoid substances when collecting from the VTM tube.

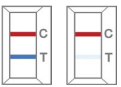
3. Add all 400 µl of collected swab specimen from the micropipette into the extraction vial after peel off the aluminum foil seal.
4. Follow Steps 4 – 7 of the **Direct Nasopharyngeal Swab Test Procedure** above.

**Interpretation of Results**

**NOTE:** The test results should be read and interpreted at 10 minutes after the sample application and the reading and interpretation of the results should not exceed 15 minutes. The test results should not be interpreted using any instruments.

**Positive:** two distinct colored lines appear.

One red-colored line next to "C" and one blue-colored line next to "T" indicates COVID-19 positive result.



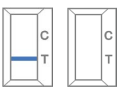

**NOTE:** The color intensity in the test region will vary depending on the amount of SARS-CoV-2 nucleocapsid protein antigen present in the sample. Any faint colored line(s) in the test region(s) should be considered as positive.

**Negative:**

One red-colored line only next to "C" indicates a negative result.


**Invalid:**

If the red-colored line in the control region "C" is not visible, the result is invalid. Re-run the test one time using the remaining specimen in the extraction vial if an invalid result is obtained during initial testing.




**Limitations**

1. False negative results may occur in patients who have indicated or whose clinical status or history would indicate they are currently taking high doses of biotin (> 10 mg per day). Biotin levels of 2.5 µg/mL have been demonstrated to result in false negative test results.
2. Negative results, should be treated as presumptive and confirmation with a molecular assay, if necessary for patient management, may be performed.

3. Failure to follow the instructions for use may adversely affect test performance and/or invalidate the test result.
4. If the differentiation of specific SARS viruses and strains is needed, additional testing, in consultation with state or local public health departments, is required.
5. Clinical performance using VTM was established on frozen specimens and performance may be different with fresh clinical specimens.
6. Extracted specimens may be frozen at -80°C and used up to 5 days after freezing and it are stable for 4 hours in extraction buffer at room temperature.
7. Results from antigen testing should not be used as the sole basis to diagnose or exclude SARS-CoV-2 infection or to determine infection status.
8. This test will indicate the presence of SARS-CoV-2 nucleocapsid protein antigen in the specimen from both viable and non-viable SARS-CoV-2 virus. 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.
9. The detection of SARS-CoV-2 nucleocapsid antigen is dependent upon proper specimen collection, handling, storage, and preparation. Failure to observe proper procedures in any one of these steps can lead to incorrect results.
10. Results from the device should be correlated with the clinical history, epidemiological data and other data available to the clinician evaluating the patient.
11. This device has been evaluated for use with human specimen material only.
12. False-negative results may occur if the concentration of the target antigen in the clinical specimen is below the detection limits of the device.
13. This device is a qualitative test and does not provide information on the viral concentration present in the specimen.
14. This test cannot rule out diseases caused by other bacterial or viral pathogens.
15. The prevalence of infection will affect the test's predictive values.
16. Positive and negative predictive values are highly dependent on prevalence. False-negative test results are more likely during peak activity when the prevalence of the disease is high. False-positive test results are more likely during the periods of low SARS-CoV-2 activity when prevalence is moderate to low.

**CONDITIONS of AUTHORIZATION for LABORATORY**

The *CareStart*™ COVID-19 Antigen test Letter of Authorization, along with the authorized Fact Sheet for Healthcare Providers, the authorized Fact Sheet for Patients, and authorized labeling are available on the FDA website: https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas.

However, to assist clinical laboratories using the *CareStart*™ COVID-19 Antigen test ("your product" in the conditions below), the relevant Conditions of Authorization are listed below:

A. Authorized laboratories[1] using your product will include with test result reports, all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.

B. Authorized laboratories using your product will use your product as outlined in the authorized labeling. Deviations from the authorized procedures, including the authorized instruments, authorized extraction methods, authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and authorized materials required to use your product are not permitted.

C. Authorized laboratories that receive your product will notify the relevant public health authorities of their intent to run your product prior to initiating testing.

D. Authorized laboratories using your product will have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.

E. Authorized laboratories will collect information on the performance of your product and report to DMD/OHT7-OIR/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov) and ACCESS BIO, INC. (Technical Support at +1-888-898-1270 or TShelp@accessbio.net) any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of your product of which they become aware.

F. All operators using your product must be appropriately trained in performing and interpreting the results of your product, use appropriate personal protective equipment when handling this kit, and use your product in accordance with the authorized labeling.

G. ACCESS BIO, INC., authorized distributors, and authorized laboratories using your product will ensure that any records associated with this EUA are maintained until otherwise notified by FDA. Such records will be made available to FDA for inspection upon request.

[1] The letter of authorization refers 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 patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation" as "authorized laboratories."

**Performance Characteristics**

**Clinical Performance**

To initially evaluate the clinical performance of the *CareStart*™ COVID-19 Antigen test, a total of 126 blinded frozen swab samples, including 106 retrospective clinical specimens and 20 contrived specimens, were tested in one (1) CLIA waived investigational site by five (5) minimally trained operators in the U.S during the 2020 COVID-19 season.

A total of 126 frozen samples consisting of 43 positive nasopharyngeal (NP) swabs, 63 negative NP swab specimens, and 20 contrived near the cut-off samples (10 positives and 10 negatives). NP swab specimens collected from the patients with COVID-19 like symptoms in the U.S during the 2020 COVID-19 season and stored in BD universal transport media tube were provided by multiple vendors in the U.S. All the NP swab specimens were confirmed as positive or negative and validated with Ct value by the FDA EUA RT-PCR as a comparator method prior to the study. The specimens were aliquoted, randomized, and blinded into sample panels that was tested by each operator, using the instructions provided by the Quick Reference Instructions (QRI).

In addition to the clinical population, a total of 20 contrived near the cut-off samples, 10 low positives near the Limit of Detection (LoD) (2x LoD), and 10 negatives (zero analytes) samples, were prepared using the inactivated SARS-CoV-2 strain spiked into the simulated nasal swab matrix, BD universal transport media. The heat-inactivated SARS-CoV-2 isolate USA-WA1/2020 was used to prepare the positive samples. The contrived near the cut-off samples were added to the clinical population and tested at the same study site by the same operators. All the study samples were randomized and assigned with unique study subject ID by the sponsor prior to testing at the study site. The expected results of the samples were completely blinded to the operators. All the samples were tested by five (5) operators according to the Quick Reference Instructions only.

A total of 126 frozen swab samples were considered evaluable in this study. The performance of the *CareStart*™ COVID-19 Antigen as compared to the RT-PCR comparator method are presented in the table below:

***CareStart*™ COVID-19 Antigen (retrospective samples) Performance against the Comparator Method**

| *CareStart*™ COVID-19 Antigen | Comparator | | |
|---|---|---|---|
| | Positive | Negative | Total |
| Positive | 38 | 0 | 38 |
| Negative | 5 | 63 | 68 |
| Total | 43 | 63 | 106 |
| Positive Percent Agreement (PPA) | 88.37% (95% CI: 75.52% – 94.93%) | | |
| Negative Percent Agreement (NPA) | 100% (95% CI: 94.25% – 100%) | | |

***Patient Demographics***

| Age Group | *CareStart*™ COVID-19 Antigen | | |
|---|---|---|---|
| | Total # | Positive | Prevalence |
| ≤5 Years of Age | 1 | 1 | 100% |
| 6-21 Years of Age | 9 | 6 | 66.67% |
| 22-59 Years of Age | 58 | 25 | 43.10% |
| ≥60 Years of Age | 37 | 10 | 27.03% |
| Unknown | 1 | 1 | 100% |

***CareStart™ COVID-19 Antigen (near the cut-off samples) Performance***

| Sample category | Overall % Agreement (result count) |
|---|---|
| True negative (zero analytes) | 100.0% (10/10) |
| Low positive (2x LoD) | 100.0% (10/10) |

**Prospective Clinical Study**

The clinical performance characteristics of *CareStart*™ COVID-19 Antigen test is currently being evaluated in a multi-site prospective study in the U.S in which NP swabs from patients are sequentially enrolled and tested. A total of five (5) investigational sites throughout the U.S are participating in the study. Testing is performed by operators with no laboratory experience and who are representative of the intended users. Operators are only using the QRI for the test without any training provided. The patients presenting the COVID-19 like symptoms within five (5) days of symptom onset at the study sites are enrolled. An FDA EUA RT-PCR assay for the detection of SARS-CoV-2 from a NP or nasal swab is utilized as the comparator method for the study. The initial six (6) positive patient results are presented as below.

***CareStart™ COVID-19 Antigen Initial Performance against the Comparator Method***

| *CareStart*™ COVID-19 Antigen | Comparator | | |
|---|---|---|---|
| | Positive | Negative | Total |
| Positive | 5 | 0 | 5 |
| Negative | 1 | 17 | 18 |
| Total | 6 | 17 | 23 |
| Positive Percent Agreement (PPA) | 83.33% (95% CI: 43.65% – 97.00%) | | |
| Negative Percent Agreement (NPA) | 100% (95% CI: 81.57% – 100%) | | |

***Patient Demographics***

| Age Group | *CareStart*™ COVID-19 Antigen | | |
|---|---|---|---|
| | Total # | Positive | Prevalence |
| ≤5 Years of Age | 0 | 0 | N/A |
| 6-21 Years of Age | 6 | 3 | 50.00% |

| | | | |
|---|---|---|---|
| 22-59 Years of Age | 12 | 2 | 16.67% |
| ≥60 Years of Age | 5 | 1 | 20.00% |

**Analytical Sensitivity: Limit of Detection (LoD)**

The LoD for direct swab was established using heat-inactivated SARS-CoV-2 isolate USA-WA1/2020 (NR-52286). The strain was spiked into the pooled human nasal swab matrix obtained from multiple healthy volunteers eluted in VTM and confirmed as SARS-CoV-2 negative by RT-PCR to prepare positive samples. The estimated LoD found from the initial two-fold serial dilution test was confirmed by testing 20 replicates. The confirmed LoD for direct swab was $8 \times 10^2$ $TCID_{50}$/ml.

The LoD for swab in VTM (BD universal transport media) was established using heat-inactivated SARS-CoV-2 isolate USA-WA1/2020 (NR-52286). The two-fold serial diluted strain stocks were spiked into each of 3 ml human nasal swab matrix obtained from multiple healthy volunteers eluted in 3 ml VTM tube. The estimated LoD found from the initial two-fold serial dilution test was confirmed by testing 20 replicates. The confirmed LoD for swab in VTM was $6.4 \times 10^3$ $TCID_{50}$/ml.

**Analytical Specificity: Cross Reactivity (Exclusivity) and Microbial Interference**

The potential cross-reactivity (exclusivity) of a panel of common organisms was evaluated with SARS-CoV-2 negative samples using the *CareStart*™ COVID-19 Antigen test. Potential microbial interference was evaluated with samples containing heat-inactivated SARS-CoV-2 isolate USA-WA1/2020 at approximately 3x LoD. A total of 8 bacteria were tested at a target concentration of approximately $10^7$ cfu/ml with the exception of *Mycoplasma pneumoniae*, which was tested at a final concentration of $1.5 \times 10^3$ cfu/ml. The 18 viruses were tested at concentrations between $10^{5.2}$ and $10^{7.9}$ $TCID_{50}$/ml. All negative samples gave negative results at the concentrations of the potentially cross-reactive common organisms tested showing no cross-reactivity with *CareStart*™ COVID-19 Antigen assay. All samples with SARS-CoV-2 strain tested positive showing no microbial interference at the concentrations of the potentially interfering common organisms tested.

| Potential Cross-Reactant | | |
|---|---|---|
| Adenovirus 1 | MERS-Coronavirus, Irradiated Lysate | *Bodetella pertussis* |
| Adenovirus 7 | Parainfluenza virus type 1 | *Candida albicans* |
| Enterovirus 71, Tainan/4643/1998 | Parainfluenza virus type 2 | *Chlamydophila pneumoniae* |
| Human coronavirus (OC43) | Parainfluenza virus type 3 | *Haemophilus influenzae* |
| Human coronavirus (229E) | Parainfluenza virus type 4 | *Legionella pneumophila* |
| Human coronavirus (NL63) | Respiratory syncytial virus Type B | *Mycoplasma pneumoniae* |
| Human metapneumovirus (hMPV) | Rhinovirus | *Staphylococcus aureus* |
| Influenza A/Michigan/45/2015 | SARS-Coronavirus | *Staphylococcus epidermidis* |
| Influenza B/Wisconsin/01/2010 | Pooled human nasal wash | *Streptococcus pneumoniae* |

| Potential Cross-Reactant |
|---|
| *Streptococcus pyogenes, Group A* |

To estimate the likelihood of cross-reactivity with SARS-CoV-2 of organisms that were not available for wet testing, *in silico* analysis using the Basic Local Alignment Search Tool (BLAST) managed by the National Center for Biotechnology Information (NCBI) was used to assess the degree of protein sequence homology.

https://blast.ncbi.nlm.nih.gov/Blast.cgi?PAGE=Proteins&PROGRAM=blastp&BLAST_PROGRAMS=blastp&PAGE_TYPE=BlastSearch&BLAST_SPEC=blast2seq&DATABASE=n/a&QUERY=&SUBJECTS=

- The homology between SARS-CoV-2 nucleocapsid protein and human coronavirus HKU1 nucleocapsid protein is relatively low, at 36.7% across 86.4% of sequences, but cross-reactivity cannot be ruled out.
- The homology between SARS-CoV-2 nucleocapsid protein and Mycobacterium tuberculosis total protein (3,991 proteins) is relatively low, homology-based cross-reactivity can be ruled out.
- The homology between SARS-CoV-2 nucleocapsid protein and Pneumocystis jirovecii total protein (3,745 proteins) is relatively low, homology-based cross-reactivity can be ruled out.
- The homology between SARS-CoV-2 nucleocapsid protein and human coronavirus 229E nucleocapsid protein is relatively low, at 28.8% across 72.1% of sequences, but cross-reactivity cannot be ruled out. However, a result of the cross-reactivity wet study showed that CareStart™ COVID-19 Antigen had no cross-reactivity against human coronavirus 229E.
- No homologous protein was detected as a result of in silico assay with all the proteins (686 proteins) of Mycoplasma pneumoniae and the nucleocapsid protein (NP) of SARS-CoV-2. So, cross-reactivity of CareStart™ COVID-19 Antigen against Mycoplasma pneumoniae can be ruled out.

**Endogenous Interfering Substances Effect**

To assess substances with the potential to interfere with the performance of the *CareStart*™ COVID-19 Antigen, positive and negative samples were tested with the addition of potentially interfering substances. The SARS-CoV-2 target concentration in the positive samples was approximately 2x LoD. All samples tested produced expected results, demonstrating that the *CareStart*™ COVID-19 Antigen test performance was not affected by any of the 30 potentially interfering substances listed in the table below at the concentrations tested.

| Potential Interfering Substances | Concentration | Potential Interfering Substances | Concentration |
|---|---|---|---|
| Acetaminophen | 10 mg/ml | Mometasone | 1 mg/ml |
| Acetyl salicylic acid | 15 mg/ml | Mucin | 2% |
| Beclomethasone | 0.5 mg/ml | Mupirocin | 1 mg/ml |

| Potential Interfering Substances | Concentration | Potential Interfering Substances | Concentration |
|---|---|---|---|
| Benzocaine | 5 mg/ml | OTC Throat drop (Halls) | 15% |
| Budesonide | 2 mg/ml | OTC Throat drop (Ricola) | 15% |
| Chlorpheniramine maleate | 5 mg/ml | OTC Nasal spray (Afrin) | 15% |
| Dexamethasone | 1 mg/ml | OTC Nasal spray (VicksSinex) | 15% |
| Dextromethorphan HBr | 2 mg/ml | OTC Nasal spray (Zicam) | 15% |
| Diphenhydramine HCl | 5 mg/ml | Oxymetazoline HCl | 10 mg/ml |
| Ephedrine HCl | 10 mg/ml | Phenylephrine HCl | 5 mg/ml |
| Flunisolide | 5 mg/ml | Phenylpropanolamine | 5 mg/ml |
| Fluticasone | 1 mg/ml | Tobramycin | 1 mg/ml |
| Guaiacol Glyceryl Ether | 20 mg/ml | Triamcinolone | 1 mg/ml |
| Histamine Dihydrochloride | 10 mg/ml | Whole Blood | 4% |
| Menthol | 10 mg/ml | Zanamivir | 1 mg/ml |

The interfering effects of biotin concentrations ranging between 625 ng/mL and 10 µg/mL were tested in a separate study. Biotin concentrations up to 1.25 µg/ml did not lead to false results. Biotin concentrations ≥2.5 µg/ml can cause false-negative COVID-19 results with the *CareStart*™ COVID-19 Antigen.

**High-dose Hook Effect**

The *CareStart*™ COVID-19 Antigen was tested up to $10^5$ $TCID_{50}$/ml of heat-inactivated SARS-CoV-2 strain and no high-dose hook effect was observed.

**Point of Care Use**

The *CareStart*™ COVID-19 Antigen was demonstrated at near patient or Point of Care (POC) testing that non-laboratory personnel can perform the test accurately in the intended use environment. In addition, the robust use of the *CareStart*™ COVID-19 Antigen for near patient or Point of Care (POC) testing was demonstrated by thirteen (13) Flex studies.

**Technical Support**

For questions, or to report a problem, please call Technical Support at +1-888-898-1270 (Available Hours: Mon. to Fri.: 8 a.m. – 5 p.m.) or TShelp@accessbio.net (24/7 available).

Test system problems may also be reported to the FDA using the MedWatch reporting system (phone: 1-800 FDA-1088; fax: 1-800 FDA-1078: or http://www.fda.gov/medwatch).

## Description of Symbols

| Symbol | Descriptions |
|---|---|
| IVD | *In vitro* diagnostic medical device<br>Indicates a medical device that is intended to be used as an *in vitro* diagnostic medical device. |
| | Consult instructions for use<br>Indicates the need for the user to consult the instructions for use. |
| | Manufacturer<br>Indicates the medical device manufacturer. |
| LOT | Batch code<br>Indicates the manufacturer's batch code so that the batch or lot can be identified. |
| | Do not re-use<br>Indicates a medical device that is intended for one use, or uses on a single patient during a single procedure. |
| | Use by date<br>Indicates the date after which the medical device is not to be used. |
| CONTROL + | Positive control<br>Indicates a control material that is intended to verify the results in the expected positive range. |
| CONTROL − | Negative control<br>Indicates a control material that is intended to verify the results in the expected negative range. |

| Symbol | Descriptions |
|---|---|
| REF | Catalog number<br>Indicates the manufacturer's catalog number so that the medical device can be identified. |
| | Caution<br>Indicates the need for the user to consult the instructions for use for important cautionary information such as warnings and precautions that cannot, for a variety of reasons, be presented on the medical device itself. |
| | Date of manufacture<br>Indicates the date when the medical device was manufactured. |
| | Temperature limit<br>Indicates the temperature limits to which the medical device can be safely exposed. |
| | Do not use if the package is damaged<br>Indicates a medical device that should not be used if the package has been damaged or opened. |
| Σ | Contains sufficient for <n> tests<br>Indicates the total number of IVD tests that can be performed with the IVD. |
| ℞ | Prescription-only |

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**Quick Reference Instructions for *CareStart*™ COVID-19 Antigen** | **Rapid Diagnostic Test for Detection of SARS-CoV-2 Antigen**

## For Emergency Use Authorization (EUA) Only

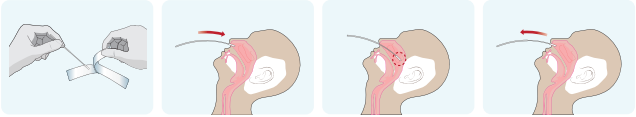
Rx Only IVD 2°C - 30°C

The *CareStart*™ COVID-19 Antigen test is a lateral flow immunochromatographic assay intended for the qualitative detection of the nucleocapsid protein antigen from SARS-CoV-2 in nasopharyngeal swab specimens directly collected from individuals who are suspected of COVID-19 by their healthcare provider within five days of symptom onset.

**IMPORTANT!**

- Refer to the Package Insert for Warnings and Precautions, Specimen Collection Procedures, Storage and Handling Conditions, and Quality Control Recommendations.
- Warning and Precautions - All kit components can be discarded as Biohazard waste according to local guidelines. Refer to the product safety data sheet for risk and safety phrases and disposal information.
- Biotin Interference: False negative results may occur in patients who have indicated or whose clinical status or history would indicate they are currently taking high doses of biotin (> 10 mg per day). Biotin levels of 2.5 µg/mL have been demonstrated to result in false negative test results.
- The extracted sample must be used within 4 hours of preparation when stored at room temperature.
- Refer to the CDC Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens from Persons for Coronavirus Disease 2019 (COVID-19): https://www.cdc.gov/coronavirus/2019-nCoV/lab/guidelines-clinical-specimens.html

## SPECIMEN COLLECTION AND HANDLING



1 Remove a nasopharyngeal swab from the pouch.

2 Place the swab into one of patient's nostrils until it reaches the posterior nasopharynx; keep insert until resistance is equivalent to that from the ear to the nostril of the patient.

3 Slowly rotate 3-5 times the swab over the surface of the posterior nasopharynx.

4 Slowly remove the swab from the nostril while rotating it.

In the USA: This test has not been FDA cleared or approved; this test has been authorized by FDA under an EUA for use by authorized laboratories; use by laboratories certified under the CLIA, 42 U.S.C. §263a, that meet requirements to perform moderate, high or waived complexity tests. This test is authorized for use at the Point of Care (POC), i.e., in patient care settings operating under a CLIA Certificate of the Waiver, Certificate of Compliance, or Certificate of Accreditation. This test has been authorized only for the detection of proteins from SARS-CoV-2, not for any other viruses or pathogens. In the USA - this test is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of the virus that causes 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 authorization is terminated or revoked sooner.

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REF RCHM-02071

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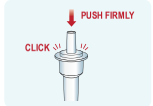
**Quick Reference Instructions for *CareStart*™ COVID-19 Antigen** | **Rapid Diagnostic Test for Detection of SARS-CoV-2 Antigen**

## TEST PROCEDURES


1 Peel off aluminum foil seal from the top of the extraction vial containing the extraction buffer.


2 Place the swab into the extraction vial. Rotate the swab vigorously at least 5 times.

3 Remove the swab by rotating against the extraction vial while squeezing the sides of the vial to release the liquid from the swab. Properly discard the swab.




4 Close the vial by pushing the cap firmly onto the vial.


5 Mix thoroughly by flicking the bottom of the tube.


6 Invert the extraction vial and hold the sample vertically above the sample well. Squeeze the vial gently. Allow three (3) drops of sample to fall into the sample well.

**NOTE** Refer to the Package Insert for the cautions.


### Result Interpretation

**Positive**


SARS-CoV-2 antigen present, does not rule out co-infection with other pathogens. The color intensity in the test region will vary depending on the amount of SARS-CoV-2 antigen present in the sample. Any faint colored line(s) in the test region(s) should be considered as positive.

**Negative**


Negative results are presumptive. Negative test results do not preclude infection and should not be used as the sole basis for treatment or other patient management decisions, including infection control decisions, particularly in the presence of clinical signs and symptoms consistent with COVID-19. If COVID-19 is still suspected based on exposure history, it is recommended that these results be confirmed by a molecular testing method, if necessary for patient management.

**Invalid**


If the red-colored line in the control region "C" is not visible, the result is invalid. Re-run the test one time using the remaining specimen in the extraction vial if an invalid result is obtained during initial testing.

### External Control Swab Test

It is recommended that positive and negative external control swabs are run once with every new lot, shipment, and each new user. External positive and negative control swabs are provided in the kit. The external control should be tested using the nasopharyngeal swab test procedure provided in this package insert or the quick reference instruction card.

**Access Bio, Inc.**