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DEPARTMENT OF PUBLIC SAFETY
MAINE EMERGENCY MEDICAL SERVICES
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OPERATIONAL BULLETIN

Bulletin #	Title		Date Issued
#2021-10-20-01	Information Regarding the Use of Access Bio, Inc. CareStart COVID-19 Antigen Tests		October 20, 2021
Superseded	**Released By:**	**Source:**	**Page(s)**
N/A	Maine EMS	Maine EMS, Maine CDC	1 and Attachments
Approved By:	J. Sam Hurley, MPH, EMPS, NRP (Maine EMS Director)		

It has come to our attention that the Maine Department of Health and Human Services is having difficulty obtaining BinaxNOW testing kits due to a national shortage. As such, they have procured Access Bio, Inc. CareStart COVID-19 Antigen tests to supplement their BinaxNOW inventory. These tests function similarly, in that they are a lateral flow rapid antigen test. They can be performed by using both anterior nasal and nasopharyngeal swabbing; however, unless otherwise trained, all persons should utilize anterior nasal swabbing.

In order for Maine EMS entities to use this test, the individual completing the test MUST have completed the Access Bio CareStart Instructional Video (2 minutes and 41 seconds) that can be found online at https://www.youtube.com/watch?v=Vh3ejrlo9vU (QR code below links to the video). It is important that persons administering the test appropriately document which test that was used in the online reporting tool by selecting CareStart rather than BinaxNOW. All negative and positive results MUST be reported to Maine CDC using the RedCap Tool (see the Maine EMS Playbook for the link). The product inserts can be found as attachments to this bulletin.

Despite this being a different test, it does not change Maine EMS's current guidance as defined in the playbook and other rules about the utilization of rapid antigen testing. Agencies may request additional tests, including the Access Bio CareStart devices, by completing the Maine DHHS Online Request form.

Don't hesitate to reach out to Maine EMS if you have any additional questions by emailing maine.ems@maine.gov or calling (207) 626-3860.

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With offices located at the Central Maine Commerce Center, 45 Commerce Drive, Suite 1, Augusta, ME 04330

CareStart™

COVID-19 Antigen

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

REF **RCHM-02071**

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

Package Insert
(Instructions for Use)

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 or anterior nasal swab specimens directly collected from individuals who are either suspected of COVID-19 by their healthcare provider within first five days of symptom onset, or from individuals without symptoms or other epidemiological reasons to suspect COVID-19 when tested twice over two or three days with at least 24 hours and no more than 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 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 or anterior nasal 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 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.

For serial testing programs, additional confirmatory testing with a molecular test for negative results may be necessary, if there is a high likelihood of SARS-CoV-2 infection, such as an individual with a close contact with COVID-19 or with suspected exposure to COVID-19 or in communities with high prevalence of infection. Additional confirmatory testing with a molecular test for positive results may also be necessary, if there is a low likelihood of SARS-CoV-2 infection, such as in individuals without known exposures to SARS-CoV-2 or residing in communities with low prevalence of infection.

The *CareStart*™ COVID-19 Antigen is intended for use in point of care settings and operated by healthcare professionals or trained users specifically instructed in the use of the *CareStart*™ COVID-19 Antigen and proper infection control procedures. 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.

The *CareStart*™ COVID-19 Antigen is a rapid (approximately 10 minutes) chromatographic immunoassay for the direct detection of the presence or absence of SARS-CoV-2 antigens in the respiratory specimens taken from patients with signs and symptoms who are suspected of COVID-19, or taken from asymptomatic individuals being tested serially, as described in the authorized intended use. The test is intended to be interpreted visually in both laboratory and near patient testing environments without an instrument.

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 or anterior nasal swab specimens directly collected from individuals who are suspected of COVID-19 by their healthcare provider within the first five days of symptom onset, or who are asymptomatic and undergoing serial testing, as described in the intended use.

Nasopharyngeal and anterior nasal 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 line 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 extraction buffer solution.
Nasal (or nasopharyngeal) swab	20 each	Swabs for 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 swab
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 product has not been FDA cleared or approved, but 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 product 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.
- 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 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 declaration is terminated or authorization is revoked sooner.
- This product 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.
- The SARS-CoV-2 positive control swabs have been prepared from recombinant viral proteins and do not contain infectious material.
- 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 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

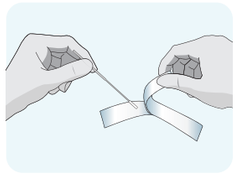
Acceptable specimen type for testing with the *CareStart*™ COVID-19 Antigen is a direct nasopharyngeal and anterior nasal swab specimen. It is essential that correct specimen collection and preparation methods be followed. Inadequate specimen collection, improper specimen handling and/or transport may yield false results; therefore, specimen collection requires specific training and guidance due to the importance of specimen quality to obtain accurate test results. Specimens 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

Swab Sample Collection Procedure

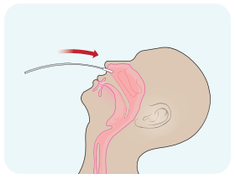
Nasopharyngeal Swab Collection

Procedural Notes

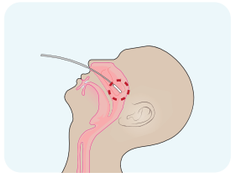
- Process the test sample immediately after collection.
- Use only recommended nasopharyngeal swab for specimen collection.
- Collect the specimen wearing safety gloves to avoid contamination.
- Do not touch the tip (specimen collection area) of the swab.
- Collect samples as soon as possible within 5 days of symptom onset.



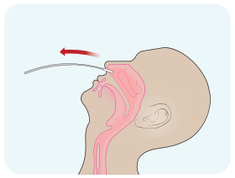
1
Remove a nasopharyngeal swab from the pouch.



2
Tilt patient's head back 70 degrees. Gently and slowly insert 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.

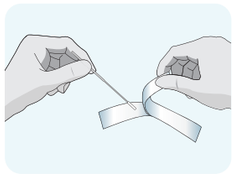


4
Leave swab in place for several seconds to absorb secretions. Slowly remove the swab from the nostril while rotating it.

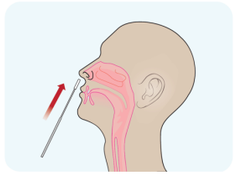
Anterior Nasal Swab Collection

Procedural Notes

- Process the test sample immediately after collection.
- Use only provided or recommended anterior nasal 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 within 5 days of symptom onset.



1
Remove a nasal swab from the pouch.



2
Insert the swab into one of patient's nostrils up to 1 inch from the edge of the nostril.

Description of Symbols

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

	Caution 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.		**Do not use if the package is damaged** Indicates a medical device that should not be used if the package has been damaged or opened.
	Date of manufacture Indicates the date when the medical device was manufactured.		**Contains sufficient for <n> tests** Indicates the total number of IVD tests that can be performed with the IVD.
	Temperature limit Indicates the temperature limits to which the medical device can be safely exposed.	Rx	**Prescription-only**

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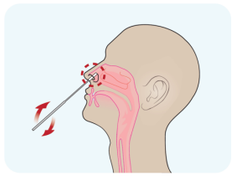
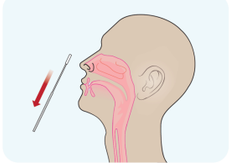
AccessBio

Document number: IFU-RCHM71-E Revision number: E Effective date: Apr. 15, 2021



3 Slowly roll the swab 5 times over the surface of the nostril. Using the same swab, repeat this collection process in the other nostril.
Take approximately 15 seconds to collect the specimen.



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

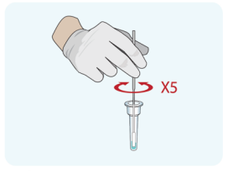
Test Procedures

Procedural Notes

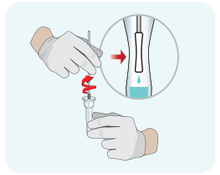
- Allow test devices, reagents, specimens, and/or controls to equilibrate to room temperature (15~30°C) prior to testing.
- Remove the *CareStart*™ COVID-19 Antigen test device and extraction vial from its foil pouch immediately before testing.
- The *CareStart*™ COVID-19 Antigen kit IS INTENDED to be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

Direct Swab Test Procedure

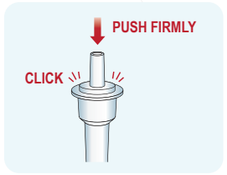
1 Peel off aluminum foil seal from the top of the extraction vial containing the extraction buffer



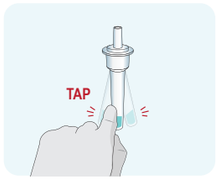
2 Place the swab into the extraction vial. Rotate the swab vigorously at least 5 times.



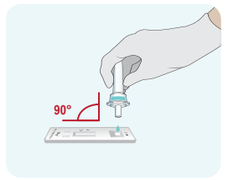
3 Remove the swab by rotating against the extraction vial while squeezing the sides of the vial to release the liquid from the swab. Properly discard the swab.



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.

⚠Warning

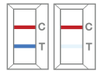
The false positive, false negative, or invalid results may occur if the test is interpreted outside of the interpretation window.

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" indicate 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.

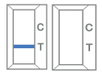
Negative:

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

NOTE: Negative results should be treated as presumptive and confirmation with a molecular assay, if necessary, for patient management, may be performed.

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.



Serial Testing Results Reporting

For serial testing programs, additional confirmatory testing with a molecular test for negative results may be necessary, if there is a high likelihood of COVID-19, such as, an individual with a close contact with COVID-19 or with suspected exposure to COVID-19 or in communities with high prevalence of infection. 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 low prevalence of infection.

Limitations

1. 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 when tested twice over two or three days with at least 24 hours and no more than 48 hours between tests, and performance may differ in these populations. A study to support use for serial testing will be completed.
2. 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 (>10mg per day). Biotin levels of 2.5 µg/mL have been demonstrated to result in false negative test results.
3. Negative results, should be treated as presumptive and confirmation with a molecular assay, if necessary for patient management, may be performed.
4. Failure to follow the instructions for use may adversely affect test performance and/or invalidate the test result.
5. If the differentiation of specific SARS viruses and strains is needed, additional testing, in consultation with state or local public health departments, is required.
6. Extracted specimens 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. The performance of this test was established based on the evaluation of a limited number of clinical specimens collected between September 2020 and December 2020. 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. 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.
17. 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 FDAwebsite: 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 must 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 must 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 must notify the relevant public health authorities of their intent to run your product prior to initiating testing.

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

E. Authorized laboratories must 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 must 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 – Nasopharyngeal Swab

The clinical performance characteristics of the *CareStart*™ COVID-19 Antigen test using nasopharyngeal swab specimen were evaluated in a multi-site prospective study in the U.S. between September 2020 and November 2020 against an FDA Emergency Use Authorized RT-PCR molecular assay as a comparator method. A total of three (3) POC investigational sites throughout the U.S. participated in the study. To be enrolled in the study, patients had to be presenting at the participating study centers with COVID-19 like symptoms and meet inclusion/exclusion criteria. All patients presented with fever or at least two symptoms of COVID-19 infection. The patients presenting the COVID-19 like symptoms within five (5) days of symptom onset at the study sites were enrolled.

The first collected nasopharyngeal or anterior nasal swab was collected from one nostril from each subject using standard collection methods for the comparator method. The second collected nasopharyngeal swab from the same nostril was tested directly on the *CareStart*™ COVID-19 Antigen test to demonstrate the agreement with the comparator method.

Testing was performed by six (6) operators with no laboratory experience and who were representative of the intended users. Operators were only using the QRI for the test without any training provided.

A total of 180 nasopharyngeal swab specimens collected from individual symptomatic patients (within 5 days of onset) were considered evaluable. The performance of the *CareStart*™ COVID-19 Antigen test compared to the comparator method is presented in the tables below.

***CareStart*™ COVID-19 Antigen nasopharyngeal clinical performance within 5 days of symptom onset against the comparator method**

CareStart™ COVID-19 Antigen	Comparator		
	Positive	Negative	Total
Positive	30	1	31
Negative	2	147	149
Total	32	148	180
Positive Percent Agreement (PPA)	93.75% (95% CI: 79.85% – 98.27%)		
Negative Percent Agreement (NPA)	99.32% (95% CI: 96.27% – 99.88%)		

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.

Patient Demographics

Age Group	*CareStart*™ COVID-19 Antigen		
	Total #	Positive	Prevalence
≤5 Years of Age	0	0	0.00%
6-21 Years of Age	22	3	13.64%
22-59 Years of Age	134	27	20.15%
≥60 Years of Age	24	2	8.33%

Positive results broken down by days since symptom onset:

Days Since Symptom Onset	Cumulative RT-PCR Positive (+)	Cumulative *CareStart*™ COVID-19 Antigen Positive (+)	PPA	95% Confidence interval	
1	0	0	-	-	-
2	7	7	100.00%	64.57%	100.00%
3	15	15	100.00%	79.62%	100.00%
4	23	22	95.65%	79.01%	99.23%
5	32	30	93.75%	79.85%	98.27%

Clinical Performance – Anterior Nasal Swab

The clinical performance characteristics of the *CareStart*™ COVID-19 Antigen test using anterior nasal swab specimen were evaluated in a multi-site prospective study in the U.S. between November 2020 and December 2020 against an FDA Emergency Use Authorized RT-PCR molecular assay as a comparator method. A total of three (3) Point-of-Care investigational sites throughout the U.S. participated in the study. To be enrolled in the study, patients had to be presenting at the participating study centers with COVID-19 like symptoms and meet inclusion/exclusion criteria. All patients presented with fever or at least two symptoms of COVID-19 infection. The patients presenting the COVID-19 like symptoms within five (5) days of symptom onset at the study sites were enrolled. Clinical studies in asymptomatic patients undergoing serial testing are ongoing to establish the clinical performance.

Two (2) nasal swabs were collected using the provided swabs. One (1) swab was tested on the *CareStart*™ COVID-19 Antigen test and the second swab was processed in transport media for the comparator method. Collection order for the swab to be tested on the *CareStart*™ COVID-19 Antigen test and the swab for reference testing was randomized.

Testing was performed by eight (8) operators with no laboratory experience and who were representative of the intended users. Operators were only using the QRI for the test without any training provided.

A total of 92 nasal swab specimens collected from individual symptomatic patients (within 5 days of onset) were considered evaluable. The performance of the *CareStart*™ COVID-19 Antigen test compared to the comparator method is presented in the tables below.

***CareStart*™ COVID-19 Antigen anterior nasal clinical performance within 5 days of symptom onset against the comparator method**

CareStart™ COVID-19 Antigen	Comparator		
	Positive	Negative	Total
Positive	34	0	34
Negative	5[b]	53	58
Total	39	53	92
Positive Percent Agreement (PPA)	87.18% (34/39) (95% CI: 73.29%-94.40%)		
Negative Percent Agreement (NPA)	100.00% (53/53) (95% CI: 93.24%-100.00%)		

[b]*COVID-19 was not detected in Q/5 False Negative specimens using an alternative FDA-EUA molecular Assay*

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.

Patient Demographics

Age Group	*CareStart*™ COVID-19 Antigen		
	Total #	Positive	Prevalence
≤5 Years of Age	1	1	100.00%
6-21 Years of Age	38	13	34.21%
22-59 Years of Age	47	20	42.55%
≥60 Years of Age	6	0	0%

Positive results broken down by days since symptom onset:

Days Since Symptom Onset	Cumulative RT-PCR Positive (+)	Cumulative *CareStart*™ COVID-19 Antigen Positive (+)	PPA	95% Confidence interval	
0	3	3	100%	43.85%	100.01%
1	11	10	90.91%	62.27%	98.38%
2	24	21	87.50%	69.00%	95.66%
3	33	29	87.88%	72.68%	95.19%
4	37	32	86.49%	72.02%	94.09%
5	39	34	87.18%	73.30%	94.40%

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 x 10^2 $TCID_{50}$/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 x 10^8 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*
		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.

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
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 10^8 $TCID_{50}$ /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).

REF RCHM-02071

QRI-RCHM-E / Rev. C / Apr. 15, 2021

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 1°C 30°C

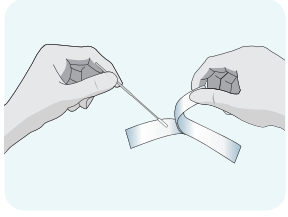
The *CareStart*™ COVID-19 Antigen test is a lateral flow immunochromatographic assay intended for the qualitative detection of the nucleocapsid protein antigen from SARS-CoV-2 in nasopharyngeal or anterior nasal swab specimens directly collected from individuals who are either suspected of COVID-19 by their healthcare provider within first five days of symptom onset, or from individuals without symptoms or other epidemiological reasons to suspect COVID-19 when tested twice over two or three days with at least 24 hours and no more than 48 hours between tests.

IMPORTANT!

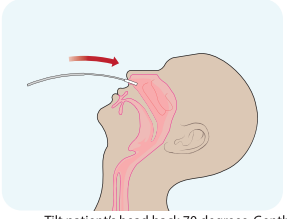
- Refer to the Package Insert for Warnings and Precautions, Specimen Collection Procedures, Storage and Handling Conditions, and Quality Control Recommendations.
- Warning and Precautions - All kit components can be discarded as Biohazard waste according to local guidelines. Refer to the product safety 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

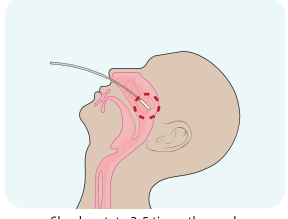
Nasopharyngeal (NP) Swab Collection



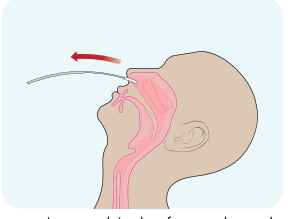
1 Remove a nasopharyngeal swab from the pouch.



2 Tilt patient's head back 70 degrees. Gently and slowly insert 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.

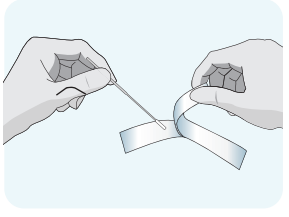


3 Slowly rotate 3-5 times the swab over the surface of the posterior nasopharynx.

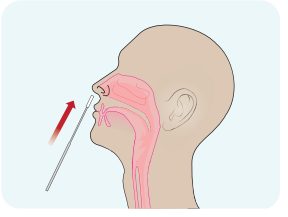


4 Leave swab in place for several seconds to absorb secretions. Slowly remove the swab from the nostril while rotating it.

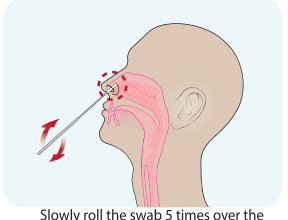
Anterior Nasal Swab Collection



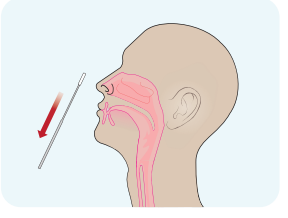
1 Remove a nasal swab from the pouch.



2 Insert the swab into one of patient's nostrils up to 1 inch from the edge of the nostril.



3 Slowly roll the swab 5 times over the surface of the nostril. Using the same swab, repeat this collection process in the other nostril. Take approximately 15 seconds to collect the specimen.



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

In the USA, this product has not been FDA cleared or approved, but 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 product 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 product has been authorized only for the detection of proteins from SARS-CoV-2, not for any other viruses or pathogens. In the USA, - 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 detection and/or diagnosis of the virus that causes COVID-19 under Section 564(b)(1) of the FederalFood, Drug and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization is revoked sooner.

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Somerset, NJ 08873, USA

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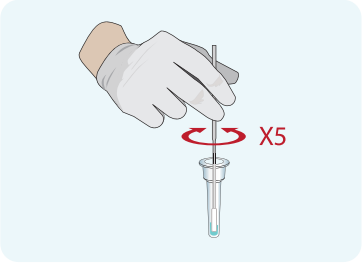
Email: TShelp@accessbio.net

REF RCHM-02071

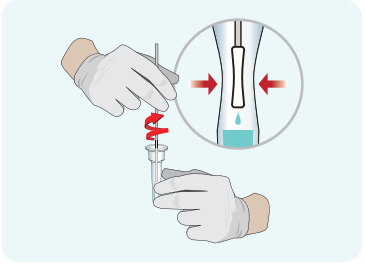
Quick Reference Instructions for *CareStart*™ COVID-19 Antigen | **Rapid Diagnostic Test for Detection of SARS-CoV-2 Antigen**

TEST PROCEDURES

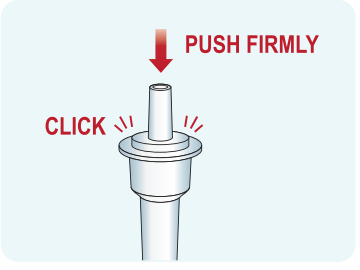
1 Peel off aluminum foil seal from the top of the extraction vial containing the extraction buffer.



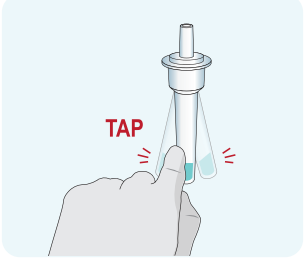
2 Place the swab into the extraction vial. Rotate the swab vigorously at least 5 times.



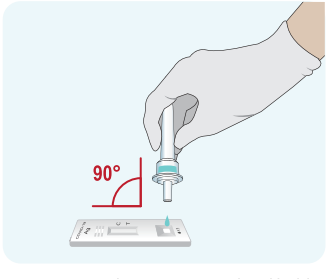
3 Remove the swab by rotating against the extraction vial while squeezing the sides of the vial to release the liquid from the swab. Properly discard the swab.



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



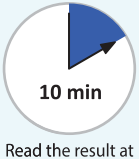
5 Mix thoroughly by flicking the bottom of the tube.



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.

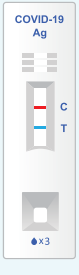
Start the timer



Read the result at 10 minutes. The test result should not be read after 15 minutes.

Warning

The false positive, false negative, or invalid results may occur if the test is interpret outside of the interpretation window.



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, or in those who have been in contact with the virus. 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.

If used on asymptomatic individuals for serial testing, a second test should be performed with at least 24 hours (and no more than 48 hours) between tests. For serial testing, additional confirmatory testing with a molecular test for negative results may be necessary, if there is a high likelihood of SARS-CoV-2 infection, such as, an individual with a close contact or with suspected exposure to COVID-19 or in communities with high prevalence of infection. Additional confirmatory testing with a molecular test for positive results may also be necessary, if there is a low likelihood of SARS-CoV-2 infection, such individuals without known exposures to SARS-CoV-2 or residing in communities with low prevalence of infection.