CorDx COVID-19 Ag Test

For use under emergency use authorization (EUA) only
For *in vitro* diagnostic use only
For use with anterior nasal swab specimens

INSTRUCTIONS FOR USE (IFU)
HEALTHCARE PROVIDER

Scan for instructions and timer

For technical support, please email **support@cordx.com**.

1. INTENDED USE

The CorDx COVID-19 Ag Test is a lateral flow immunoassay device intended for the qualitative detection of nucleocapsid protein antigen from the SARS-CoV-2 virus.

This test is authorized for non-prescription home use with self-collected anterior nasal (nares) swab samples from individuals aged 14 years or older or adult collected anterior nasal (nares) swab samples from individuals aged two years or older. This test is authorized for individuals with symptoms of COVID-19 within the first 7 days of symptom onset when tested at least twice over three days with at least 48 hours between tests, and for individuals without symptoms or other epidemiological reasons to suspect COVID-19, when tested at least three times over five days with at least 48 hours between tests.

The CorDx COVID-19 Ag Test does not differentiate between SARS-CoV and SARS-CoV-2.

Results are for the identification of SARS-CoV-2 nucleocapsid protein antigen, which is generally detectable in anterior nasal (nares) swab specimens during the acute phase of infection. Positive results indicate the presence of viral antigens, but clinical correlation with past medical history and other diagnostic information is necessary to determine infection status. Positive results do not rule out bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause of disease. Individuals who test positive with the CorDx COVID-19 Ag Test should self-isolate and seek follow-up care with their physician or healthcare provider as additional testing may be necessary.

All negative results are presumptive and confirmation with a molecular assay, if necessary for patient management, may be performed. Negative results do not rule out SARS-CoV-2 infection and should not be used as the sole basis for treatment or patient management decisions, including infection control measures such as isolating from others and wearing masks. Negative results should be considered in the context of an individual's recent exposures, history, and the presence of clinical signs and symptoms consistent with COVID-19.

Individuals who test negative and continue to experience COVID-19 like symptoms of fever, cough and/or shortness of breath may still have SARS-CoV-2 infection and should seek follow up care with their physician or healthcare provider.

Individuals should provide all results obtained with this product to their healthcare provider for public health reporting and to receive appropriate medical care. All healthcare providers will report all test results they receive from individuals who use the authorized product to relevant public health authorities in accordance with local, state, and federal requirements using appropriate LOINC and SNOMED codes, as defined by the Laboratory In Vitro Diagnostics (LIVD) Test Code Mapping for SARS-CoV-2 Tests provided by CDC.

The CorDx COVID-19 Ag Test is intended for non-prescription self-use and/or as applicable an adult lay user testing another person 2 years of age or older in a non-laboratory setting. The CorDx COVID-19 Ag Test is only for use under the Food and Drug Administration’s Emergency Use Authorization. This product has not been FDA cleared or approved.

IMPORTANT ! How to Use This Test

- Serial testing should be performed in all individuals with negative results; individuals with symptoms of COVID-19 and initial negative results should be tested again after 48 hours. Individuals without symptoms of COVID-19, and with initial negative results, should be tested again after 48 hours and, if the 2nd test is also negative, a 3rd time after an additional 48 hours. You may need to purchase additional tests to perform this serial (repeat) testing.
- If you test negative but continue to have symptoms of COVID-19, and both your first and second tests are negative, you may not have COVID-19, however you should follow-up with your healthcare provider.
- If your test is positive, then proteins from the virus that causes COVID-19 have been found in your sample and you likely have COVID-19.

2. EXPLANATION OF THE TEST

COVID-19 (short for 'Coronavirus Disease 2019') is a disease first recognized in 2019 that is based by a type of novel coronavirus called SARS-CoV-2. Due to its rapid spread, the World Health Organization (WHO) recognized the disease as a global pandemic on March 11, 2020. Individuals with COVID-19 may have a range of symptoms including fever and/or symptoms of acute respiratory illness (i.e. cough, dyspnea) although some individuals experience mild symptoms or are asymptomatic. The virus is spread primarily from person to person through respiratory particles, even by individuals without symptoms.

The CorDx COVID-19 Ag Test is a rapid, immunochromatographic membrane assay that uses highly sensitive monoclonal antibodies to detect nucleocapsid protein from SARS-CoV-2 from anterior nasal swab specimens. The test kit includes the: test cassette, swab, tube with sample processing solution, tube holder (back of the box) and the QRI.

The test strip enclosed in a cassette housing is comprised of the following components: sample pad, reagent pad, reaction membrane, and absorbing pad. The reagent pad contains colloidal-gold conjugated with a monoclonal antibody against the nucleocapsid protein of SARS-CoV-2; the reaction membrane contains the secondary antibody for the nucleocapsid protein of SARS-CoV-2. The whole strip is fixed inside a plastic cassette.

When the sample extract is added into the sample well, conjugates dried onto the reagent pad are dissolved and migrate along with the sample. If SARS-CoV-2 nucleocapsid antigen is present in the sample, a complex formed between the anti-SARS-2 conjugate and the viral antigen will be captured by the specific anti-SARS-2 monoclonal antibody coated on the test line region (T). Absence of the test line (T) suggests a negative result. To serve as a procedural control, a red line will always appear in the control line region (C) indicating that proper volume of sample has been added and membrane wicking has occurred.

3. MATERIALS AND REAGENTS PROVIDED

The CorDx COVID-19 Ag Test kit configurations are indicated below:

	Number of tests/kit	2 tests/kit	4 tests/kit	5 tests/kit	8 tests/kit	10 tests/kit	12 tests/kit	20 tests/kit
Reagent/ Material	Test cassette	2	4	5	8	10	12	20
	Swab	2	4	5	8	10	12	20
	Tube with sample processing solution	2	4	5	8	10	12	20
	Tube holder (back of box)	2	2	2	2	2	2	2
	User Instructions	1	1	1	1	1	1	1

4. MATERIALS REQUIRED BUT NOT PROVIDED

Clock, timer or stopwatch

5. WARNINGS, PRECAUTIONS, AND SAFETY INFORMATION

- Read all instructions carefully before performing the test. Failure to follow the instructions may result in inaccurate test results.
- If you skipped or incorrectly performed one or more steps, repeat the test with a new sample and cassette.
- In the USA, this product has not been FDA cleared or approved, but has been authorized by FDA under an Emergency Use Authorization. This product has been authorized only for the detection of proteins from SARS-CoV-2, not for any other viruses or pathogens. The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization is revoked sooner.
- **Serial testing should be performed in individuals with negative results at least twice over three days (with 48 hours between tests) for symptomatic individuals and three times over five days (with at least 48 hours between tests) for asymptomatic individuals. You may need to purchase additional tests to perform this serial (repeat) testing.**
- If you have had symptoms longer than 7 days you should consider testing at least three times over five days with at least 48 hours between tests.
- An anterior nasal swab sample can be self-collected by an individual aged 14 years and older. Children aged 2 to 13 years should be tested by an adult.
- Do not use on anyone under 2 years of age.
- Wear a safety mask or other face-covering when collecting a specimen from a child or another individual.
- Do not use if any of the test kit contents or packaging is damaged.
- Test components are single-use. Do not re-use.

- Do not use kit past its expiration date. For information about current expiration dates for at -home OTC COVID-19 diagnostic tests, visit *At-Home OTC COVID-19 Diagnostic Tests*
- Do not touch the swab tip.
- Once opened, the test card should be used within 60 minutes.
- Do not read test results before 10 minutes or after 30 minutes. Results read before 10minutes or after 30 minutes may lead to a false positive, false negative, or invalid result.
- If uncertain how to proceed, contact Technical Assistance at **support@cordx.com.**
- This product is only for the detection of proteins from SARS-CoV-2, not for any other viruses or pathogens.
- When collecting an anterior nasal swab sample, only use the swab provided in the kit.
- Inadequate or inappropriate specimen collection may yield false negative test results.
- Testing should be performed in an area with good lighting.
- Dispose of all materials in household waste.
- Wash hands thoroughly or use hand sanitizer before and after the test.
- Keep testing kit and kit components away from children and pets before and after use. Avoid contact with your skin, eyes, nose, or mouth. Do not ingest any kit components. The reagent solution contains harmful chemicals (see table below). If the solution contacts your skin, eyes, nose, or mouth, flush with large amounts of water. **If irritation persists, seek medical advice:** *https://www.poisonhelp.org* **or *1-800-222-1222*.**

Chemical Name	Harms (GHS Code) for each ingredient	Concentrations
Triton X-100	Harmful if swallowed (H302) Causes skin irritation (H315) Causes serious eye damage (H318)	0.5%
ProClin 300	Harmful if swallowed (H302) Harmful if inhaled (H332) Causes severe skin burns and eye damage (H314) May cause an allergic skin reaction (H317)	0.05%

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

6. STORAGE AND STABILITY

Store the CorDx COVID-19 Ag Test between 36-86°F (2-30°C) in a place out of direct sunlight and out of reach of children. Reagents and devices must be used at room temperature (59-86°F/15-30°C). The unsealed cassette is valid for 1 hour. It is recommended to use the test kit immediately after opening. The expiration date assigned at manufacturing is on the package. For information about current expiration dates for at-home OTC COVID-19 diagnostic tests, visit *At-Home OTC COVID-19 Diagnostic Tests*

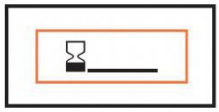
7. QUALITY CONTROL

Each CorDx COVID-19 Ag Test has a built-in “Control” region which serves as an internal procedural control when a colored line appears in the control line region (“C line”). The “C line” should always appear if the test has been performed correctly. If the “C line” does not appear at 10 minutes, the test result is invalid. It is recommended to review the instructions again and repeat the test with a new sample and a new cassette. If the problem persists, please stop using the product and contact CorDx for technical support.

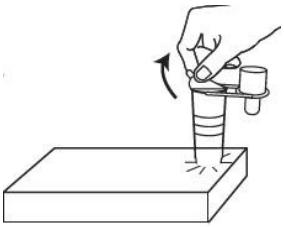
8. TEST PROCEDURES

TEST PREPARATION

- Wash hands before testing.

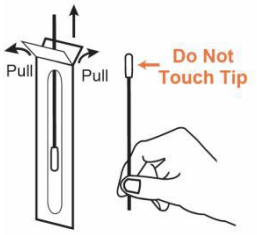


- Check Expiration Date on the package.
  Do not use expired test kit!
  For information about current expiration dates, visit *At-Home OTC COVID-19 Diagnostic Tests*



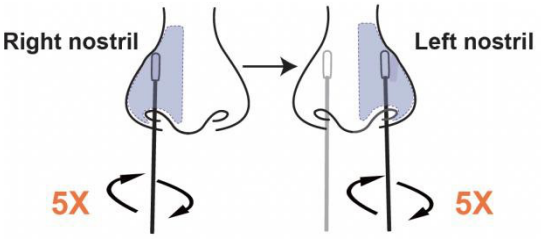
- Remove the test cassette from the pouch and place it on a clean, flat surface.
- Insert the tube in the pre-made hole on the back of the kit box.
- Remove the foil from the top of the tube.

STEP 1: COLLECT SAMPLE



(1) Remove the swab from the pouch.

Note: Be careful not to touch the swab tip (soft end) with hand.



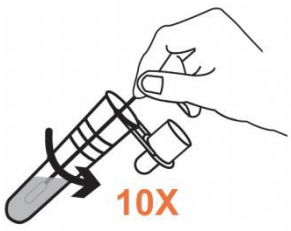
(2) Carefully insert the swab tip into one nostril About **1/2** to **3/4 inch**. Firmly and slowly rotate the swab 5 times, brushing against the inside walls of the nostril to ensure both mucus and cells are collected.
Do not push the swab further if you meet resistance.
For young children do not insert more than **1/2** inch.

(3) Using the **same swab**, repeat this process for the other nostril to ensure an adequate sample is collected from both nostrils.

Note: Failure to swab properly may cause Incorrect results.

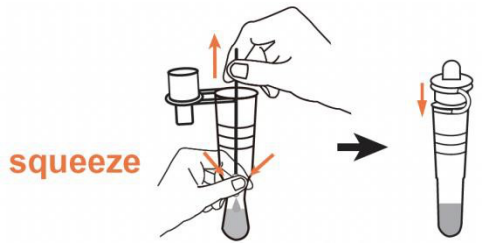
STEP 2: PROCESS SAMPLE

(4) Insert the swab into the bottom of the tube.



(5) Rotate the swab at least **10 times** while pressing the swab head against the bottom and side of the tube.

(6) Remove the swab while squeezing the sides of the tube to express as much liquid as possible from the swab.

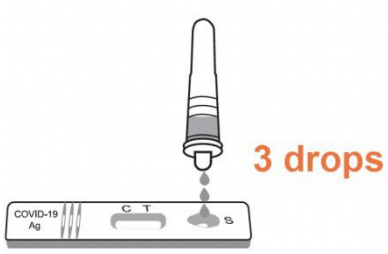


(7) Attach the dropper tip firmly onto the tube.

STEP 3: ADD SAMPLE

(8) Gently squeeze the tube and dispense 3 drops of solution in the sample well.

Note: A false negative or invalid result may occur if less than 3 drops of fluid are added to the Sample Well.

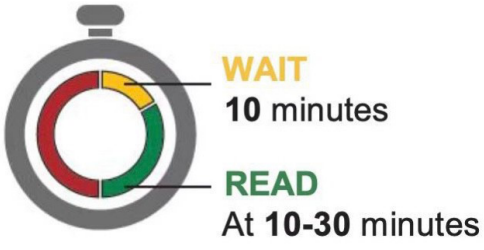


STEP 4: READ RESULT

(9) **Wait** 10 minutes.

(10) **Read** the result at 10 minutes.

Do not read the result after 30 minutes.



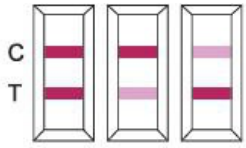
Note: The result is valid when read at 10-30 minutes. If a POSITIVE result is obtained within 10 minutes, it should also be considered valid.

9. TEST INTERPRETATION

Repeat testing is needed to improve test accuracy. Please follow the table below when interpreting test results.

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

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



POSITIVE

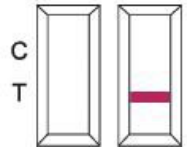
COVID-19 Positive (+)

If the Control (C) line and the Test (T) line are visible, the test is positive. Any faint visible colored test (T) line with the control line (C) should be read as positive.

Repeat testing does not need to be performed if patients have a positive result at any time.

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

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

 **NEGATIVE**	***COVID-19 Negative (-)*** If the Control (C) line is visible, but the Test (T) line is not visible, the test is negative. **To increase the chance that the negative result for COVID-19 is accurate, you should:** • **Test again in 48 hours if the individual has symptoms on the first day of testing.** • **Test 2 more times at least 48 hours apart if the individual does not have symptoms on the first day of testing.** A negative test result indicates that the virus that causes COVID-19 was not detected in the sample. A negative result does not rule out COVID-19. There is a higher chance of false negative results with antigen tests compared to laboratory-based tests such as PCR tests. If the test is negative but COVID-19-like symptoms, e.g., fever, cough, and/or shortness of breath continue, follow up testing for SARS-CoV-2 with a molecular test or testing for other respiratory diseases should be considered. If applicable, seek follow up care with the primary health care provider. All negative results should be treated as presumptive and confirmation with a molecular assay may be necessary if there is a high likelihood of SARS-CoV-2 infection, such as in an individual with a close contact with COVID-19 or with suspected exposure to COVID-19 or in communities with high prevalence of infection. Negative results do not rule out SARS-CoV-2 infection and should not be used as the sole basis for treatment or patient management decisions, including infection control decisions.
 **INVALID**	***Invalid*** If the control (C) line is not visible, the test is invalid. Re-test with a new swab and new test device.

10. LIMITATIONS

- The performance of this test was established based on the evaluation of a limited number of clinical specimens collected between March 2022 and May 2022. The clinical performance has not been established for 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.
- There is a higher chance of false negative results with antigen tests than with laboratory -based molecular tests due to the sensitivity of the test technology. This means that there is a higher chance this test will give a false negative result in an individual with COVID-19 as compared to a molecular test, especially in samples with low viral load.
- All COVID-19 antigen test negative results are presumptive and confirmation with a molecular assay may be necessary.
- If the patient continues to have symptoms of COVID-19, and both the patient's first and second tests are negative, the patient may not have COVID-19, however additional follow-up may be needed.

- If the test is positive, then proteins from the virus that causes COVID-19 have been found in the sample and the individual likely has COVID-19.
- This test is read visually and has not been validated for use by those with impaired vision or color-impaired vision.
- Incorrect test results may occur if a specimen is incorrectly collected or handled.
- This test detects both viable (live) and nonviable SARS-CoV-2. Test performance depends on the amount of virus (antigens) in the sample and may or may not correlate with viral culture results performed on the same sample.
- This device is only used for testing direct human anterior nasal swab specimens. Viral transport media (VTM) should not be used with this test.
- Negative test results are not indicative of the presence/absence of other viral or bacterial pathogens.
- Positive test results do not exclude co-infection with other pathogens.
- Positive test results do not difference between SARS-CoV-2 and SARS-CoV.
- If the differentiation of specific coronaviruses and strains is needed, additional testing, in consultation with state and local public health departments, is required.

11. PERFORMANCE CHARACTERISTICS

11.1 Limit of Detection (Analytical Sensitivity)

The Limit of Detection (LoD) of the CorDx COVID-19 Ag Test was established using serial dilutions of UV-irradiated SARS-CoV-2 virus. Contrived samples were prepared by spiking the strain into a pooled nasal cavity wash from presumed negative human donors.

The preliminary LoD determined by testing a 2-fold dilution series of three replicates per concentration was confirmed by testing 20 replicates. The confirmed LoD for the CorDx COVID-19 Ag Test was $1.25x10^4$ $TCID_{50}$/mL which is equivalent to $6.25x10^2$ $TCID_{50}$/swab based upon the testing procedure of the study.

11.2 CorDx Variant Testing

A study was performed in May 2022 to determine the inclusivity of the CorDx COVID-19 Ag Test on detecting SARS-CoV-2 Delta and Omicron variants as assessed by its Limit of Detection. Serial diluted Gamma-irradiated SARS-CoV-2 Delta and Omicron variants (obtained from commercial sources) were spiked into negative sample matrix to determine the LoD for each tested variant using 3 lots of tests. Based on the results, the CorDx COVID-19 Ag Test detects SARS-CoV-2 Delta variant with LoD at $2.5x10^4$ $TCID_{50}$/ mL ($1.25x10^3$ $TCID_{50}$/swab) and detects SARS-CoV-2 Omicron variant with LoD at $3.75x10^4$ $TCID_{50}$/ mL ($1.875x10^3$ $TCID_{50}$/swab). The assay can detect these variants at 2- 3x LOD of the original SARS-CoV-2 virus and thus displaying comparable sensitivity and acceptable inclusivity for the Delta and Omicron variants.

NIH/RADx Variant Testing

An independent study was conducted by the National Institutes of Health (NIH) as a component of the Rapid Acceleration of Diagnostics (RADx®) initiative in January 2023. The performance of this test in detecting the Omicron variant of SARS-CoV-2 was evaluated in a dilution series of clinical specimens which were positive for the Omicron variant. The clinical specimens used to prepare this dilution series were not identical to the previous specimen pools prepared and tested by RADx® to

assess performance with the Omicron variant. Results from this dilution series cannot be compared to other specimens pools and do not indicate that a test will have different clinical performance compared to other EUA authorized tests. Compared to an EUA authorized RT-PCR method, the CorDx COVID-19 Ag Test detected 100% of the live Omicron samples at a Ct-value of 26.7 (n=5). Testing was also compared to two additional EUA-authorized OTC antigen tests (Assay #1 and Assay #2). Omicron dilutions at lower viral concentrations (Ct-values greater than 26.7) were not detected by the CorDx COVID-19 Ag Test in this study.

Omicron BQ.1.1 Live Pool 1	Average N2-Ct (n=9)	Assay #1 Percent Positive (n=5)	Assay #2 Percent Positive (n=5)	CorDx COVID-19 Ag Test Percent Positive (n=5)
Dilution 1	18	100	100	100
Dilution 2	19.4	100	100	100
Dilution 3	20	100	100	100
Dilution 4	21.5	100	100	100
Dilution 5	23	100	100	100
Dilution 6	24.4	100	100	100
Dilution 7	25.4	0	0	100
Dilution 8	26.7	0	0	100
Dilution 9	27.7	0	0	0
Dilution 10	28.7	0	0	0
Dilution 11	29.8	0	0	0
Dilution 12	30.6	0	0	0

11.3 Cross Reactivity (Analytical Specificity) and Microbial Interference

Cross reactivity (analytical specificity) and microbial interference studies were performed to determine if the CorDx COVID-19 Ag Test reacts with non-SARS-CoV-2 respiratory pathogens and other microorganisms that are likely to be encountered in the clinical sample. Each microorganism was evaluated in the absence and presence of inactivated SARS-CoV-2 virus (3xLoD) to see if false positive and false negative test results may occur. Study results showed that no cross reactivity or interference was observed with the following 30 microorganisms at the concentration tested in the table below.

Substance	Concentration	Cross Reactivity	Microbial Interference Results
Human coronavirus 229E	$1x10^5$ $TCID_{50}$/mL	No cross-reactivity	No interference
Human coronavirus OC43	$1x10^5$ $TCID_{50}$/mL	No cross-reactivity	No Interference
Human coronavirus NL63	$1x10^5$ $TCID_{50}$/mL	No cross-reactivity	No Interference
MERS-coronavirus	$1x10^5$ $TCID_{50}$/mL	No cross-reactivity	No Interference
SARS-coronavirus (Gamma-irradiated virus in Vero E6 cells in DMEM)	$1x10^5$ PFU/mL	No cross-reactivity	No Interference
SARS-coronavirus (Gamma-irradiated virus in PBS)	$1x10^7$ PFU/mL	No cross-reactivity	No Interference
Human Adenovirus 1	$1x10^6$ $TCID_{50}$/mL	No cross-reactivity	No Interference
Human Metapneumovirus 3 (hMPV-3) Type B1	$1x10^5$ $TCID_{50}$/mL	No cross-reactivity	No Interference
Parainfluenza virus Type 1	$1x10^7$ $TCID_{50}$/mL	No cross-reactivity	No Interference
Parainfluenza virus Type 2	$1x10^5$ $TCID_{50}$/mL	No cross-reactivity	No Interference
Parainfluenza virus Type 3	$1x10^7$ $TCID_{50}$/mL	No cross-reactivity	No Interference
Parainfluenza virus Type 4A	$1x10^5$ $TCID_{50}$/mL	No cross-reactivity	No Interference
Influenza A /Perth/16/09 (H3N2)	$1x10^5$ $TCID_{50}$/mL	No cross-reactivity	No Interference
Influenza A/California/07/09 (H1N1)	$1x10^5$ $TCID_{50}$/mL	No cross-reactivity	No Interference
Influenza B/Brisbane/60/08 (Victoria lineage)	$4.68 x10^4$ $TCID_{50}$/mL	No cross-reactivity	No interference
Influenza B/Wisconsin/01/10(Yamagata lineage)	$1x10^5$ $TCID_{50}$/mL	No cross-reactivity	No Interference
Enterovirus B111 2015 isolate	$1x10^6$ $TCID_{50}$/mL	No cross-reactivity	No Interference
Respiratory syncytial virus	$1x10^6$ $TCID_{50}$/mL	No cross-reactivity	No Interference
Rhinovirus Type 1A	$1x10^5$ $TCID_{50}$/mL	No cross-reactivity	No Interference
Haemophilus influenzae type b (Eagan)	$1x10^7$ CFU/mL	No cross-reactivity	No Interference
Streptococcus pneumoniae Z022	$1x10^7$ CFU/mL	No cross-reactivity	No Interference
Streptococcus pyogenes Z018	$1x10^7$ CFU/mL	No cross-reactivity	No Interference
Candida albicans Z006	$1x10^7$ CFU/mL	No cross-reactivity	No Interference
Pooled human nasal wash – representative of normal respiratory microbial flora	NA	No cross-reactivity	No Interference
Bordetella pertussis A639	$1x10^7$ CFU/mL	No cross-reactivity	No Interference
Mycoplasma pneumoniae M129	$1x10^7$ CFU/mL	No cross-reactivity	No Interference
Chlamydia pneumoniae	$1x10^7$ IFU/mL	No cross-reactivity	No Interference
Legionella pneumophila Philadelphia	$1x10^7$ CFU/mL	No cross-reactivity	No Interference
Staphylococcus aureus MRSA; COL	$1x10^7$ CFU/mL	No cross-reactivity	No Interference
Staphylococcus epidermidis MRSE; PR62A	$1x10^7$ CFU/mL	No cross-reactivity	No Interference

To estimate the likelihood of cross reactivity for 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. Human coronavirus HKU1, Mycobacterium tuberculosis and Pneumocystis jirovecii were analyzed as shown below.

- Homology exists between the SARS-CoV-2 Nucleocapsid protein and Human Coronavirus HKU1. BLASTP results showed 36 sequence IDs. Sequence ID AGT17773.1 and AGW27840.1 has the highest alignment score (199) and is 39.1% homologous across 76% of the sequences. This is relatively low sequence homology, however, the possibility of cross -reactivity cannot be completely ruled out.
- Based on the *in silico* sequence homology analysis, no significant homology was found between the SARS-CoV-2 Nucleocapsid protein and the Mycobacterium tuberculosis. indicating an unlikelihood of cross-reactivity.
- No significant homology was found between the SARS-CoV-2 Nucleocapsid protein and the Pneumocystis jirovecii, indicating an unlikelihood of cross-reactivity.

11.4 Endogenous Interfering Substances

The following substances, naturally present in respiratory specimens or that may be artificially introduced, were evaluated.

The negative samples and positive samples (viral titer 3xLoD) were tested in triplicate in the presence of the potentially interfering substances. The performance of the CorDx COVID-19 Ag Test was not affected by any of the 14 potentially interfering substances listed in the table below at the tested concentration.

Substance	Concentration	# Neg Result / Total # Neg	# Pos Result/ Total # Pos	Interference Results
Whole Blood	4%	3(-)/3	3(+)/3	No interference
Mucin	0.5%	3(-)/3	3(+)/3	No Interference
Chloraseptic (Methol/Benzocaine)	1.5 mg/mL	3(-)/3	3(+)/3	No Interference
Naso GEL (NeilMed)	5% v/v	3(-)/3	3(+)/3	No Interference
CVS Nasal Drops (Phenylephrine)	15% v/v	3(-)/3	3(+)/3	No Interference
Afrin (Oxymetazoline)	15% v/v	3(-)/3	3(+)/3	No Interference
CVS Nasal Spray (Cromolyn)	15% v/v	3(-)/3	3(+)/3	No Interference
Zicam	5% v/v	3(-)/3	3(+)/3	No Interference
Homeopathic (Alkalol)	10% v/v	3(-)/3	3(+)/3	No Interference
Sore Throat Phenol Spray	15% v/v	3(-)/3	3(+)/3	No Interference
Tobramycin	4 µg/mL	3(-)/3	3(+)/3	No Interference
Mupirocin	10 mg/mL	3(-)/3	3(+)/3	No Interference
Fluticasone Propionate	5% v/v	3(-)/3	3(+)/3	No Interference
Tamiflu (Oseltamivir Phosphate)	5 mg/mL	3(-)/3	3(+)/3	No Interference

11.5 High Dose Hook Effect

No hook effect was observed for specimens containing SARS-CoV-2 viral concentration as high as $4.57x10^6$ $TCID_{50}$/ mL.

11.6 Flex Studies

The robustness of the CorDx COVID-19 Ag Test kit for home/OTC use was demonstrated by eight flex studies, including:
Specimen extraction delay study, Extracted specimen loading delay study, Swab rotation number variability study, Extracted specimen volume variability study, Test result reading time variability study, Disturbance during analysis study, Lighting conditions study, Temperature and humidity conditions study.

11.7 Usability and User Comprehension Studies

Of the 473 subjects enrolled in the clinical study, 32 were enrolled in the human factors arm of the study to evaluate the human user experience and comprehension of the CorDx COVID-19 Ag Test and labeling. This subset of subjects included 17 self-collecting and 15 lay users collecting from another lay user.

The usability portion of the human factors assessment evaluated the ability of users to perform the entire test procedure in a simulated home-setting environment. The entire test procedure was performed by each individual participant using the kit. The participants were observed by study personnel during the whole procedure and any difficulties were recorded.

The user comprehension portion of the human factors assessment studied user comprehension of test results (interpreting mock positive, negative and invalid results) and instructions for use to verify that users can accurately interpret the test results and carry out any follow up actions. The participants were provided a panel of mock test devices to interpret following completion of the investigational testing during the subject's first visit.

Evaluation of the human user experience indicated high usability of the CorDx COVID-19 Ag Test. Of the subjects that participated in the human factors assessment, 96.9% of the subjects found the instructions clear and easy to follow, 100% of the subjects found sample collection easy to perform, and 100% of the subjects found their test results easy to read. Additionally, 92.5% of the mock tests were interpreted correctly by the subjects. Overall, 92.4% of all essential steps were completed samples and run the CorDx COVID-19 Ag Test were performed correctly. 74% of all non-essential steps were performed correctly by the subjects.

12. CLINICAL PERFORMANCE

The clinical performance of the CorDx COVID-19 Ag Test was evaluated in a prospective clinical study completed at seven (7) sites throughout the United States. The study evaluated 383 symptomatic individuals aged 2 years or older who were either experiencing fever, or two or more symptoms associated with COVID-19, and presented within 7 days of symptom onset.

The subject either self-collected one sample from their anterior nasal passages (from both nostrils), or had one sample collected from him/her by another individual. Upon reviewing the CorDx COVID-19 Ag Test's Quick Reference Instructions, the subject self-collected, or collected from another individual, an anterior nares sample and test the sample using the CorDx COVID-19 Ag Test. A matched mid-turbinate nasal swab sample was also taken from each study subject by a healthcare professional for testing on a high- sensitivity, FDA EUA-authorized RT-PCR method as the comparator.

Of the 383 symptomatic subjects, 39 (10.2%) were COVID-19 positive and 344 (89.8%) were COVID-19 negative by the comparator test.

Test results from the CorDx COVID-19 Ag Test (investigational test) were compared to highly sensitive molecular FDA EUA Authorized SARS-CoV-2 assay to determine the test performance.

Table 1: CorDx COVID-19 Ag Test Performance Against Comparator

Subjects	Comparator Positives	Comparator Negatives	Total
CorDx COVID-19 Ag Test Positives	35	1	36
CorDx COVID-19 Ag Test Negatives	4	343	347
Total	39	344	383
Positive Percent Agreement = 89.7% (95% CI: 76.4 to 95.9%)			
Negative Percent Agreement = 99.7% (95% CI: 98.4 to 100.0%)			

13. FREQUENTLY ASKED QUESTIONS (FAQ)

1) WHAT ARE THE KNOWN AND POTENTIAL RISKS AND BENEFITS OF THE TEST?

Potential risks include:

a. Possible discomfort during sample collection.
b. Possible incorrect test result (see Warnings and Result Interpretation sections for more information).

Potential benefits include:

a. The results, along with other information, can help you and your healthcare provider make informed recommendations about your care.
b. The results of this test may help limit the potential spread of COVID-19 to your family and others in your community.

For more information on EUAs go here: *https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization*

2) WHAT IS THE DIFFERENCE BETWEEN AN ANTIGEN AND MOLECULAR TEST?

There are different kinds of tests for the SARS-CoV-2 virus that causes COVID-19. Molecular tests detect genetic material from the virus. Antigen tests, such as the CorDx COVID-19 Ag Test, detect proteins from the virus. Due to the lower sensitivity of antigen tests, there is a higher chance this test will give you a false negative result when you have COVID-19 than a molecular test would.

3) HOW ACCURATE IS THIS TEST?

Clinical studies have shown that antigen tests more accurately determine whether you are infected with the virus that causes COVID-19 when taken multiple times across several days. Repeat testing improves test accuracy. This serial testing approach is recommended to minimize the risk of incorrect results.

4) WHAT IF I HAVE A POSITIVE TEST RESULT?

A positive result means that it is very likely you have COVID-19 because proteins from the virus that causes COVID-19 were found in your sample. You should self-isolate from others and contact a healthcare provider for medical advice about your positive result.

5) WHAT IF I HAVE A NEGATIVE TEST RESULT?

A negative test result indicates that antigens from the virus that causes COVID-19 were not detected in your sample. However, if you have symptoms of COVID-19, and your first test is negative, you should test again in 48 hours since antigen tests are not as sensitive as molecular tests. If you do not have symptoms and received a negative result, you should test at least two more times with 48 hours in between tests for a total of three tests. If you have a negative result, it does not rule out SARSCoV-2 infection; you may still be infected and you may still infect others. It is important that you work with your healthcare provider to help you understand the next steps you should take.

6) WHAT DOES AN INVALID TEST RESULT MEAN?

An invalid result means the test was not able to tell if you have COVID-19 or not. If the test is invalid, a new swab should be used to collect a new nasal specimen and you should test again with a new test.

14. SERIAL TESTING

A prospective clinical study was conducted between January 2021 and May 2022 as a component of the Rapid Acceleration of Diagnostics (RADx) initiative from the National Institutes of Health (NIH). A total of 7,361 individuals were enrolled via a decentralized clinical study design, with a broad geographical representation of the United States. Per inclusion criteria, all individuals were asymptomatic upon enrollment in the study and at least 14 days prior to it and did not have a SARS-CoV-2 infection in the three months prior to enrollment. Participants were assigned to one of three EUA authorized SARS-CoV-2 OTC rapid antigen tests to conduct serial testing (every 48 hours) for 15 days. If an antigen test was positive, the serial-antigen testing result is considered positive.

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

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

Out of the 7,361 participants enrolled in the study, 5,609 were eligible for analysis. Among eligible participants, 154 tested positive for SARS-CoV-2 infection based on RT-PCR, of which 97 (62%) were asymptomatic on the first day of their infection, whereas 57 (39%) reported symptoms on the first day of infection. Pre-symptomatic subjects were included in the positive percent agreement (PPA) of asymptomatic individuals, if they were asymptomatic on the first day of antigen testing, regardless of whether they developed symptoms at any time after the first day of testing.

Performance of the antigen test with serial testing in individuals is described in Table 2.

Table 2: Data establishing PPA of COVID-19 antigen serial testing compared to the molecular comparator single day testing throughout the course of infection with serial testing. Data is from all antigen tests in study combined.

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

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

2 Tests = two (2) tests performed an average of 48 hours apart. The first test performed on the indicated day and the second test performed 48 hours later.

3 Tests = three (3) tests performance an average of 48 hours apart. The first test performed on the indicated day, the second test performed 48 hours later, and a final test performed 48 hours after the second test.

15. SYMBOLS

	Do not re-use		Use-by date (Expiration date)		Catalogue number
	Batch code		Consult instructions for use		Keep dry
	Store at 36~86°F /2~30℃		Manufacturer		Keep away from sunlight
	In vitro diagnostic medical device		Caution		Do not use if package is damaged and consult instructions for use

CorDx, Inc.
9540 Waples St. Unit C, San Diego, CA 92121

Manufacturing sites:
CorDx, Inc.
8940 Kenamar Dr, San Diego, CA 92121,
3719 North Peachtree Rd, Suite 200, Chamblee, GA 30341
Core Technology Co., Ltd.
No.30, Area 9, Douda Avenue, Fangshan District, Beijing 102433, China

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