For Emergency Use Authorization (EUA) only
For IN VITRO Diagnostic use only

ADEXUSDx® COVID-19 Test

For detection of SARS-CoV-2 total antibody in human venous whole blood, serum, and plasma

Read this product insert completely before using the test. Follow the instructions carefully when performing the test. Failure to follow instructions may result in inaccurate test results.

STORAGE:

Store at 15-30°C (59-86°F)

NAME AND INTENDED USE:

The ADEXUSDx® COVID-19 Test is an *in vitro* lateral-flow immunoassay intended for qualitative detection of total antibodies to SARS-CoV-2 in human whole blood or plasma (EDTA), and serum. The ADEXUSDx® COVID-19 Test is intended for use as an aid in identifying individuals with an adaptive immune response to SARS-CoV-2, indicating recent or prior infection. At this time, it is unknown for how long antibodies persist following infection and if the presence of antibodies confers protective immunity. Testing is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. 263a, to perform moderate or high complexity tests.

Results are for the detection of SARS-CoV-2 antibodies. Total antibodies to SARS-CoV-2 are generally detectable in blood several days after initial infection, although the duration of time antibodies are present post-infection is not well characterized. Individuals may have detectable virus present for several weeks following seroconversion.

Laboratories within the United States and its territories are required to report all positive results to the appropriate public health authorities.

The sensitivity of ADEXUSDx® COVID-19 Test early after infection is unknown. Negative results do not preclude acute SARS-CoV-2 infection. If acute infection is suspected, direct testing for SARS-CoV-2 is necessary.

False positive results for ADEXUSDx® COVID-19 Test may occur due to cross-reactivity from pre-existing antibodies or other possible causes. Due to the risk of false positive results, confirmation of positive results should be considered using second, different total antibody assay.

The ADEXUSDx® COVID-19 Test is only for use under the Food and Drug Administration's Emergency Use Authorization. For prescription use only. For *in vitro* diagnostic use only.

SUMMARY AND EXPLANATION:

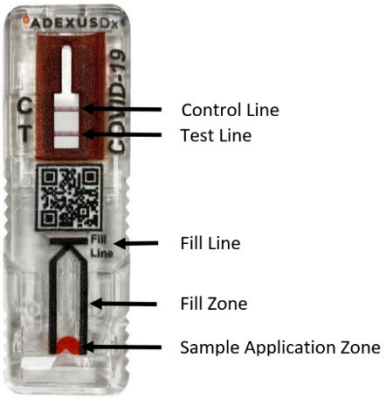
Coronaviruses are a large family of viruses that are common among humans and several known different species of animals. Seven known types of human coronaviruses (HCoV) lead to respiratory diseases among humans. These coronaviruses include: 1) HCoV-229E, 2) HCoV-NL63, 3) HCoV-OC43, 4) HCoV-HKU1, 5) SARS-CoV, 6) MERS-CoV, and 7) the novel Coronavirus Disease 2019 (COVID-19). Discovered in 2019 in Wuhan, China, COVID-19 is

caused by infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Individuals infected with the virus report a mild to severe respiratory illness with fever, cough, and shortness of breath, and other symptoms which can rapidly lead to severe pneumonia, septic shock, multiple organ failure, and death.

TEST PRINCIPLE:

To run the test, a sample (whole blood or plasma (EDTA), or serum) is applied in the Sample Application Zone of the cassette to fill the Fill Zone [**Figure 1**]. When enough sample is in the Fill Zone, the sample flows into a dry porous test strip composed of a plasma-separating membrane and a series of analytical membranes. The sample first passes through the plasma-separating membrane, which binds the erythrocytes in whole blood samples to prevent them from interfering with the test. The membrane also contains two separate colloidal gold conjugate materials: SARS-CoV-2 recombinant antigen conjugated with colloidal gold and rabbit IgG conjugated with colloidal gold. The SARS-CoV-2 specific antibody in the sample binds to the gold labeled SARS-Cov-2 recombinant antigen in the upstream region of the test strip and the complex is captured by immobilized SARS-CoV-2 antigen at the test line location as it flows downstream. The appearance of a visible test line indicates the sample contains a detectable level of SARS-CoV-2 antibody. Rabbit IgG conjugated with colloidal gold will flow past the test line region and bind to the polyclonal anti-rabbit antibody in the control line location of the analytical membranes, resulting in the appearance of a procedural control line. Test ("T") and Control ("C") Lines on each cassette are visually read for this qualitative test. The control line and the test line may differ in color intensity. The intensity of the test line will vary depending on the concentration of SARS-CoV-2 specific antibody present in the specimen. However, a quantitative value for SARS-CoV-2 cannot be determined by this qualitative test. The color intensity of the lines will increase slowly with time due to sample evaporation; the test result can be read as early as 15 minutes but must be read within 30 minutes to be valid. A line of any signal intensity at the test line indicates a positive result. If the test line is absent, the appearance of the control line assures that the sample was applied correctly, and that proper chromatography occurred in the test. A visible control line with an absent test line assures that the negative result was not due to improper test performance. If there is no control line, then the result is invalid.

Figure 1. ADEXUSDx® COVID-19 Test schematic



MATERIALS PROVIDED:

Each box of fifty (50) tests contains the following items:

- Fifty (50) sealed aluminum pouches containing one (1) ADEXUSDx® COVID-19 Test and one (1) desiccant.
- One (1) Instructions For Use
- One (1) Product Insert

Each box of twenty-five (25) tests contains the following items:

- Twenty-five (25) sealed aluminum pouches containing one (1) ADEXUSDx® COVID-19 Test and one (1) desiccant.
- One (1) Instructions For Use
- One (1) Product Insert

MATERIALS REQUIRED BUT NOT PROVIDED:

- Watch or timer
- Gloves
- Liquid transfer device
- Negative and positive control set

WARNINGS:

- For *in vitro* diagnostic use under Emergency Use Authorization only.
- Use of this product is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. § 263a, to perform moderate and high complexity tests.
- Read the Product Insert completely before using this assay. Follow the instructions carefully. Failure to follow instructions may result in inaccurate test results.
- Use of ADEXUSDx® COVID-19 Test with sample types not specifically approved for use with this device may result in inaccurate test results.
- The ADEXUSDx® COVID-19 Test should be performed at 15 - 30°C (59 - 86°F).

PRECAUTIONS:

SAFETY PRECAUTIONS

- Specimens may be infectious. Use universal precautions when performing this assay.
- Use routine laboratory precautions. Avoid any contact between hands, eyes, or mouth during sample collection and testing.
- Use appropriate personal protective equipment (laboratory coat, gloves, and eye protection) during patient sample handling. Wash hands thoroughly after handling specimens.
- All samples and materials used in this test procedure must be disposed in a biohazard waste container. Proper handling and disposal methods should be established according to local regulations.

HANDLING PRECAUTIONS

- DO NOT USE the test if desiccant packet is missing. Discard test and use a new test.
- DO NOT USE the test if the pouch was not sealed.

- DO NOT USE the test beyond the expiration date stated on the pouch. Always check expiration date prior to performing test.
- DO NOT REUSE the test. Each test device is for single use only.
- Ensure finger is completely dry before performing fingerstick.
- Perform test procedure and read results in a well-lit area.

STORAGE AND STABILITY:

The ADEXUSDx® COVID-19 Tests should be stored in sealed pouches at 15 - 30°C (59 - 86°F) until the expiration date. DO NOT FREEZE. Do not open sealed pouch until you are ready to perform the test.

SPECIMEN COLLECTION:

The ADEXUSDx® COVID-19 Test must be performed on human whole blood or plasma (EDTA), or serum samples.

VENOUS WHOLE BLOOD (EDTA)

- In an EDTA tube, collect blood by following laboratory procedure for venipuncture.
- Venous whole blood samples may be stored at room temperature for up to 4 hours prior to testing.
- Venous whole blood samples may be refrigerated for up to 3 days prior to testing.
- Venous whole blood must NOT be frozen.

PLASMA (EDTA)

- In an EDTA tube, collect blood by following laboratory procedure for venipuncture.
- Process blood to obtain plasma.
- Plasma samples must be refrigerated if not tested immediately after collection.
- Plasma samples may be refrigerated for up to 3 days prior to testing.
- Plasma samples must be frozen at -20°C (-4°F) or colder if not tested within 3 days post collection.

SERUM

- In an appropriate tube (no anticoagulant), collect blood by following laboratory procedure for venipuncture.
- Process blood to obtain serum.
- Serum samples must be refrigerated if not tested immediately after collection.
- Serum samples may be refrigerated for up to 3 days prior to testing.
- Serum samples must be frozen at -20°C (-4°F) or colder if not tested within 3 days post collection.

SPECIMEN SHIPPING:

If venous whole blood, serum, or plasma specimens are to be shipped, they should be packed in compliance with regulations covering the transportation of etiologic reagents. Venous whole blood samples, serum and plasma specimen should be shipped refrigerated with cold packs or wet ice.

TEST PROCEDURE:

Follow these instructions to get an accurate result. Failure to follow the instructions or modification to the test system instructions will result in the test no longer meeting the requirements for Emergency Use Authorization.

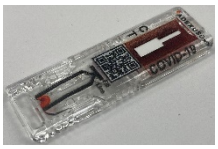
PREPARATION

1. Make sure you have a watch or timer ready.
2. If you wear contacts or glasses, make sure that you are wearing them when you read the result.
3. Wear gloves.

DIRECTIONS

1. Open test pouch

Open a sealed pouch containing one (1) ADEXUSDx® COVID-19 Test and desiccant packet. Remove the test from the pouch and discard the desiccant packet. **DO NOT REMOVE THE CAP.** Lay the test on a flat surface.

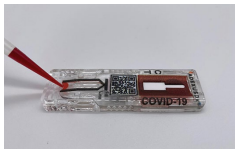


2. Collect the sample

Collect 40 µL of sample using a liquid transfer pipette.

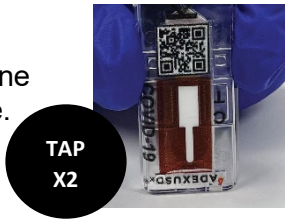
3. Apply the sample to the test

Apply the sample slowly into the Sample Application Zone until the Fill Zone is full and the Fill Line is reached. The transfer device should be at an angle as shown to minimize any air bubbles.



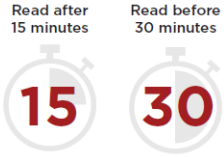
4. Tap the test twice

After filling the Fill Zone, hold the test with the Sample Application Zone facing up and tap the opposite end of the test twice on a hard surface. Then, lay the test on a flat surface.



5. Set a timer

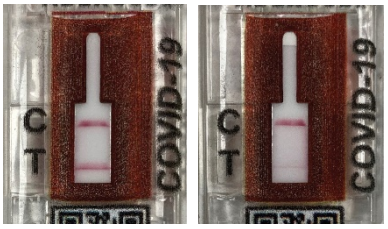
Set a timer for 15 minutes. Read the result after 15 minutes. Do not read the result after 30 minutes.



INTERPRETATION OF TEST RESULTS

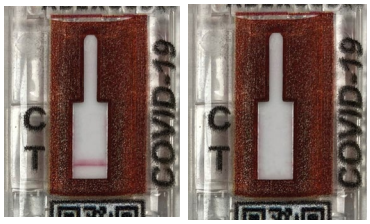
"C" & "T" Lines
Lines may appear at two locations, marked "C" and "T".
"C" stands for Control Line; it tells you if the test has worked.
"T" stands for Test Line; it tells you if the test is positive or not.

Positive Results
A positive result has TWO LINES, one at the "C" and one at the "T". The intensity of the lines may vary, so look carefully as **lines might be faint.**



Negative Result
A line at the "C" and no line at the "T" indicate a negative result.

Invalid Result
If NO line appears at the "C", the test has not worked. You must retest using a new test.



QUALITY CONTROL:

Procedure controls are intrinsic to the cassette. In addition, the ADEXUSDx® COVID-19 Control Set is available for use. It includes a positive and a negative plasma control. Both positive and negative controls should be tested on each new shipment of reagents.

LIMITATIONS OF PROCEDURE:

- Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions. The sensitivity of the test early after infection is unknown.
- False positive results may occur due to cross-reactivity from pre-existing antibodies or other possible causes.
- Samples with positive results should be confirmed with alternative testing method(s) and clinical findings before a diagnostic determination is made.
- A negative result can occur if the quantity of antibodies for the SARS-CoV-2 virus present in the specimen is below the detection limit of the assay, or if the virus has undergone minor amino acid mutation(s) in the epitope recognized by the antibody used in the test.

- A positive result may not indicate previous SARS-CoV-2 infection. Consider other information, including clinical history and local disease prevalence, in assessing the need for a second but different serology test to confirm an immune response.
- It is not known at this time if the presence of antibodies to SARS-CoV-2 confers immunity to reinfection.
- Correct performance of sample collection and storage is crucial for the test results.
- The test is qualified for use with whole blood or plasma (ETDA), and serum.
- The test should not be used for screening donated blood.

CONDITIONS OF AUTHORIZATION FOR THE LABORATORY:

The ADEXUSDx® COVID-19 Test Letter of Authorization, along with the authorized Fact Sheet for Healthcare Providers, the authorized Fact Sheet for Patients, and authorized labeling are available on the FDA website: **TBD by FDA**

Authorized laboratories using the ADEXUSDx® COVID-19 Test ("your product" in the conditions below), must adhere to the Conditions of Authorization indicated in the Letter of Authorization as listed below:

1. Authorized laboratories* using your product will include with test result reports, all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.
2. Authorized laboratories using your product will use your product as outlined in the Instructions for Use. Deviations from the authorized procedures, including the authorized clinical specimen types, authorized control materials, and authorized materials required to use your product are not permitted.
3. Authorized laboratories that receive your product will notify the relevant public health authorities of their intent to run your product prior to initiating testing.
4. Authorized laboratories using your product will have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
5. Authorized laboratories will collect information on the performance of your product and report to DMD/OHT7- OIR/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov) and NOWDiagnostics, Inc. (techsupport@nowdx.com) 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.
6. All laboratory personnel using your product must be appropriately trained in immunoassay techniques and use appropriate laboratory and personal protective equipment when handling this kit and use your product in accordance with the authorized labeling. All laboratory personnel using the assay must also be trained in and be familiar with the interpretation of results of the product.
7. Authorized distributors, and authorized laboratories using your product will ensure that any records associated with this EUA are maintained until otherwise notified by FDA. Such records will be made available to FDA for inspection upon request.

*The letter of authorization refers to, "Laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform moderate and high complexity tests" as "authorized laboratories."

PERFORMANCE EVALUATION:

CLINICAL AGREEMENT

Clinical performance of the ADEXUSDx® COVID-19 Test was evaluated with serum or plasma samples collected at clinical sites or donor collection centers from the following cohorts:

- 182 individuals who test positive for COVID-19
- 291 specimens collected prior to December 2019

Sensitivity:

Sensitivity was assessed using 182 serum and plasma specimens collected at clinical sites or donor collection centers from COVID-19 patients who tested positive with an emergency use authorized molecular test (PCR).* The samples were tested according to the ADEXUSDx® COVID-19 Test Instructions For Use (IFU) Transfer Device Method (Nonwaived).

*If present/known, other basic information related to sample population, comparator method, specimen collection date, date of onset of symptoms were collected.

Data analysis and conclusions:

Results with the ADEXUSDx® COVID-19 test and positive percent agreement (PPA) with the PCR results are recorded in **Tables 1 and 2**.

Table 1. ADEXUSDx® COVID-19 Test agreement with PCR test results

		PCR
		Positive
ADEXUSDx® COVID-19 Test	Positive	174
	Negative	8

Positive Percent Agreement (174/182) = 95.6% (91.6%,97.8%)

Table 2. Positive agreement by days post PCR test

Days post PCR test	Positive	Negative	PPA (95% CI)
≤7	131	7	94.9% (89.9%, 97.5%)
8 – 14	24	1	96.0% (80.5%, 99.3%)
15 – 21	13	0	100% (77.2%, 100.0%)
≥22	6	0	100% (61.0%, 100.0%)

Additional Sensitivity Study:

Two hundred EDTA plasma samples, collected from convalescent plasma donors who had documented SARS-CoV-2 disease, yielded a sensitivity of 98% (196/200) using the ADEXUSDx® COVID-19 Test.

Specificity

Specificity was assessed with 291 serum and plasma specimens collected prior to December 2019 (prior to the COVID-19 pandemic) and sourced from commercial vendors in the United States. The samples were tested according to the ADEXUSDx® COVID-19 Test Instructions For Use (IFU) Transfer Device Method (Nonwaived).

Data analysis and conclusions:

Results with the ADEXUSDx® COVID-19 test and negative percent agreement (NPA) between results obtained from the ADEXUSDx® COVID-19 Test and PCR results are recorded in **Table 3**.

Table 3. ADEXUSDx® COVID-19 Specificity Results

		Specimens prior to December 2019
ADEXUSDx® COVID-19 Test	Positive	5
	Negative	286

Negative Percent Agreement (286/292) = 98.3% (96.0%,99.3%)

Combining the results of Specimens Collected Prior to 2019 (**Table 3**) and the potential Cross-Reactant specimens (**Table 6**) gives an overall specificity of 98.5% (326/331).

Positive and Negative Predictive Values

Positive and Negative Predictive values (PPV and NPV) are calculated based on the sensitivity of 95.6% and overall specificity of 98.5% using an assumed prevalence of 5%.

PPV: 77.1% (58.3%, 88.8%)

NPV: 99.8% (99.5%, 99.9%)

MATRIX EQUIVALENCY

The equivalency of matrices and their effect on the performance of the ADEXUSDx® COVID-19 Test were evaluated using prospectively collected matched EDTA plasma (reference matrix), EDTA venous whole blood, and serum specimens from five (5) asymptomatic donors who tested negative for SARS-CoV-2 with an EUA molecular assay and 5 positive EDTA plasma specimens obtained retrospectively. Each EDTA plasma positive specimen was spiked into one of the EDTA plasma negative specimens to achieve low positive and moderate positive samples. The EDTA plasma positive specimens were also spiked into the matched EDTA venous whole blood and serum negative specimens at the same dilutions factors as the low positive and moderate positive samples with the reference matrix. Each spiked sample retained >= 90% of the original specimen matrix. The prepared samples as well as the original negative specimens in

each matrix were tested in duplicate randomly by two operators who were blinded to the sample information. The results of the EDTA venous whole blood and serum specimens and spiked samples were compared to the results of the matched EDTA plasma specimens and spiked samples for each subject. We have reported both positive and negative percent agreement for each matrix with respect to the reference matrix in **Tables 4 and 5**.

Table 4. ADEXUSDx® COVID-19 Test Equivalency of Results Between Matched Serum and EDTA Plasma Matrices

		EDTA Plasma	
		Positive	Negative
Serum	Positive	40	0
	Negative	0	20

Positive Percent Agreement (40/40) = 100%
Negative Percent Agreement (20/20) = 100%

Table 5. ADEXUSDx® COVID-19 Test Equivalency of Results Between Matched Venous Whole Blood and EDTA Plasma Matrices

		EDTA Plasma	
		Positive	Negative
Venous Whole Blood	Positive	40	0
	Negative	0	20

Positive Percent Agreement (40/40) = 100%
Negative Percent Agreement (20/20) = 100%

CROSS-REACTIVITY

Cross-reactivity of the ADEXUSDx® COVID-19 Test has been evaluated by testing serum and plasma samples positive for the potential cross-reactants in **Table 6**, which were banked prior to December 2019 and sourced from commercial vendors.

Cross-reactivity was assessed using serum and plasma from individuals with underlying diseases in the acute or convalescent stages of infection for the underlying condition. Some samples, as indicated in Table 3 were positive for multiple potential cross-reactants. Devices from 1 lot were used in this study. No reactivity was detected with the cross reactants (see results in **Table 6**).

Table 6. List of potential cross-reactants with SARS-CoV-2 and performance of the ADEXUSDx® COVID-19 Test in cross-reactivity study.

Potential cross-reactant*	**Results**		
	n	**+**	**-**
ANA	5	0	5
Anti-Coronavirus NL63	4	0	4
Anti-Coronavirus 229E	5	0	5

Anti-Hepatitis B	5	0	5
Anti-Hepatitis C	5	0	5
Anti-Influenza A	6	0	6
Anti-Influenza B	6	0	6
Anti-RSV IgG	5	0	5
Anti-RSV IgM	6	0	6
Total	**47**	**0**	**47**

**One sample contained potential reactants anti-RSV IgM and anti-coronavirus 229E. One sample contained potential reactants anti-RSV IgG, anti-RSV IgM and anti-coronavirus 229E. Three samples contained potential reactants anti-Influenza A and anti-Influenza B. One sample contained potential reactants anti-Influenza B and anti-RSV IgM.*

INQUIRIES AND GENERAL INFORMATION:

Visit website c19development.com/

ORDERING INFORMATION:

Laboratories may contact c19development.com/order/ to place an order.

TECHNICAL INFORMATION:

Email techsupport@nowdx.com

MANUFACTURER:

NOWDiagnostics, Inc.
1200 Stewart Place
Springdale, AR 72764
Phone: 1-844-207-3370
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Website: www.nowdx.com

AUTHORIZED REPRESENTATIVE:

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Via Campobello, 1 – 00071 Pomezia
Roma (Italy)
Phone: +39 06 87678028

SYMBOL LEGEND:

	Do Not Reuse
	Use by or Expiration Date
	Catalog Number or Product Code
	Manufacturer
	Consult Instructions for Use
	Store between 15°C – 30°C

IVD	For in vitro diagnostic use only
LOT	Lot Number
Σ	Tests per kit
EC REP	Authorized Representative