Celltrion DiaTrust™ COVID-19 Ag Home Test

Healthcare Provider Instructions for Use

For use under the Emergency Use Authorization (EUA) only

For in vitro diagnostic use

[INTENDED USE]

Celltrion DiaTrust™ COVID-19 Ag Home Test is a lateral flow immunoassay intended for the qualitative detection of nucleocapsid protein and receptor binding domain (RBD) antigens from SARS-CoV-2. This test is authorized for non-prescription home use with self-collected and adult-collected mid-turbinate nasal swab samples from individuals 14 years or older. This test is authorized for individuals with symptoms of COVID-19 within the first seven (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 Celltrion DiaTrust™ COVID-19 Ag Home Test does not differentiate between SARS-CoV and SARS-CoV-2.

Results are for the identification of SARS-CoV-2 nucleocapsid and RBD protein antigens which are generally detectable in mid-turbinate 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 and the agent detected may not be the definitive cause of disease. Individuals who test positive with the Celltrion DiaTrust™ COVID-19 Ag Home 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. 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 (LVID) Test Code Mapping for SARS-CoV-2 Tests provided by CDC.

The Celltrion DiaTrust™ COVID-19 Ag Home Test is intended for non-prescription self-use or an adult testing another person 14 years or older in a non-laboratory setting. The Celltrion DiaTrust™ COVID-19 Ag Home Test is only for in vitro diagnostic use under the Food and Drug Administration's Emergency Use Authorization. This product has not been FDA cleared or approved.

[SUMMARY AND EXPLANATION]

Coronavirus is a group of viruses that belongs to the Family Coronaviridae; a type of RNA virus of 27 - 32 kb commonly found in birds and mammals including human. Coronavirus is divided into four genera: alpha, beta, gamma and delta. The virus causes illness ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV).

Coronavirus disease 2019 (COVID-19) is a new strain caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The disease originated from Wuhan city of China in December 2019. The World Health Organization (WHO) publicly named this virus 'COVID-19' and declared it a pandemic and a Public Health Emergency of International Concern. The infection is typically spread from one person to another via direct contact or respiratory droplets from cough or sneeze. Latent period from exposure to onset of symptoms is between one to fourteen days (four to seven days on average). Common symptoms and signs of infection include fever, cough, shortness of breath and breathing difficulties. In severe cases, infections can cause pneumonia, severe acute respiratory syndrome, kidney failure and even death.

Due to the wide variety of symptoms, it is difficult to differentiate COVID-19 from other existing respiratory viruses or bacteria. Diagnosing COVID-19 through isolating the virus or detecting specific genes from the collected respiratory droplet specimens is a challenge in terms of time and accessibility as it requires long hours, well-equipped laboratory and advanced technology which are often not available to many public. The test is designed to detect antigen to SARS-CoV-2, and it will help assess if an individual has COVID-19 antigen within 15 minutes r.

[TEST PRINCIPLE]

The Celltrion DiaTrust™ COVID-19 Ag Home Test is a lateral flow immunoassay test. The Celltrion DiaTrust™ COVID-19 Ag Home Test is designed to detect antigens from the SARS-CoV-2 from direct mid-turbinate swab samples from symptomatic individuals for serial testing for use at least twice over three days with at least 48 hours between tests or asymptomatic individuals (without symptoms or other epidemiological reasons to suspect COVID-19) for serial testing for use at least three times over five days with at least 48 hours between tests. This test is also authorized to detect antigens from the SARS-CoV-2 from direct mid-turbinate swab samples from individuals aged 14 years or older with symptoms of COVID-19 within the first seven days of symptom onset. This test is authorized for non-prescription home use with mid-turbinate nasal swab specimens from individuals aged 14 years and older. The Celltrion DiaTrust™ COVID-19 Ag Home Test is validated for use from direct specimens testing without transport media.

A nitrocellulose membrane strip in the device having a test line and a control line, wherein the test line is pre-coated with anti-mouse monoclonal antibody to SARS-CoV-2 to detect SARS-CoV-2 nucleocapsid and RBDs from the SARS-CoV-2 spike proteins, and the control line is coated with goat anti-mouse IgG. When the extracted swab specimen is dispensed into to the sample well, the specimen migrates towards the conjugate pad, which contains conjugated antibodies with colloidal gold directed against the SARS-CoV-2 antigen. When the sample contains SARS-CoV-2 antigens, an antigen-antibody-conjugate complex is formed. The sample-conjugate complex then passes over the membrane until it reaches the capture zone (test line). Here, the complex is bound to immobilized antibodies and form visible colored band in the test line. The sample then migrates across the membrane along the strip until it reaches the control line where excess conjugate binds and produces a second visible line on the membrane. This control line indicates that the sample has migrated across the membrane as intended and indicates that the test was correctly performed. This test does not use biotin-Streptavidin/avidin chemistry in any of the steps for coupling reagents.

[MATERIALS SUPPLIED]

Kit components	Quantity			
	1 Test Kit	2 Tests Kit	5 Tests Kit	25 Tests Kit
Test cassette with test strip	1 ea/box	2 ea/box	5 ea/box	25 ea/box
Extraction buffer (0.3 mL / test tube)[1]	1 ea/box	2 ea/box	5 ea/box	25 ea/box
Filter cap	1 ea/box	2 ea/box	5 ea/box	25 ea/box
Swab	1 ea/box	2 ea/box	5 ea/box	25 ea/box
Instructions for Use	1 ea/box	1 ea/box	1 ea/box	1 ea/box

[1] Extraction buffer is provided in the sealed test tube.

[MATERIALS REQUIRED BUT NOT PROVIDED]

- Celltrion DiaTrust™ COVID-19 Ag Home Test Application (Celltrion SafeKey)
- Smartphone for using App, Celltrion SafeKey (Android 10 or newer, iOS 14.2 or newer)
- Compatible computer for web-based App (https://celltrion.safekey.tools)

[WARNINGS, PRECAUTIONS, AND SAFETY INFORMATION]

- For in vitro diagnostic use only
- Read all instructions carefully before performing the test. Failure to follow the instructions may result in inaccurate test results.
- In the USA, this product has not been FDA cleared or approved, but has been authorized by FDA under an Emergency Use Authorization (EUA). 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.
- Wear a safety mask or other face-covering when collecting a specimen from a child or another individual.
- Do not use this test for individuals under 14 years of age. The swab included in the kit is designed for collection of samples from adults and additional safety measures are needed for safe collection in children under 14 years of age.
- A mid-turbinate nasal swab sample can be self-collected by an individual age 14 years and older.
- All the results within the United States and its territories are required to be reported to the appropriate public health authorities.
- This product has been authorized only for the detection of proteins from SARS-CoV-2, not for any

other viruses or pathogens.

- Do not use the kit past its expiration date.
- Keep sealed until usage, and once opened use immediately.
- Test samples immediately after collection.
- Do not use the test device if the pouch is damaged or open.
- Test components are single-use. Do not re-use the device.
- This test is intended for diagnosis of coronavirus infection by detecting COVID-19 antigen, but should not be used as a sole criterion for the determination of SARS-CoV-2 infection. Other laboratory tests and clinical information (signs and symptoms) should be used and considered for diagnosis.
- Inadequate or inappropriate sample collection may yield false test results.
- To obtain accurate results, the test must be performed as indicated in this Instructions for Use
- Once opened, the test card should be used within 1 hour.
- **Do not read test results before 15 minutes or after 20 minutes. Results read before 15 minutes or after 20 minutes may lead to a false positive, false negative or invalid result.**
- Inadequate or improper nasal swab sample collection may result in false negative test results.
- Do not touch the swab tip.
- **Keep testing kit and kit components away from children and pets before and after use. Avoid contact with skin and eyes. Do not ingest any kit components. The reagent solution contains harmful chemicals (see table below). If the solution contacts your skin and eyes, flush with large amounts of water. If irritation persists, seek medical advice: https://www.poisonhelp.org or 1-800-222-1222.**

Chemical Name (CAS)	Material Safety Data Sheet	GHS Code for each ingredient	Conc.
Sodium Azide (26628-22-8)	Material Safety Data Sheet	Acute Tox.2 (oral), H300 Acute Tox.1 (dermal), H310	0.09%

- Discard Celltrion DiaTrust™ COVID-19 Ag Home Test in accordance with local, state and federal regulations or accreditation requirements.
- 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

[LIMITATIONS]

- There is a higher chance of false negative results with antigen tests than with laboratory-based molecular tests. This means that there is a higher chance this test will give you a false negative result in an individual with COVID-19 as compared to a molecular test, especially in samples with low viral load.
- Serial testing (i.e., testing every day or every other day) is more likely to detect COVID-19, especially when you do not have any symptoms.
- This test detects both viable (live) and non-viable 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.
- A negative test result may occur if the level of antigens in a sample is below the detection limit of the test or if the sample was collected or transported improperly.
- Failure to follow the Test Procedure may adversely affect test performance and/or invalidate the test result.
- Test results must be evaluated in conjunction with other clinical data available to the physician.

- Positive test results do not rule out co-infections with other pathogens.
- This test is read visually and has not been validated for use by those with impaired vision of color-impaired vision.
- Incorrect test results may occur if a specimen is incorrectly collected or handled.
- Negative test results are not intended to rule in other non-SARS-CoV-2 viral or bacterial infections.
- 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.
- If the differentiation of specific coronaviruses and strains is needed, additional testing, in consultation with state or local public health departments, is required.
- The amount of antigen in a sample may decrease as the duration of illness increases. Specimens collected after seven days are more likely to be negative compared to RT-PCR.
- The performance of this test was established based on the evaluation of a limited number of clinical specimens collected between March and July of 2021. 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.
- The Celltrion DiaTrust™ COVID-19 Ag Home Test does not differentiate between SARS-CoV and SARS-CoV-2.

[REAGENT STORAGE AND STABILITY]

An unopened test device should be stored at 2-30°C (36-86°F). The shelf-life of the test device is stable until the expiration date marked on the label. An opened test device is stable up to 1 hour after released from the aluminum pouch. If the tests were refrigerated, keep them at room temperature for 30 minutes prior to use. For the most current expiration dates of this test, please refer to: http://www.fda.gov/covid-tests.

[QUALITY CONTROL]

A procedural internal control is built in the 'control line (c)' of the device and is used to ensure that the applied specimen has migrated well into the device. It is coated with goat anti-mouse IgG and a red colored line will always appear when the test is performed properly.

External run controls are not required to use the Celltrion DiaTrust™ COVID-19 Ag Home Test.

[TEST PROCEDURE]

When opening the test device, download the mobile application (Celltrion SafeKey) using QR code from Instructions for Use provided with the test kit and follow the instructions as described in the mobile application.

1. Test Preparation

   Following the instruction in the mobile application, when you are ready to proceed with the test, tear open the two aluminum pouches.

1) Prepare the aluminum pouch containing the test device and place it on the testing surface along with the reagents from the second aluminum pouch - test tube filled with the extraction buffer and filter cap. In case the tests were refrigerated, keep them ambient for 30 minutes to let it reach the room temperature.

** Testing should be completed within 30-60 minutes of opening the pouch.*

2) Remove the test device, test tube and filter cap from the aluminum pouches and place it on a flat surface just prior to starting test.

3) Scan the QR code on the test device through your mobile phone camera. If you are having difficulty scanning the QR on the test device, you may type the serial number into the input box on the application page. The serial number is printed on the test device.

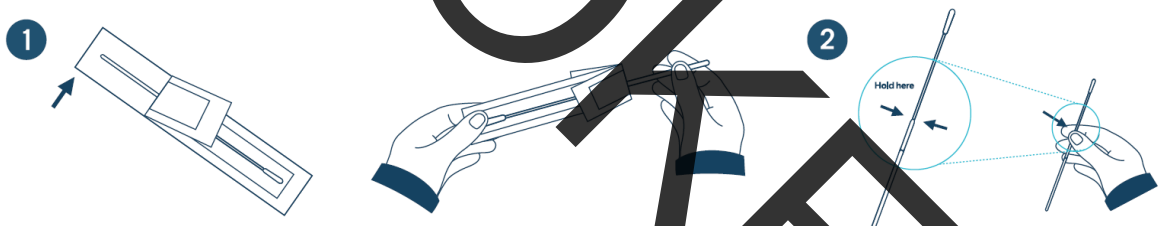
4) Fill out the requested personal information and symptoms about the person who will be tested.

2. Specimen collection (CDC guideline):

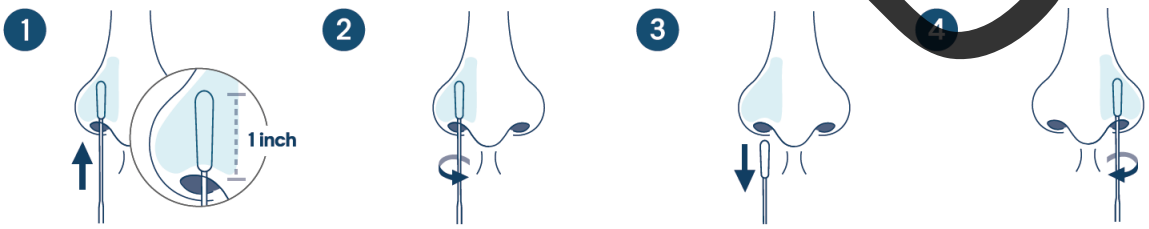
Use only the swabs provided with the test kit (FA/FANAB01 and Miraclean Technology, Item No. 96000) for specimen collection following the instruction on the mobile application.

1) Make sure extraction buffer tube and filter cap are also readily available before starting sample collection, as the collected swab sample must be immediately inserted into the extraction buffer tube for sample extraction. After swabbing, immediately insert the swab into extraction buffer tube. Do not leave the sampled swab dry in open air as it may result in incorrect test results.

2) Peel open the swab package and take the swab out. Do not touch the soft tip or lay it down on any surfaces. Hold the swab near the middle where it's thin (at the second notch; refer to image below).



3) Insert the entire soft end of the swab straight back into your nostril less than one inch (about 2cm) or until resistance is felt. Slowly swirl the swab, gently rubbing it along the insides of your nasal passage several times. Gently remove the swab. Using the same swab, repeat this process in your other nostril.



Note: The swab included in the kit is designed for collection of samples from adults. Do not collect swabs from children under 14 years of age.

3. Test method

1) Put the tip of the swab into the test tube. Move the swab up and down at least 10 times to

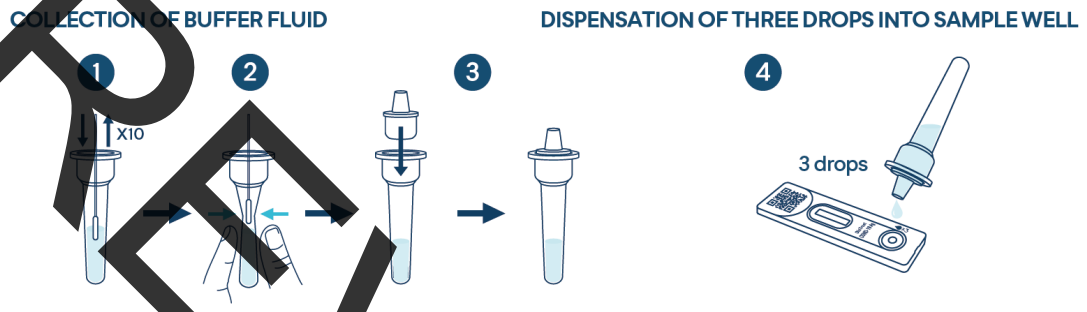
properly mix the fluid.

2) Squeeze the tube while removing the swab to squeeze out as much liquid from the swab as possible.

Note: *False negative results can occur if the specimen is not properly mixed or too vigorously mixed.*

3) Place the filter cap on the test tube.

4) Immediately dispense three drops of the sample extract (100 µL) into the well at the bottom of the test device. On the mobile application, tap the "Completed" button to start a 15-minute timer.



** If you have dropped the test device after sample application, please discard the test device and restart the test using a new test device.*

Note: *Adding only one drop of solution or the entire vial may result in false negative results.*

5) Read results at 15 minutes after applying the sample. Do not read results after 20 minutes. On the mobile application, images of four potential results will be displayed. Click the image that best represents your result for the presence of red colored lines in the device window next to each of the two letters, C (Control) and T (Test). Follow the instructions based on your test result.

Note: False negative or false positive results can occur if results are read before 15 minutes or after 20 minutes.

6) Dispose the remainder of the test in general waste.

[INTERPRETATION OF RESULTS]

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

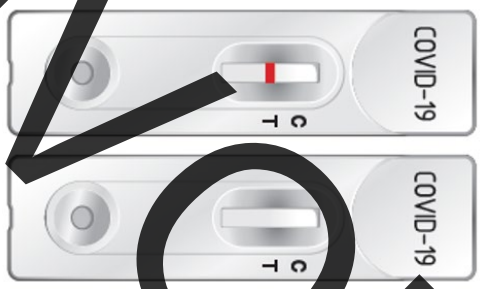
Results should be considered in the context of an individual's recent exposures, history, and the presence of clinical signs and symptoms consistent with COVID-19.

- Negative result: If no red colored line appears in the test line (T) and a red colored line is present on the control region (C), then the result is negative. A negative result indicates viral antigens were not detected in the specimen and the individual is presumed negative for COVID-19.
    - **To increase the chance that the negative result for COVID-19 is accurate, you should:**
        - **Test again in 48 hours if you have symptoms on the first day of testing.**
        - **Test 2 more times at least 48 hours apart if you do 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 disease 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.

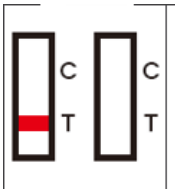
- Positive result: If red colored line is visible in the test line (T) and control line (C), the result is positive. A positive result indicates that viral antigens from COVID-19 were present in the specimen and the individual is positive for COVID-19.
    - **Repeat testing does not need to be performed 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 Celltrion DiaTrust™ COVID-19 Ag Rapid 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.

- Invalid result: If there is no red colored line in the control region (C), the result is invalid.
  - In case of an invalid test result: Re-test with a new swab and new test device. If the test result is still invalid, contact your doctor or local COVID-19 center. An invalid result does not indicate if the individual did or did not have COVID-19 and should be repeated.



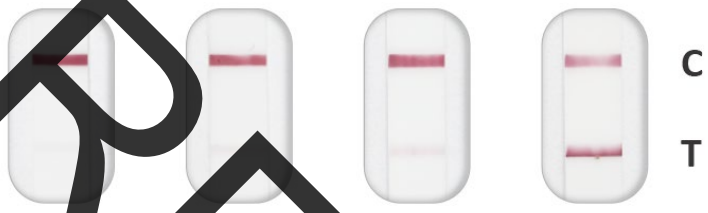
	**COVID-19 NEGATIVE (-)** If no red colored line appears in the test line (T Line Level 0) and a red colored line is present on the control region (C Line Level 1 ~ 11), then the result is negative. **To increase the chance that the negative result for COVID-19 is accurate, you should:** **· Test again in 48 hours if you have symptoms on the first day of testing.** **· Test 2 more times at least 48 hours apart if you do 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 your sample. A negative result is presumptive, meaning it is not certain that you do not have COVID-19. You may still have COVID-19 and you may still be contagious. There is a higher chance of false negative results with antigen tests compared to laboratory-based tests such as PCR. If you test negative and continue to experience COVID-19-like symptoms, (e.g., fever, cough, and/or shortness of breath) you should seek follow up care with your health care provider.
	**COVID-19 POSITIVE (+)** If a red colored line is visible in the test line (T Line Level 1 ~ 11) and control line (C Line Level 1 ~ 11), the result is positive. You do not need to perform repeat testing if you have a positive result at any time. A positive test result means that the virus that causes COVID-19 was detected in your sample and it is very likely you have COVID-19 and are contagious. Please contact your doctor/primary care physician or your local health authority immediately and 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).



INVALID

If there is no red colored line in the control region (C Line Level 0), the result is invalid. Re-test with a new swab and new test device.

These are photos of actual positive results. Please note that the test line can show up faintly. This faint line still indicates a positive result.



[PERFORMANCE CHARACTERISTICS]

Analytical testing is conducted with the nasopharyngeal swab specimen, and the matrix equivalency study is conducted to support mid-turbinate nasal swab as the specimen type.

1) Limit of detection (LoD)

LoD studies determine the lowest detectable concentration of SARS-CoV-2. The LoD was determined by limiting dilution studies using SARS-CoV-2 virus inactivated by beta-Propiolactone (BPL).

Negative sample was prepared by collecting nasopharyngeal swab samples from healthy donors (negative clinical matrix) eluted in PBS.

The positive standard materials are prepared with the six different concentrations of SARS-CoV-2 inactivated virus (Conc. 6.3×10^5 $TCID_{50}$/mL, NMC-nCoV02 #24) that is serially diluted in PBS and negative clinical matrix.

The diluted positive standard materials are applied to the swab tip with 100 µL of approximate absorption volume. The extraction buffer tubes are prepared and each swab samples are inserted into each extraction buffer tubes. The swab was moved up and down inside the tube 10 times and taken out by pressing to remove the extracted liquid. The filter cap was equipped onto the test tube, then three drops of extracts (100 µL) was dispensed into the sample inlet. The result was read 15 minutes after applying the sample.

Serial dilutions of the inactivated SARS-CoV-2 were tested in 5 replicates. The lowest concentration at which all 5 replicates were positive was treated as the tentative LoD for each test. Based on this testing, the tentative LoD was 3.2×10^1 $TCID_{50}$/mL.

The LoD of each test was then confirmed by testing 20 replicates with concentrations near the tentative limit of detection. The final LoD of Celltrion DiaTrust™ COVID-19 Ag Home Test was determined to be the lowest concentration resulting in positive detection more than 95% of the time, which is at least 19 out of 20 replicates.

In conclusion, the limit of detection (LoD) of Celltrion DiaTrust™ COVID-19 Ag Home Test for NP swab is 3.2×10^1 $TCID_{50}$/mL. Based upon the testing procedure for this study the LoD of 3.2×10^1 $TCID_{50}$/mL equates to 3.2×10^0 $TCID_{50}$/swab.

2) **OMICRON TESTING**

The performance of this test device in the detection of the Omicron variant of SARS-CoV-2 was evaluated in a dilution series of clinical specimens which were positive for the Omicron variant. This testing was conducted by the National Institutes of Health (NIH) as a component of the Rapid Acceleration of Diagnostics (RADx®) initiative. Specimen pools were prepared by the RADx team using clinical pooled samples from currently circulating Omicron strains and tested by RADx to assess performance with the Omicron variant. Results from this dilution series cannot be compared to other specimen 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 Celltrion™ DiaTrust Covid-19 Ag Home Test detected 100% of live virus Omicron samples at a Ct-value of 23.3 (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 23.3) were not detected by the Celltrion diatrust Covid-19 Ag Home Test in this study.

Omicron Pool 1 – Live Omicron Clinical Samples	Ct N2 Avg (N=9)	Assay#1 Percent Positive N=5	Assay#2 Percent Positive N=5	Celltrion Diatrust Percent Positive N=5
Dilution 1	19.4	100	100	100
Dilution 2	20.6	100	100	100
Dilution 3	21.6	100	100	100
Dilution 4	22.4	100	100	100
Dilution 5	23.3	100	100	100
Dilution 6	24.5	0	100	0
Dilution 7	25.6	0	100	0
Dilution 8	26.5	0	0	0
Dilution 9	27.7	0	0	0
Dilution 10	28.5	0	0	0
Dilution 11	29.4	0	0	0
Dilution 12	30.3	0	0	0

3) Cross-reactivity (Analytical specificity) and Microbial Interference Studies

Wet-testing:

The study was performed to evaluate the cross-reactivity of the Celltrion DiaTrust™ COVID-19 Ag Home Test.

Nasopharyngeal swab sample from healthy donors (negative clinical matrix) were collected and eluted in extraction buffer to be used as a negative standard material. For each test, the diluted sample was added to a sterile nasal swab before conducting the test according to the instruction for use. Positive standard materials (NMC-nCoV02 #24, 6.3×10^5 $TCID_{50}$/mL) were spiked into negative sample and were diluted to make low concentration level (6.3×10^1 $TCID_{50}$/mL, approx. 2xLoD) for testing.

Potential cross-reactive organisms listed in the below table were prepared at the concentration of 10^5

PFU/mL or higher for viruses and 10^6 CFU/mL or higher for bacteria. They were spiked into the negative and low positive samples and were tested in 3 replicates. A total of 31 pathogens listed in the below table showed no cross-reactivity with the Celltrion DiaTrust™ COVID-19 Ag Home Test.

List of organisms		**Testing conc.**	**Test result**	
			Negative (No. of negative/ No. of replicates)	**Low Positive** (No. of positive/ No. of replicates)
Other high priority pathogens from the same virus family	Coronavirus OC43	4.4×10^7 PFU/mL	3/3	3/3
	Coronavirus 229E	3×10^6 PFU/mL	3/3	3/3
	Coronavirus NL63	1×10^5 $TCID_{50}$/mL	3/3	3/3
	MERS-coronavirus	1.183×10^5 $TCID_{50}$/mL	3/3	3/3
Other high priority organisms	Human adenovirus 1	7×10^7 PFU/mL	3/3	3/3
	Human adenovirus 3	2.4×10^6 PFU/mL	3/3	3/3
	Human adenovirus 5	4.0×10^7 PFU/mL	3/3	3/3
	Human adenovirus 7	2.0×10^8 PFU/mL	3/3	3/3
	Respiratory syncytial virus A	8.0×10^5 PFU/mL	3/3	3/3
	Respiratory syncytial virus B	2.4×10^6 PFU/mL	3/3	3/3
	Parainfluenza 1	2.8×10^5 PFU/mL	3/3	3/3
	Parainfluenza 2	2×10^7 PFU/mL	3/3	3/3
	Parainfluenza 3	8×10^5 PFU/mL	3/3	3/3
	Parainfluenza 4a	1.3×10^8 PFU/mL	3/3	3/3
	Rhinovirus 1	1.4×10^5 PFU/mL	3/3	3/3
	Metapneumovirus	6×10^5 PFU/mL	3/3	3/3
	Human enterovirus	1×10^5 PFU/mL	3/3	3/3
	Influenza A H1N1	2×10^5 PFU/mL	3/3	3/3
	Influenza A H3N2	4.9×10^6 PFU/mL	3/3	3/3
	Influenza B	1×10^6 PFU/mL	3/3	3/3
	Mycoplasma pneumonia (whole organism)	1×10^7 CFU/mL	3/3	3/3
	Streptococcus pyogenes	1×10^6 CFU/mL	3/3	3/3
	Bordetella pertussis	1×10^6 CFU/mL	3/3	3/3
	Streptococcus pneumoniae	1×10^6 CFU/mL	3/3	3/3
	Legionella pneumophila	1×10^6 CFU/mL	3/3	3/3
	Haemophilus influenzae	1×10^6 CFU/mL	3/3	3/3
	Candida albicans	1×10^6 CFU/mL	3/3	3/3
	Chlamydia pnuemoniae	2.0×10^7 $TCID_{50}$/mL	3/3	3/3
	Pooled human nasal wash	100%	3/3	3/3

List of organisms		Testing conc.	Test result	
			Negative (No. of negative/ No. of replicates)	**Low Positive** (No. of positive/ No. of replicates)
	Staphylococcus epidermidis	1×10^6 CFU/mL	3/3	3/3
	Staphylococcus aureus	1×10^6 CFU/mL	3/3	3/3

In-silico:

To estimate the likelihood of cross-reactivity with SARS-CoV-2 virus in the presence of organisms that were not available for wet testing, *in silico* analysis was used to assess the degree of protein sequence homology.

- Human coronavirus HKU1: 25% homology was found between SARS-CoV-2 Receptor Binding Domain spike proteins and HKU1 spike protein, and 44% homology was found between SARS-CoV-2 Nucleocapsid protein and HKU1 Nucleocapsid protein. Therefore, cross-reactivity cannot be ruled out.
- *Pneumocystis jirovecii*: No significant similarity was found between SARS-CoV-2 RBD spike protein / nucleocapsid protein and *P. jirovecii*. But minor similarity was found between some partial proteins of P. jirovecii RU 7and SARS-CoV-2 RBD spike protein / nucleocapsid protein. Therefore, cross-reactivity cannot be ruled out.
- *Mycobacterium tuberculosis*: No significant similarity was found between *M. tuberculosis* and SARS-CoV-2 RBD spike protein / nucleocapsid protein despite of increasing expect threshold.
- SARS-CoV: 72% homology was found between SARS-CoV-2 Receptor Binding Domain spike proteins and SARS-CoV spike protein, and 96% homology was found between SARS-CoV-2 Nucleocapsid protein and SARS-CoV Nucleocapsid protein. Therefore, cross-reactivity is highly likely.
- The Celltrion DiaTrust™ COVID-19 Ag Home Test does not differentiate between SARS-CoV and SARS-CoV-2.

4) Endogenous interference substances study:

Test to evaluate interference of the Celltrion DiaTrust™ COVID-19 Ag Home Test was performed.

Extraction buffer was used as negative sample. Positive standard materials were spiked into negative sample and were diluted to make low concentration level (6.3×10^1 $TCID_{50}$/mL, approx. 2xLoD) for testing.

Potential interfering substances were added to the negative and positive samples and were tested using the Celltrion DiaTrust™ COVID-19 Ag Home Test in 3 replicates. The test results demonstrated that 48 interfering substances did not affect the performance of Celltrion DiaTrust™ COVID-19 Ag Home Test.

No.	Interfering substances	Testing conc.	Negative	Negative + Interfering substances	Low positive	Low pos. + Interfering substances
1	Whole blood	4%	3/3*	3/3*	3/3**	3/3**
2	Mucin	0.5%	3/3*	3/3*	3/3**	3/3**
3	Chloraseptic	1.5 mg/mL	3/3*	3/3*	3/3**	3/3**

No.	Interfering substances	Testing conc.	Negative	Negative + Interfering substances	Low positive	Low pos. + Interfering substances
4	NeilMed NasoGel	5% v/v	3/3*	3/3*	3/3**	3/3**
5	CVS Nasal drops	15% v/v	3/3*	3/3*	3/3**	3/3**
6	Afrin (Oxymetazoline)	15% v/v	3/3*	3/3*	3/3**	3/3**
7	Sodium cromoglycate (CVS nasal spray, Cromolyn)	15% v/v	3/3*	3/3*	3/3**	3/3**
8	Zicam	15% v/v	3/3*	3/3*	3/3**	3/3**
9	Homeopathic (Alkalol)	1:10 dilution	3/3*	3/3*	3/3**	3/3**
10	Sore throat Phenol Spray	15% v/v	3/3*	3/3*	3/3**	3/3**
11	Tobramycin	5 µg/mL	3/3*	3/3*	3/3**	3/3**
12	Mupirocin	10 mg/mL	3/3*	3/3*	3/3**	3/3**
13	Fluticasone Propionate	5% v/v	3/3*	3/3*	3/3**	3/3**
14	Tamiflu (Oseltamivir Phosphate)	5 mg/mL	3/3*	3/3*	3/3**	3/3**
15	Albumin, human	3000 mg/dL	3/3*	3/3*	3/3**	3/3**
16	Bilirubin	500 µmol/L	3/3*	3/3*	3/3**	3/3**
17	Hemoglobin	500 mg/dL	3/3*	3/3*	3/3**	3/3**
18	Cholesterol	20 µmol/L	3/3*	3/3*	3/3**	3/3**
19	Triglyceride	1000 mg/dL	3/3*	3/3*	3/3**	3/3**
20	Biotin	0.75 mg/mL	3/3*	3/3*	3/3**	3/3**
21	Sodium citrate	25 mg/mL	3/3*	3/3*	3/3**	3/3**
22	Heparin	100 U/mL	3/3*	3/3*	3/3**	3/3**
23	EDTA	5 µmol/L	3/3*	3/3*	3/3**	3/3**
24	K3-EDTA	20 mg/mL	3/3*	3/3*	3/3**	3/3**
25	Diphenhydramine hydrochloride	5 mg/mL	3/3*	3/3*	3/3**	3/3**
26	Acetaminophen	199 µmol/L	3/3*	3/3*	3/3**	3/3**
27	Acetylsalicylic acid	3.62 mmol/L	3/3*	3/3*	3/3**	3/3**
28	Ibuprofen	2.425 mmol/L	3/3*	3/3*	3/3**	3/3**
29	Olopatadine hydrochloride	5 mg/mL	3/3*	3/3*	3/3**	3/3**
30	Hanmi Ko-and-Cool Nasal Spray (Chlorpheniramine Maleate 250 mg/ 100 mL, Xylometazoline Hydrochloride 0.1 g/100 mL)	10%(v/v)	3/3*	3/3*	3/3**	3/3**
31	Samchundang Narista-S Nasal Spray (Chlorpheniramine Maleate 2.5 mg/mL, Dipotassium Glycyrrhizinate 3 mg/mL, Naphazoline	10%(v/v)	3/3*	3/3*	3/3**	3/3**

No.	Interfering substances	Testing conc.	Negative	Negative + Interfering substances	Low positive	Low pos. + Interfering substances
	Hydrochloride 0.5 mg/mL)					
32	Sodium chloride	20 mg/mL	3/3*	3/3*	3/3**	3/3**
33	Zanamivir	5 mg/mL	3/3*	3/3*	3/3**	3/3**
34	Oseltamivir	10 mg/mL	3/3*	3/3*	3/3**	3/3**
35	Artemether-lumefantrine	50 µmol/L	3/3*	3/3*	3/3**	3/3**
36	Doxycycline hyclate	70 µmol/L	3/3*	3/3*	3/3**	3/3**
37	Quinine	150 µmol/L	3/3*	3/3*	3/3**	3/3**
38	Lamivudine	1 mg/mL	3/3*	3/3*	3/3**	3/3**
39	Erythromycin	81.6 µmol/L	3/3*	3/3*	3/3**	3/3**
40	Ciprofloxacin	30.2 µmol/L	3/3*	3/3*	3/3**	3/3**
41	Rheumatoid factor positive plasma	20%(v/v)	3/3*	3/3*	3/3**	3/3**
42	Neutrogena lotion (glycerin)	1% (v/v)	3/3*	3/3*	3/3**	3/3**
43	Hand sanitizer (ethyl alcohol)	1% (v/v)	3/3*	3/3*	3/3**	3/3**
44	Hand soap (benzalkonium chloride)	1% (v/v)	3/3*	3/3*	3/3**	3/3**
45	Laundry detergent (C12-15 pareth-7 and sodium laureth-12 sulfate)	1% (v/v)	3/3*	3/3*	3/3**	3/3**
46	Bleach (sodium hypochlorite)	1% (v/v)	3/3*	3/3*	3/3**	3/3**
47	Surface sanitizer (citric acid)	1% (v/v)	3/3*	3/3*	3/3**	3/3**
48	Dish-washing liquid (sodium lauryl sulfate)	1% (v/v)	3/3*	3/3*	3/3**	3/3**

*: Negative / **: Positive

5) High-dose Hook effect

Pooled nasopharyngeal specimens were used as clinical matrix, and SARS-CoV-2 virus inactivated by beta-Propiolactone (BPL) was spiked to make various high concentration levels of SARS-CoV-2 antigens. Prepared samples of each concentration levels were tested using Celltrion DiaTrust™ COVID-19 Ag Home Test in 3 replicates following instructions.

No high-dose hook effect was observed up to 6.3×10^5 $TCID_{50}$/mL, approx. 20,000xLoD.

SARS-CoV-2 inactivated virus (6.3×10^5 $TCID_{50}$/mL)		
$TCID_{50}$/mL (concentration)	**Test results (No. of positives/ No. of replicates)**	
	Lot 1	**Lot 2**
3.2×10^1 [1xLoD]	3/3	3/3

1.3×10^2 [4xLoD]	3/3	3/3
1.5×10^4 [500xLoD]	3/3	3/3
6.3×10^5 [20,000xLoD]	3/3	3/3

6) Flex study

The robust use of Celltrion DiaTrust™ COVID-19 Ag Home Test was demonstrated by ten (10) Flex studies: temperature and humidity, delay in sample testing, delay in result reading, extraction buffer volume variability, swab mixing expression variability, disturbance during testing, testing on non-level surface, impact of light sources, test device held at 90° angle and disturbance during analysis - receiving a phone call while the mobile app is running.

7) Clinical performance

The clinical evaluation of the Celltrion DiaTrust™ COVID-19 Ag Home Test was evaluated by testing a total of 211 prospectively collected direct mid-turbinate nasal swab samples, consisted of 36 positive and 175 negative samples from individuals with signs and symptoms of COVID-19 in United States, aged 14 years and older at four clinical sites. Mid-turbinate nasal swabs were collected and tested by each study participant, eluted in the extraction buffer and tested with the device immediately, using only the QRI and App. Results of each samples were confirmed by FDA EUA RT-PCR.

According to the test results, clinical performance results of the Celltrion DiaTrust™ COVID-19 Ag Home Test was as follows:

Table 1. Demographic and Clinical Characteristics

Characteristic		Total number	Total Positive by RT-PCR	% Positive
Age Range	14-24	41	9	9/41 (22.0%)
	25-64	164	25	25/164 (15.2%)
	≥65	6	2	2/6 (33.3%)
Sex				
Female		110	14	14/110 (12.7%)
Male		101	22	22/101 (21.8%)
Total		211	36	36/211 (17.1%)

Table 2. Observations of Symptomatic Subjects

Symptomatic Data		Reference PCR Results		
		Positive	Negative	Total
DiaTrust™ COVID-19 Ag Home Test	Positive	31	1	32
	Negative	5	174	179
	Total	36	175	211

PPA: 86.1% (95% CI: 71.3% - 93.9%)

NPA: 99.4% (95% CI: 96.8% - 99.9%)

Table 3. PPA and NPA by days since onset of symptoms

Days since symptom onset	PPA (95% CI)	NPA (95% CI)
1	75.0% (3/4) (95% CI: 30.1% - 95.4%)	95.8% (23/24) (95% CI: 79.8% - 99.3%)
2	100.0% (8/8) (95% CI: 67.6% - 100.0%)	100.0% (40/40) (95% CI: 91.2% - 100.0%)
3	100.0% (9/9) (95% CI: 70.1% - 100.0%)	100.0% (38/38) (95% CI: 90.8% - 100.0%)
4	85.7% (6/7) (95% CI: 48.7% - 97.4%)	100.0% (30/30) (95% CI: 88.6% - 100.0%)
5	66.7% (2/3) (95% CI: 20.8% - 93.9%)	100.0% (24/24) (95% CI: 86.2% - 100.0%)
6	100.0% (2/2) (95% CI: 34.2% - 100.0%)	100.0% (12/12) (95% CI: 75.8%-100.0%)
7	33.3% (1/3) (95% CI: 6.1%-79.2%)	100.0% (7/7) (95% CI: 64.6%-100.0%)

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 4.

Table 4: 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 FIRIST 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.

[ASSISTANCE]

If you have any questions regarding the use of this product or if you want to report a test system problem, please contact Humasis Co., Ltd. (via email: info@humasis.com, via phone: +82-31-8085-6284) or Celltrion USA, Inc. (via email: celltrionusa.CS@celltrion.com, or via phone: (201) 499-1844). Test system problems may also be reported to the FDA through the MedWatch medical products reporting program (phone: 800.FDA.1088; fax: 800.FDA.0178; http://www.fda.gov/medwatch).

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