Celltrion DiaTrust™ COVID-19 Ag Rapid Test

Instructions for Use For Healthcare Providers

For use under the Emergency Use Authorization (EUA) only

For in vitro diagnostic use

For Prescription Use only

INTENDED USE

Celltrion DiaTrust™ COVID-19 Ag Rapid Test is a lateral flow immunoassay intended for the qualitative detection of nucleocapsid protein and receptor binding domain (RBD) protein antigens in direct mid-turbinate nasal swab specimens from individuals who are suspected of COVID-19 by their healthcare provider within the first seven (7) days of symptom onset when tested at least twice over three days with at least 48 hours between tests, or from 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. Testing is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet the requirements to perform high complexity, moderate complexity, or waived tests. This product is authorized for use at the Point of Care (POC), i.e., in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation.

The Celltrion DiaTrust™ COVID-19 Ag Rapid 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 nasal swab specimens during the acute phase of infection. Positive results indicate the presence of viral antigens, but clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. Positive results do not rule out bacterial infection or co-infection with other viruses and the agent detected may not be the definite cause of disease.

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

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 decisions such as isolating from others and wearing masks. Negative results should be considered in the context of a patient's recent exposures, history and the presence of clinical signs and symptoms consistent with COVID-19.

The Celltrion DiaTrust™ COVID-19 Ag Rapid Test is intended for use by healthcare professionals or operators who are proficient in performing tests in point of care settings. The Celltrion DiaTrust™ COVID-19 Ag Rapid 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.

TEST PRINCIPLE

The Celltrion DiaTrust™ COVID-19 Ag Rapid Test is a lateral flow immunoassay test. The Celltrion DiaTrust™ COVID-19 Ag Rapid Test is designed to detect antigen from the SARS-CoV-2 in human mid-turbinate nasal swab specimens from symptomatic individuals who are suspected of COVID-19 by their healthcare provider when serial tested twice over three days with at least 48 hours between tests, or from asymptomatic individuals (e.g., individuals without symptoms or other epidemiological reasons to suspect COVID-19), when serial tested at least three times over five days with at least 48 hours between tests. The Celltrion DiaTrust™ COVID-19 Ag Rapid 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.

MATERIALS PROVIDED

- Test devices packaged individually in aluminum pouch (25 test/box)
- Disposable test tube with 0.3 mL of extraction buffer (25 ea/box)
- Filter cap (25 ea/box)
- Sterilized swabs for specimen collection (25 ea/box)
- Quick reference instruction (1 ea)
- Positive control swab (1 ea/box)
- Negative control swab (1 ea/box)

MATERIALS REQUIRED BUT NOT PROVIDED

- Timer
- Any necessary personal protective equipment

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.

SPECIMEN STORAGE AND STABILITY

Swab specimens should be tested immediately after collection. If immediate testing is not possible, specimens should be stored immediately into extraction buffer and may be stored for up to 4 hours until testing. If testing cannot be performed within this time, a new specimen should be collected and tested.

QUALITY CONTROL

An external positive control is needed to confirm that the device performs as intended and that the test procedure is conducted correctly. 0.1 µg/mL of non-infectious recombinant SARS-CoV-2 RBD antigen and 0.1 µg/mL non-infectious recombinant SARS-CoV-2 nucleoprotein antigen is dried onto the swab. This control swab should be tested once with every new lot and shipment, on a daily basis, for each new user, or according to the quality control procedures established for each laboratory.

A sterile swab is included as an external negative control to confirm that the device performs as intended and that the test procedure is conducted correctly. This control swab should be tested once with every new lot and shipment, on a daily basis, for each new user, or according to the quality control procedures established for each laboratory.

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 and the test procedure was properly done. It is coated with goat anti-mouse IgG and a colored line will always appear when the test is performed properly.

CHEMICAL HAZARD AND SAFETY INFORMATION

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).

Hazardous ingredients for the extraction buffer

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%

The extraction buffer solution in the extraction buffer tube contains a hazardous ingredient as shown in above table. If the extraction buffer solution contacts your skin or eye, flush with large amounts of water. . In case the irritation persists, please seek medical advice at: https://www.poisonhelp.org or 1-800-222-1222

PRECAUTIONS AND WARNINGS

- For use under Emergency Use Authorization Only.
- For in vitro diagnostic use only.
- For prescription use only.
- Read all instructions completely and carefully before performing the test. Failure to follow all 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) for use by authorized laboratories certified under the CLIA that meet the requirements to perform high or moderate complexity, or waived tests. This product is authorized for use at the Point of Care (POC), i.e., in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation.
- This product has been authorized only for the detection of proteins from SARS-CoV-2, not for any other viruses or pathogens. The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of *in vitro* diagnostic tests for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or the 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 the individual has had symptoms longer than 7 days you should consider testing them at least three times over five days with at least 48 hours between tests.**
- Use appropriate precautions in the collection, handling and storage of patient samples. Refer to CDC Interim Guidelines for Collection, Handling and Transportation of clinical specimens from persons with Coronavirus Disease 2019 (COVID-19) at https://www.cdc.gov/coronavirus/2019-nCoV/lab/guidelines-clinical-specimens.html, and to WHO's Interim guidance for Laboratory testing for coronavirus disease (COVID-19) in suspected human cases at http://www.who.int/publications-detail/laboratory-testing-for-2019-novel-coronavirus-in-suspected-human-cases-20200117, as amended and supplemented. Refer to the WHO website for additional publications.
- Federal Law restricts this device to sale by or on the order of a licensed practitioner (US only).
- Laboratories within the United States and its territories are required to report all results to the appropriate public health laboratories.
- Do not use kit past its expiration date.
- Keep sealed until usage, and once opened use immediately.
- Do not use if any of the test kit contents or packaging is damaged.
- Do not use the test device if the pouch is damaged or the device is seriously broken.
- Test components are single-use. Do not re-use.
- Do not touch the swab tip.
- Handle all specimens safely as potentially infectious.
- 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.**
- All samples, even after the extraction procedure, and reagents containing biological materials used

for the assay must be considered as potentially able to transmit infectious agents; accordingly samples, reagents and the waste must be handled with utmost care and disposed of in compliance with the laboratory guidelines and the statutory provisions in force in each country.

- This test is intended for assessment 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 methods and clinical information (signs and symptoms) should be used and considered for diagnosis.
- Discard Celltrion DiaTrust™ COVID-19 Ag Rapid 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
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Safety Precautions

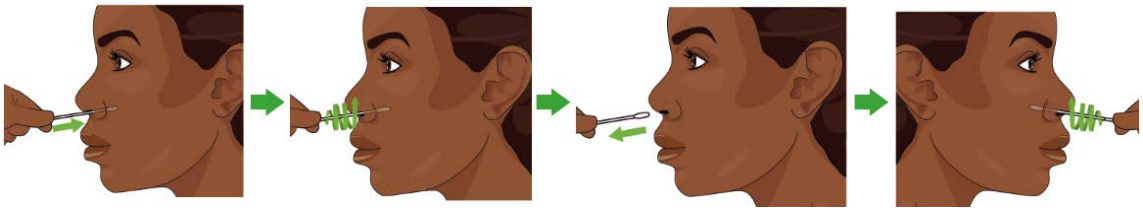
- Specimens may be infectious. Use Universal Precautions when performing this assay.
- Use routine laboratory precautions. Do not eat, drink, or smoke in the area where samples are being handled and testing is being conducted. Avoid any contact between hands, eyes or mouth during sample collection and testing.
- Wear personal protective equipment (PPE) in accordance with laboratory and institutional policies, such as laboratory coats, disposable gloves, and eye protection when handling patient samples.
- Wear a safety mask or other face-covering when collecting a specimen from a child or another individual.
- Wash hands thoroughly after handling specimens and used cartridge.
- Dispose of used test device in a biohazard waste container. Proper handling and disposal methods should be established according to local regulations.
- Avoid splashing or aerosolization of samples or reagents as droplets are a means of transmission of SARS-CoV-2 virus. All drops and spills must be wiped up with an appropriate disinfectant such as a sodium hypochlorite solution with 0.5% active chlorine, and all soiled materials must be disposed of as infectious waste.

TEST PROCEDURE

1. Specimen collection (CDC guideline):

   Use only the swabs provided with the test kit (FA/FANAB01 and Miraclean Technology, Item No. 96000) for specimen collection. Make sure extraction buffer tube and filter cap is also readily available before starting sample collection, as collected swab sample need to 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 affect the performance of the test.

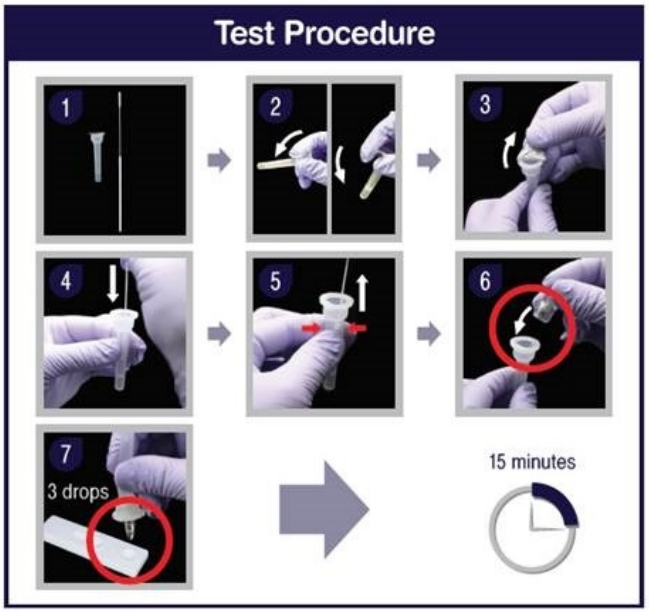
   [Mid-turbinate Nasal Swab]



Tilt patient's head back 70 degrees. Use a flocked tapered swab. While gently rotating the swab, insert it less than one inch (about 2 cm) into nostril parallel to the palate until resistance is met at turbinate. Rotate the swab several times against nasal wall. Remove swab, insert it into the other nostril and repeat the process.

NOTE: Do not store the swab without extraction buffer. Swabs may be stored in extraction buffer up to 4 hours after collection in room temperature. However, it is highly recommended to perform test immediately after collection for the best results.

2. Test method



1) Prepare an aluminum pouch containing the test device and place it on the testing surface along with the 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.
2) Release the test device from the aluminum pouch and place it on a flat surface just prior to starting test.
3) Collect the buffer fluid at the bottom of the test tube by shaking it and then peel off the seal of the test tube. Insert the tip of the swab with the patient specimen and move the swab up and down more than 10 times to ensure sufficient sample extraction.
4) Remove the swab while pressing against the sides of the tube to ensure maximum amount of liquid has been squeezed from the swab.
5) Equip the filter cap on the test tube and immediately dispense three drops of sample extracts (100 µL) into the sample well of the device. (If you have dropped the test device after sample application, please discard the device and restart the test using new device.)
6) Read results 15 minutes after applying the sample. Do not read results after 20 minutes. Note: False negative or false positive results could occur if the results are read before 15 minutes or after 20 minutes.

*** Avoid swabbing and inserting excessive amount of mid-turbinate nasal specimen into the test tube, as it may block the filter cap when dispensing sample extracts.*

INTERPRETATION OF RESULTS

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

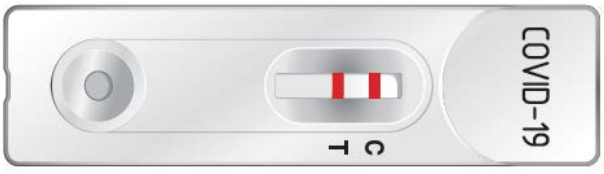
Status on first day of Testing	First Result Day 1	Second Result Day 3	Third Result Day 5	Interpretation
With Symptoms	Positive	N/A	N/A	Positive for COVID-19
	Negative	Positive	N/A	Positive for COVID-19
	Negative	Negative	N/A	Negative for COVID-19
Without Symptoms	Positive	N/A	N/A	Positive for COVID-19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

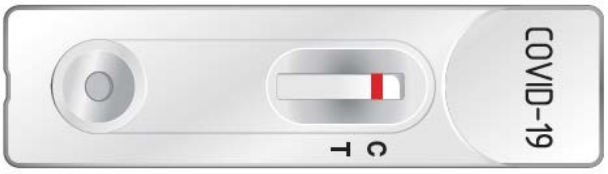
1) Celltrion DiaTrust™ COVID-19 Ag Rapid Test Controls – positive and negative:

Celltrion DiaTrust™ COVID-19 Ag Rapid Test contains one positive and one negative control to ensure that the test device is working as intended, and the test is correctly performed.

A positive control swab will give two colored lines in both test line and control line indicating a positive result.



A negative control will give a single colored control line indicating a negative result.



If incorrect control results are obtained, do not perform patient tests or report patient results. Contact technical support.

2) Examination and interpretation of patient specimen results:

Assessment of Celltrion DiaTrust™ COVID-19 Ag Rapid Test results should be performed after the positive and negative controls have been examined and determined to be valid and acceptable. If the controls are not valid, the patient results cannot be interpreted.

COVID-19 NEGATIVE (-)

Negative result: 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.**

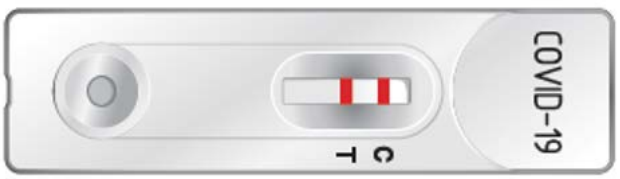
A negative test result indicates that the virus that causes COVID-19 was not detected in the sample. A negative result does not rule out COVID-19. There is a higher chance of false negative results with antigen tests compared to laboratory-based tests such as PCR tests. If the test is negative but COVID-19-like 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 disease should be considered. If applicable, seek follow up care with the primary health care provider. Note: All negative result 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

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

COVID-19 Positive (+)

Positive result: If the Control (C) line and the Test (T) line are visible, the test is positive. Any faint visible red 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.

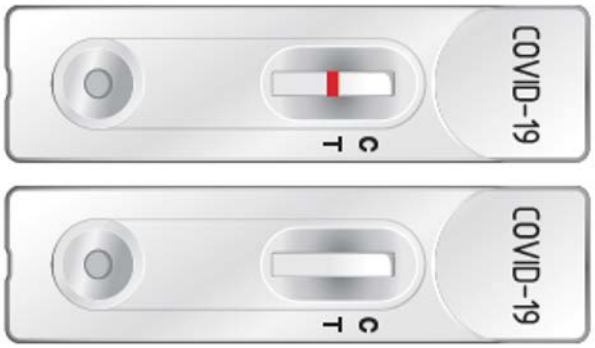


Note: A positive test result means that the virus that causes COVID-19 was detected in the sample, and it is very likely the individual has COVID-19 and is contagious. Please contact the patient's doctor/primary care physician (if applicable) and the local health authority immediately and instruct your 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-infections 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 individuals without known exposures to COVID-19 or residing in communities with low prevalence of infection.

Invalid

Invalid result: If the control (C) line is not visible, the test is invalid. Re-test with a new swab and new test device.



LIMITATIONS OF THE PROCEDURE

- Failure to follow the test procedure may adversely affect test performance and/or invalidate the test result.
- The performance of this device has not been assessed in a population vaccinated against COVID-19.
- This test detects both viable (live) and non-viable SARS-CoV-2. Test performance depends on the amount of virus (antigen) in the sample and may or may not correlate with viral culture results performed on the same sample.
- Performance has not been established for use with specimens other than mid-turbinate nasal swabs. Other specimen types have not been evaluated and should not be used with this assay.
- Test results should be considered in the context of all available clinical and diagnostic information, including patient history and other test results.
- The performance of this test was established based on the evaluation of a limited number of clinical specimens collected between February 2021 and July 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.

- 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.
- The clinical performance of this test has not been evaluated in patients without signs and symptoms of respiratory infection or other reasons to suspect COVID-19 infection, or for serial testing when tested twice over two or three days with at least 24 hours and no more than 48 hours between tests. A clinical study to support use in these individuals will be completed.
- A false negative test result may occur if the level of antigen in a sample is below the detection limit of the test or if the sample was collected or transported improperly.
- 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.
- Negative test results are not intended to rule in other non-SARS-CoV-2 viral or bacterial infections.
- The results obtained with this test should only be interpreted in conjunction with clinical findings, and the results from other laboratory tests and evaluations. This is especially important if the patient has had recent exposure to COVID-19, or clinical presentation indicates that COVID-19 is likely and diagnostic tests for other causes of illness (e.g., other respiratory illness) are negative. In this case, direct testing for the SARS-CoV-2 virus (e.g. PCR testing) should be considered.
- Positive results do not rule out co-infections with other pathogens.
- Positive test results do not differentiate between SARS-CoV-2 and SARS-CoV.
- 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.

CONDITIONS OF AUTHORIZATION FOR THE LABORATORY

The Celltrion DiaTrust™ COVID-19 Ag Rapid Test Letter of Authorization, along with the authorized Fact Sheet for Healthcare Providers, the authorized Fact Sheet for Patients, and authorized labeling are available on the FDA website: https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas. However, to assist clinical laboratories using the DiaTrust™ COVID-19 Ag Rapid Test ("your product" in the conditions below), the relevant Conditions of Authorization are listed below:

A. Authorized laboratories* using your product must include, with test result reports, all Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.
B. Authorized laboratories using your product must use your product as outlined in the "Celltrion DiaTrust™ COVID-19 Ag Rapid Test" Instructions for Use. Deviations from the authorized procedures, including the authorized instruments, authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and authorized materials required to use your product are not permitted.
C. Authorized laboratories that receive your product must notify the relevant public health authorities of their intent to run your product prior to initiating tests.
D. Authorized laboratories using your product must have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
E. Authorized laboratories must collect information on the performance of your product and report to DMD/OHT7-OIR/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov), and Celltrion USA, Inc. (via email: Diatrust@celltrion.com or via phone: (201) 499-1844) any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of your product of which they become aware.
F. All operators using your product must be appropriately trained in performing and interpreting the results of your product. Use appropriate personal protective equipment when handling this kit, and use your product in accordance with the labeling.
G. Celltrion USA, Inc., authorized distributor(s)., and authorized laboratories using your product must ensure that any records associated with this EUA are maintained until otherwise notified by the FDA. Such records will be made available to the 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, that meet requirements to perform high, moderate or waived complexity tests. This product is authorized for use at the Point of Care (POC) i.e., in patient care settings operating under CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation" as "authorized laboratories."

PERFORMANCE CHARACTERISTICS

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 Rapid 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 Rapid 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 X 10^1 $TCID_{50}$/mL equates to 3.2 X 10^0 $TCID_{50}$/swab.

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. 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 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 Rapid Test detected 100% of live virus Omicron samples at a Ct-value of 22.7 (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 22.7) were not detected by the Celltrion DiaTrust™ COVID-19 Ag Rapid Test in this study.

Omicron Pool 2 – Live Omicron Clinical Samples	**Average N2 Ct (n=9)**	**Assay #1** **Percent Positive (n=5)**	**Assay #2** **Percent Positive (n=5)**	***Celltrion DiaTrust™ COVID-19 Ag Rapid Test*** **Percent Positive (n=5)**
Omicron-Dilution 1	19.8	100	100	100
Omicron-Dilution 2	20.8	100	100	100
Omicron-Dilution 3	21.5	100	100	100
Omicron-Dilution 4	22.7	100	100	100
Omicron-Dilution 5	23.6	100	0	0
Omicron-Dilution 6	24.0	60	0	0
Omicron-Dilution 7	24.8	0	0	0
Omicron-Dilution 8	25.8	0	0	0
Omicron-Dilution 9	27.4	0	0	0
Omicron-Dilution 10	28.1	0	0	0
Omicron-Dilution 11	29.1	0	0	0

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

Wet-testing:

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

List of organisms		Testing conc.	Test result	
			Negative (No. of negative/ No. of replicates)	**Low Positive** (No. of positive/ No. of replicates)
	Candida albicans	1×10^6 CFU/mL	3/3	3/3
	Chlamydia pneumoniae	2.0×10^7 $TCID_{50}$/mL	3/3	3/3
	Pooled human nasal wash	100%	3/3	3/3
	Staphylococcus epidermidis	1×10^6 CFU/mL	3/3	3/3
	Staphylococcus aureus	1×10^6 CFU/mL	3/3	3/3

Human coronavirus HKU1 spike protein at the concentration of 10 µg/mL was spiked into negative and positive samples. It was tested in 3 replicates using the Celltrion DiaTrust™ COVID-19 Ag Rapid Test, and no cross-reactivity was observed.

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 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: 12% homology was found between SARS-CoV-2 Receptor Binding Domain spike proteins and HKU1 spike protein, and 32% homology was found between SARS-CoV-2 Nucleocapsid protein and HKU1 Nucleocapsid protein. Therefore, cross-reactivity is highly unlikely but cannot be ruled out.

Pneumocystis jirovecii: No sequence homology was found between SARS-CoV-2 RBD spike protein / nucleocapsid protein and *P. jirovecii*. Therefore, there is no cross-reactivity.

Mycobacterium tuberculosis: There was 45.6% homology across 9% of the whole sequence between *M. tuberculosis* and SARS-CoV-2 RBD spike protein. No similarity was found between *M. tuberculosis* and SARS-CoV-2 NP. Therefore, cross-reactivity is highly unlikely but cannot be ruled out.

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.

Note: The Celltrion DiaTrust™ COVID-19 Ag Rapid Test does not differentiate between SARS-CoV and SARS-CoV-2.

4) Endogenous interference substances study:
Testing to evaluate interference of the Celltrion DiaTrust™ COVID-19 Ag Rapid Test was performed.

Extraction buffer was used as negative sample. Positive standard materials were spiked into negative sample and were diluted to prepare a 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 Rapid Test in 3 replicates. The test results demonstrated that 41 interfering substances (table below) did not affect the performance of Celltrion's DiaTrust™ COVID-19 Ag Rapid 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**
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 Hydrochloride 0.5 mg/mL)	10%(v/v)	3/3*	3/3*	3/3**	3/3**
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**

No.	Interfering substances	Testing conc.	Negative	Negative + Interfering substances	Low positive	Low pos. + Interfering substances
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	10%(v/v)	3/3*	3/3*	3/3**	3/3**

*: Negative / **: Positive

5) High-dose Hook effect

Pooled nasopharyngeal specimens was 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 Rapid 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) Specimen stability

Nasopharyngeal swab samples were collected from healthy donors and were used as negative sample. Positive materials were prepared using the SARS-CoV-2 inactivated virus (NMC-nCoV02 #24, 6.3×10^5 $TCID_{50}$/mL) diluted to low positive concentration (6.3×10^1 $TCID_{50}$/mL, approx. 2xLoD) in negative sample, and 20 µL of the prepared low positive materials were coated on the swab to be used as positive sample.

Prepared negative and positive samples were mixed in extraction buffer and capped as per the instructions for use and stored in room temperature (30°C) for various time periods; immediately, and 1, 2, 3, 4, 6 hours after preparation. Samples of each condition were tested in 5 replicates for negative samples and 10 replicates for low positive samples following the instructions, using randomly selected samples of the Celltrion DiaTrust™ COVID-19 Ag Rapid Test.

Test results showed that collected nasopharyngeal swab specimen in extraction buffer is stable for testing up to 4 hours after collection in room temperature. However, it is highly recommended to perform test immediately after collection for the best results.

Time periods after storage in room temperature	**Test result**	
	Negative	**Low Positive**

	(No. of negative/ No. of replicates)	(No. of positive/ No. of replicates)
Immediately	5/5	10/10
1 hour	5/5	10/10
2 hours	5/5	10/10
3 hours	5/5	10/10
4 hours	5/5	10/10
6 hours	5/5	8/10

7) Clinical evaluation

The clinical performance of the Celltrion DiaTrust™ COVID-19 Ag Rapid Test was evaluated by testing a total of 211 prospectively collected direct mid-turbinate nasal swab samples, consisting of 36 positive and 175 negative samples from suspected COVID-19 patients in United States, aged 14 years and older at four clinical sites. Direct mid-turbinate nasal swabs were collected from each patient, eluted in the extraction buffer and tested with the device immediately, using only the QRI and App. Results of each sample were confirmed by a high-sensitivity FDA authorized RT-PCR assay.

According to the test results, clinical performance results of the Celltrion DiaTrust™ COVID-19 Ag Rapid 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 Rapid 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 symptoms 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 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.

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: Diatrust@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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