SARS-CoV-2 Rapid Antigen Test 2.0

REF		SYSTEM	IVD
9901-NCOV-08G	25	visual reading	For in vitro diagnostic use

English

Intended use
The SARS-CoV-2 Rapid Antigen Test 2.0 is a rapid chromatographic immunoassay for the qualitative detection of SARS-CoV-2 nucleocapsid antigen present in human nasopharyngeal swab samples. This test is intended as an aid in the diagnosis of SARS-CoV-2 infection in individuals with or without symptoms consistent with COVID-19.
This product is intended for professional use in laboratory and near-patient testing environments. Not for self-testing.

Summary
Coronaviruses are enveloped positive-stranded RNA viruses belonging to the Order of *Nidovirales*.[1] In late 2019 a new coronavirus was identified in a cluster of pneumonia cases.[2] The novel coronavirus, now known as SARS-CoV-2, has been classified as a member of the *Sarbecovirus* subgenus under the *Betacoronavirus* genus, and the disease associated with SARS-CoV-2 infection has been named COVID-19 (COronaVIrus Disease 2019).[3,4] Due to the rapid rise in the number of cases and the scale of worldwide spread, the World Health Organization (WHO) described the SARS-CoV-2 situation as pandemic on March 11, 2020.[5] The clinical presentation of SARS-CoV-2 can range from asymptomatic infection to severe disease and even death.[6,7] Symptoms of patients with confirmed SARS-CoV-2 infection vary from fever and dry cough to shortness of breath or difficulty in breathing. In addition, diarrhea and a loss of taste or smell have been reported after a SARS-CoV-2 infection.[6,7] Symptom onset may appear up to 14 days after exposure to the virus.[7]

Test principle
The SARS-CoV-2 Rapid Antigen Test 2.0 has 2 pre-coated lines: a "C" Control line and a "T" Test line on the surface of the nitrocellulose membrane. Both the control line and the test line in the result window are not visible before applying any specimens. Mouse monoclonal anti-SARS-CoV-2 antibody is coated on the test line region and mouse monoclonal anti-Chicken IgY antibody is coated on the control line region. Mouse monoclonal anti-SARS-CoV-2 antibody conjugated with color particles are used as detectors for the SARS-CoV-2 antigen device. During the test, the SARS-CoV-2 antigen in the specimen interacts with monoclonal anti-SARS-CoV-2 antibody conjugated with color particles making an antigen-antibody color particle complex. This complex migrates on the membrane via capillary action to the test line, where it is captured by the mouse monoclonal anti-SARS-CoV-2 antibody. A colored test line becomes visible in the result window if SARS-CoV-2 antigens are present in the sample.

Reagents
- mAb anti-SARS-CoV-2 antibody
- mAb anti-Chicken IgY
- mAb anti-SARS-CoV-2 antibody gold conjugate
- Purified chicken IgY-gold conjugate

Precautions and warnings
For in vitro diagnostic use.
Exercise the normal precautions required for handling all laboratory reagents.
Disposal of all waste material should be in accordance with local guidelines.
Safety data sheet available for professional user on request.
This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

Warning:

H317	May cause an allergic skin reaction.
H319	Causes serious eye irritation.
H412	Harmful to aquatic life with long lasting effects.

Prevention:

P261	Avoid breathing mist or vapours.
P273	Avoid release to the environment.
P280	Wear protective gloves/ eye protection/ face protection.

Response:

P333 + P313	If skin irritation or rash occurs: Get medical advice/attention.
P337 + P313	If eye irritation persists: Get medical advice/attention.
P362 + P364	Take off contaminated clothing and wash it before reuse.

Product safety labeling follows EU GHS guidance.
Contact phone: all countries: +49-621-7590
- Equilibrate the kit contents and specimens to operating temperature (15-30 °C / 59-86 °F) before testing.
- Do not use kit contents beyond the expiration date printed on the outside of the box.
- Do not re-use the test kit.
- Do not use the test kit if the pouch is damaged or the seal is broken.
- Do not use the extraction buffer of a different lot.
- Do not smoke, drink or eat while handling the sample.
- Wear personal protective equipment, such as gloves and lab coats when handling kit reagents. Wash hands thoroughly after the tests are done.
- Clean up spills thoroughly using an appropriate disinfectant.
- Handle all samples as if they contain infectious agents.
- If you suspect the presence of blood on the swab, discard the swab and repeat the test with a fresh one.
- Observe established precautions against microbiological hazards throughout testing procedures.
- Dispose of all samples and materials used to perform the test as biohazard waste. Laboratory chemical and biohazard wastes must be handled and discarded in accordance with all local, state, and national regulations.
- Prevent release into the environment, drainage system or water bodies.
- Desiccant in foil pouch is to absorb moisture and keep humidity from affecting products. If the desiccant beads change from yellow to green, the test device in the pouch should be discarded.

Storage and stability
Store the kit at 2-30 °C / 36-86 °F out of direct sunlight. Kit materials are stable until the expiry date printed on the outer box. Do not freeze the kit.
- Specimens should be tested as soon as possible after sample collection.
- Dry swab samples are stable for 2 hours at room temperature (20 ± 5 °C) and for 4 hours at 4 °C.
- Specimens in extraction buffer are stable at room temperature (20 ± 5 °C) for up to 4 hours, at 5 ± 3 °C for up to 4 hours, at -20 °C for up to 4 months and at -70 °C for up to 4 months.
- Specimens in extraction buffer are stable for 1 freeze-thaw cycle.

Materials provided
- Test device (individually in a foil pouch with desiccant)
- Extraction buffer tube and buffer tube rack
- Nozzle cap
- Sterile swab
- Instructions for Use and Quick Reference Guide

Materials required (but not provided)
- Timer
- Personal protective equipment per local recommendations or requirements
- Biohazard container

Test preparation and sample collection
Carefully read the instructions for using the SARS-CoV-2 Rapid Antigen Test 2.0. Please also see the enclosed Quick Reference Guide (QRG, with illustrations) before performing a test.

Preparing for a test
Prior to starting the procedure, test devices and reagents must be equilibrated to operating temperature (15-30 °C / 59-86 °F).
1. Check the expiry date on the back of the foil pouch. Do not use the test, if the expiry date has passed.
2. Open the foil pouch and remove the test device and the desiccant package. Use the test immediately after opening the pouch.
3. Ensure that the test device is undamaged and that the desiccant status indicator shows yellow beads (valid).
4. Consider performing a quality control (QC) as recommended in the "External quality control (QC)" section.

Collecting a sample (Nasopharyngeal swab)
1. Remove the swab from the packaging by pulling on both flaps of the plastic film. Only touch the swab at the handle, not at the tip.
2. Tilt the patient's head back slightly (approximately at a 70 degree angle).
3. Insert a sterile swab into the nostril of the patient, reaching the surface of the posterior nasopharynx.
4. Rotate the swab 3-4 times against the nasopharyngeal surface. Remove the swab from the nasal cavity carefully.

Test procedure
1. Carefully open the extraction buffer tube avoiding spillage. If buffer is spilled, do not use the tube.
2. Insert the swab into an extraction buffer tube. While squeezing the buffer tube, stir the swab at least 10 times.
3. Remove the swab while squeezing the sides of the tube to extract the liquid from the swab.
4. Press the nozzle cap tightly onto the tube.
5. Place the test device on a flat surface and apply 4 drops of extracted specimen to the specimen well of the test device.
6. Read the test result at 15-30 minutes. Do not touch or move the test device until the result can be read.

⚠ Failure to squeeze the tube can lead to incorrect results due to insufficient elution of the material into the buffer or excess buffer in the swab.
⚠ Test results that are read before 15 minutes or after 30 minutes may be incorrect.
⚠ Place the test device on a flat surface to allow optimal capillary action.
⚠ Dispense the specimen at 90 degree angle to allow for free falling drops and avoid bubbles.

Interpreting test results
- A colored line appears in the "C" section of the result window to show that the test is working properly. This is the control line (C). Even if the control line is faint or not uniform, the test should be considered to have been performed properly. If no control line is visible the test result should be considered as invalid. In case of an invalid result, consider performing an external QC and repeat the test with a new test device.
- In case of a positive result, a colored line appears in the "T" section of the result window. This line is the test line (T). Even if a test line is very faint or not uniform, the test result should be interpreted as a positive result.

⚠ The test result should not be used as the sole basis for treatment or patient management decisions, and should be considered in the context of the patient's recent exposures, history and the presence of clinical signs and symptoms consistent with COVID-19.

Internal quality control
A control line is used in the test as a procedural control. A visible control line confirms that the lateral flow of the test is successful but is not the confirmation that the specimen and buffer have been applied properly.

External quality control (QC)
- Positive and negative controls are available separately from Roche (SARS-CoV-2 Antigen Control Swab).
- It is recommended that positive and negative controls be run once for each new lot, once for each untrained operator, once for each new shipment of test kits, and as required by test procedures in these instructions and in accordance with local, state and federal regulations or accreditation requirements.

Limitations
- The test procedure, precautions and interpretation of results for this test must be followed strictly when testing.
- Failure to follow the test procedure and interpretation of test results may adversely affect test performance and/or produce invalid results.
- The test should be used for the detection of SARS-CoV-2 antigen in human nasopharyngeal swab samples.
- This is a qualitative test, therefore quantitative values of SARS-CoV-2 antigen concentration cannot be determined.
- The immune response cannot be assessed with this test and needs other testing methods.
- The test result should not be used as the sole basis for treatment or patient management decisions, and should be considered in the context of the patient's recent exposures, history and the presence of clinical signs and symptoms consistent with COVID-19.
- A negative result may occur if the concentration of antigen in a sample is below the detection limit of the test or if the sample was collected or transported improperly. Therefore a negative test result does not eliminate the possibility of SARS-CoV-2 infection, and should be confirmed by viral culture or a molecular assay, if necessary for patient management.
- Positive test results do not rule out co-infections with other pathogens.
- Positive test results do not differentiate between SARS-CoV-2 and SARS-CoV.
- Negative test results are not intended to rule in or rule out other infections.
- Clinical performance has not been established with 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.
- Rapid antigen tests perform the best when viral replication peaks, which may differ from variant to variant. For wild-type SARS-CoV-2, the viral load peaks are usually the highest from 1-3 days before symptoms onset through the first 5-7 days of illness.[8] Please monitor the latest reports for variants relevant for your geographic area for the most accurate information.

Specific performance data

Clinical evaluation
The performance of the SARS-CoV-2 Rapid Antigen Test 2.0 was evaluated by point-of-care healthcare professionals using nasopharyngeal swab samples collected during a clinical study in South Korea. An enrichment strategy was employed to increase the positive and negative pre-test probabilities. Each study participant donated two nasopharyngeal swab samples, one for testing on the SARS-CoV-2 Rapid Antigen Test 2.0 and the other for testing on the RT-PCR comparator test. In total 100 RT-PCR-positive and 402 RT-PCR-negative subjects participated in this study. This included 320 asymptomatic subjects, among whom 34 were positive and 286 were negative. 100 out of the 402 RT-PCR-negative subjects were hospitalized due to a suspected respiratory infection.

The SARS-CoV-2 Rapid Antigen Test 2.0 correctly identified 99 out of the 100 positive individuals and 401 out of the 402 negative individuals. The positive percent agreement (PPA) and negative percent agreement (NPA) with the comparator method were 99.00 % (94.55 % - 99.97 %) and 99.75 % (98.62 % - 99.99 %), respectively. The PPA and NPA for all samples, samples collected within 7 days of symptoms onset, as well as samples for which the comparator test yielded a Cycle Threshold (Ct) value below or equal to 30 are summarized in the table below.

	Positives Antigen / PCR	Negatives Antigen / PCR	PPA (95 % CI*)	NPA (95 % CI*)
Overall	99 out of 100	401 out of 402	99.00 % (94.55 - 99.97 %)	99.75 % (98.62 - 99.99 %)
Ct** ≤ 30	79 out of 79	N/A	100.00 % (95.44 - 100.00 %)	N/A
DPSO ≤ 7	65 out of 66	116 out of 116	98.48 % (91.84 - 99.96 %)	100.00 % (96.87 - 100.00 %)

*95 % confidence intervals (CI) were calculated using the exact Clopper-Pearson method.
**Ct values are commonly used to estimate the amount of the viral material in samples. A low Ct value suggests the presence of a lot of viral material, and a high Ct value suggests the presence of lower levels of viral material.

Analytical performance
1. Limit of Detection (LoD):
The SARS-CoV-2 positive specimen was prepared by spiking inactivated SARS-CoV-2 (2019-nCOV) NCCP 43326/2020/Korea strain to SARS-CoV-2 negative nasopharyngeal swab confirmed with PCR. LoD is determined as 1.46 X 10^1 $TCID_{50}$/mL for direct nasopharyngeal swabs by testing serially diluted positive specimens.

2. Cross-reactivity & microbial interference:
There was no cross-reactivity and interference with the following microbes at indicated concentrations:
Human coronavirus 229E (2.43 x 10^5 PFU/mL), Human coronavirus OC43 (3.42 x 10^5 PFU/mL), Human coronavirus NL63 (1.16 x 10^5 PFU/mL), Human coronavirus HKU1 (29.1 ng/mL), SARS-coronavirus (17.2 ng/mL), MERS-coronavirus (2.85 x 10^5 PFU/mL), Adenovirus Type 1 (1.76 x 10^6 PFU/mL), Adenovirus Type 2 (7.17 x 10^5 PFU/mL), Adenovirus Type 5 (2.78 x 10^7 PFU/mL), Adenovirus Type 6 (1.33 x 10^7 PFU/mL), Adenovirus Type 7A (7.17 x 10^5 PFU/mL), Adenovirus Type 11 (1.33 x 10^7 PFU/mL), Adenovirus Type 14 (2.85 x 10^5 PFU/mL), Adenovirus Type 40 (2.60 x 10^6 PFU/mL), Human Metapneumo virus 3 Type B1 (1.50 x 10^6 PFU/mL), Human Metapneumo virus 16 Type A1 (2.60 x 10^6 PFU/mL), Parainfluenza virus 1 (8.61 x 10^5 PFU/mL), Parainfluenza virus 2 (1.03 x 10^6 PFU/mL), Parainfluenza virus 3 (2.32 x 10^7 PFU/mL), Parainfluenza virus 4A (2.60 x 10^6 PFU/mL), Influenza A H1N1 pdm/Michigan/45/15 (8.34 x 10^5 PFU/mL), Influenza A H1N1 Brisbane/59/07 (1.00 x 10^6 PFU/mL), Influenza A H3N2 Singapore/NFIMH-16-0019/16 (8.60 x 10^5 PFU/mL), Influenza A H3N2 South Australia/55/14 (1.03 x 10^6 PFU/mL), Influenza A H3N2 Hong Kong/8/68 (3.32 x 10^5 PFU/mL), Influenza A H3N2 Victoria/361/11 (2.85 x 10^5 PFU/mL), Influenza B Massachusetts/2/12 (3.32 x 10^5 PFU/mL), Influenza B Malaysia/2506/04 (2.76 x 10^5 PFU/mL), Influenza B Lee/40 (3.32 x 10^5 PFU/mL), Influenza B Yamagata/16/88 (1.62 x 10^5 PFU/mL), Influenza B Victoria/2/87 (1.13 x 10^5 PFU/mL), Influenza B Texas/6/11 (2.51 x 10^6 PFU/mL), Influenza B Colorado/6/17 (1.13 x 10^5 PFU/mL), Influenza B Florida/02/06 (2.51 x 10^6 PFU/mL), Enterovirus Type 68 09/2014 Isolate 4 (1.03 x 10^6 PFU/mL), Respiratory syncytial virus A (7.17 x 10^5 PFU/mL), Respiratory syncytial virus B (3.42 x 10^5 PFU/mL), Rhinovirus 1A (1.16 x 10^5 PFU/mL), Rhinovirus A16 (8.61 x 10^5 PFU/mL), Rhinovirus B42 (7.17 x 10^5 PFU/mL), *Haemophilus influenzae* (NCCP 13815) (2.51 x 10^7 CFU/mL), *Haemophilus influenzae* (NCCP 13819) (3.36 x 10^7 CFU/mL), *Haemophilus influenzae* (NCCP 14581) (4.06 x 10^7 CFU/mL), *Haemophilus influenzae* (NCCP 14582) (1.05 x 10^{10} CFU/mL), *Streptococcus pneumoniae* Type 1 (KCCM 41568) (1.89 x 10^8 CFU/mL), *Streptococcus pneumoniae* Type 2 (KCCM 40410) (1.54 x 10^6 CFU/mL), *Streptococcus pneumoniae* Type 3 (KCCM 41569) (2.30 x 10^7 CFU/mL), *Streptococcus pneumoniae* Type 5 (KCCM 41570) (9.90 x 10^6 CFU/mL), *Streptococcus pyogenes* (ATCC 12344) (6.88 x 10^7 CFU/mL), *Candida albicans* (ATCC 10231) (1.84 x 10^9 CFU/mL), *Bordetella pertussis* (NCCP 13671) (6.18 x 10^7 CFU/mL), *Mycoplasma pneumoniae* (ATCC 15531) (3.37 x 10^7 CFU/mL), *Chlamydia pneumoniae* (ATCC VR-2282) (9.01 x 10^7 IFU/mL), *Legionella pneumophila* (ATCC 33155) (1.57 x 10^{10} CFU/mL), *Staphylococcus aureus* (NCCP 14647) (8.91 x 10^8 CFU/mL), *Staphylococcus epidermidis* (KCCM 35494) (6.16 x 10^8 CFU/mL).

Note: SARS-coronavirus and Human coronavirus HKU1 were tested using recombinant nucleocapsid proteins. No cross-reactivity and interference was observed. The in-silico analysis for SARS-CoV shows high probability of cross-reactivity with the SARS-CoV-2 test line. Cross-reactivity was observed using live samples of SARS-coronavirus at high concentrations. *Pneumocystis jirovecii* (PJP) and *Mycobacterium tuberculosis* have not been tested. A low probability of cross-reactivity was determined by in-silico analysis.

3. Exogenous / endogenous interference substances studies:
There was no interference with the following substances at indicated concentrations:
Chloraseptic (Menthol/Benzocaine) (1.5 mg/mL), Naso GEL (NeilMed) (5 % v/v), CVS Health Nasal Drops (Phenylephrine) (15 % v/v), Afrin (Oxymetazoline) (15 % v/v), CVS Health Oxymetazoline (15 % v/v), CVS Health Nasal Spray (Cromolyn) (15 % v/v), Zicam (5 % v/v), Homeopathic (Alkalol) (10 % v/v), Sore Throat Phenol Spray (15 % v/v), Tobramycin (4 µg/mL), Mupirocin (10 mg/mL), CVS Health Fluticasone Propionate (5 % v/v), Tamiflu (Oseltamivir Phosphate) (5 mg/mL), Soap (Sodium Lauroyl Isethionate) (5 % w/v), Facial wash (Disodium Laureth Sulfosuccinate, Sodium Laureth-6 Carboxylate) (5 % w/v), Hand Sanitizer (Ethyl alcohol) (5 % v/v), Shampoo (Sodium Laureth Sulfate, Sodium Myreth Sulfate) (5 % v/v), Toothpaste (Sodium Lauryl Sulfate, Hydrogen Peroxide, Sodium Monofluorphosphate) (5 % w/v), Dish-washing liquid (Sodium Laureth Sulfate, Lauryl / Myristyl Glucoside) (5 % v/v), Laundry Detergent (Sodium Laureth Sulfate, C12-15 alcohols ethoxylated (or C12-16), Sodium C10-16 alkylbenzenesulfonate, Disodium distyrylbiphenyl disulfonate, C12-13 pareth-2, Sodium hydroxide) (5 % v/v), Bleach (Sodium percarbonate) (5 mg/mL), Surface cleaner for multiple use (Sodium Laureth Sulfate) (5 % v/v), Surface cleaner for bathroom (Sodium hypochlorite) (5 % v/v), Body lotion (5 % w/v), Hand lotion (5 % w/v), Facial suncream SPF 50+ (5 % w/v), Whole Blood (4 % v/v), Mucin (0.5 % w/v).

4. High-dose hook effect:
Cultured SARS-CoV-2 virus was spiked into negative clinical matrix. SARS-CoV-2 cultured virus did not show hook effect up to 4.45 X 10^5 $TCID_{50}$/mL.

5. Variants of concern:
Lab testing showed that the SARS-CoV-2 Rapid Antigen Test 2.0 can qualitatively detect major variants of concern including Delta and Omicron variants. Emerging variants are continuously monitored.

A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

References

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2 Wu et al. Nature. 2020. 579:265–9.
3 Coronaviridae Study Group of the International Committee on Taxonomy of Viruses. Nat Microbiol. 2020. 5:536–44.
4 https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-%28covid-2019%29-and-the-virus-that-causes-it
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7 Centers for Disease Control and Prevention. https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html. Accessed 6 Jan 2021.
8 World Health Organization (WHO). Antigen-detection in the diagnosis of SARS-CoV-2 infection using rapid immunoassays. Interim guidance. 11 September 2020.

Symbols
The manufacturer uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard:

GTIN	Global Trade Item Number
UDI	Unique Device Identifier
SYSTEM	Systems on which reagents can be used
	Distributor

CE

SD BIOSENSOR
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L23SCR21EN01R0
Issue date: 2023.03

09695150001
2023-07 V 2.0