SARS-CoV-2 Rapid Antigen Test Nasal

REF		SYSTEM
9901-NCOV-03G	25	visual reading

English

Intended use

The SARS-CoV-2 Rapid Antigen Test Nasal is a rapid chromatographic immunoassay for the qualitative detection of SARS-CoV-2 nucleocapsid antigen present in human nasal samples. This test is intended to detect antigen from SARS-CoV-2 in individuals suspected of COVID-19 or with known or suspected exposure to SARS-CoV-2. This product is intended for professional use in laboratory and Point of Care environments, or self-collection under the supervision of a healthcare worker.

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 Nasal has two 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 samples. 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 sample 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. The intensity of the colored test line varies depending upon the amount of SARS-CoV-2 antigen present in the sample.

Reagents

- mAb anti-COVID-19 antibody
- mAb anti-Chicken IgY
- mAb anti-COVID-19 antibody-gold conjugate
- Purified chicken IgY-gold conjugate
- Recombinant COVID-19 nucleocapsid protein (positive controls)

Negative controls do not contain active ingredients.

Precautions and warnings

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 dust/fume/gas/mist/vapours/spray.
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.

For customers in the European Economic Area: Contains SVHC: octyl/nonylphenol ethoxylates. For use as part of an IVD method and under controlled conditions only – acc. to Art. 56.3 and 3.23 REACH Regulation.

- 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 buffer of different lot.
- 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.
- 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.

Product safety labeling follows EU GHS guidance.

Contact phone: all countries: +49-621-7590

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.

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.

Materials provided

- Test device (individually in a foil pouch with desiccant)
- Extraction buffer tube and buffer tube rack
- Nozzle cap
- Sterile swab
- Instruction for Use and Quick Reference Guide
- Positive and negative controls

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 Nasal. Please also see the enclosed Quick Reference Guide (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 immediatedly after opening the pouch.
3. Ensure that the test device is undamaged and that the desiccant status indicator shows valid (yellow).
4. Perform a quality control (QC) as required according to the Instructions for Use of the QC material.

Collecting a sample (Nasal 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 slightly back (approximately 70 degree angle).
3. Insert the sterile swab into the nostril with the most secretion. While rotating the swab, insert the swab 2 cm (slightly less than 1 inch) parallel to the palate (not upwards) towards the throat into the nostril until resistance is met at turbinates. Do not apply pressure.
4. Rotate the swab 4 times for about 15 seconds against the nasal wall and remove it from the nostril.
5. Repeat step 3 to 4 with the same swab in the other nostril.
6. If the sample is collected by the patient the swab must be handed over to the healthcare worker on a sterile tray to avoid contamination.

Specimens must be collected from both nostrils using the same swab.

Test procedure (to be performed by healthcare worker)

1. Insert the swab into an extraction buffer tube. While squeezing the buffer tube, stir the swab more than 10 times.
2. Remove the swab while squeezing the sides of the tube to extract the liquid from the swab.
3. Press the nozzle cap tightly onto the tube.
4. Place the test device on a flat surface and apply 4 drops of extracted sample at a 90 degree angle to the specimen well of the test device.
5. Read the test result in 15-30 minutes.

⚠ Without the tube squeezing process, improper results may occur due to the large amount of buffer absorption by the swab.

⚠ Do not read test results after 30 minutes. It may give false results.

Interpreting test results

- A colored line appears in the top section of the result window to show that the test is working properly. This line is the control line (C). The control line always appears if the test result is valid. Even if the control line is faint or not uniform, the test should be considered to be performed properly. 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. If no control line is visible the test result should be considered as invalid.
- In case of a positive result, a colored line appears in the lower section of the result window. This line is the test line of the SARS-CoV-2 antigen (T). Even if the test line is very faint or not uniform the test result should be interpreted as a positive result. If SARS-CoV-2 antigens are not present in the sample, no color appears in the test line.

⚠ Positive results should be considered in conjunction with the patient's clinical history and other data available.

External quality control (QC)

- Positive and negative controls are supplied with each kit or available separately from Roche (SARS-CoV-2 Antigen Control Swab).
- Positive and negative controls should be performed as real specimens.
- It is recommended that positive and negative controls be run once for each new lot, once for each untrained operator, as required by test procedures in these instructions and in accordance with local, state and federal regulations or accreditation requirements.

Preparing a QC

1. Check the expiry date on the foil pouch of the controls. Do not use the controls if the expiry date has passed.
2. Open the pouch of the positive or negative control and put the positive or negative control swab into an extraction buffer tube. Stir the swab more than 5 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.

QC procedure

1. Place the test device on a flat surface and apply 3 drops of extracted sample at a 90 degree angle to the specimen well of the test device.
2. Read the test result in 15-30 minutes.

⚠ Do not read test results after 30 minutes. It may give false results.

Result	Interpretation
Positive result with positive control	Pass
Negative result with negative control	Pass
Negative result with positive control	Fail
Positive result with negative control	Fail
Control line not visible	Invalid. Repeat with a new test device.

Limitations

- The test procedure, precautions and interpretation of results for this test must be followed strictly when testing.
- The test should be used for the detection of SARS-CoV-2 antigen in human nasal 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 a 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 or ELISA, 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 coronavirus infections.

Specific performance data

Clinical evaluation

Clinical performance of the SARS-CoV-2 Rapid Antigen Test Nasal was evaluated using nasal swab samples from 468 subjects in a prospective study at a clinical center in Germany. The study cohort included adults at high risk for SARS-CoV-2 infection according to clinical suspicion. 179 subjects underwent nasal sampling performed by healthcare professionals and 289 subjects followed written instructions to obtain a nasal swab sample by themselves. Self-collection was performed under the supervision of healthcare workers without interference or assistance. Test procedures and result reading were always performed by healthcare professionals. RT-PCR tests (Roche **cobas®** SARS-CoV-2 and TibMolbiol SARS-CoV-2 E-gene assay) using combined nasopharyngeal/oropharyngeal swab samples were used as the comparator methods. Nasal sampling always preceded the combined NP/OP sampling.

Test sensitivity & specificity

The following tables summarize the patient and performance characteristics of the SARS-CoV-2 Rapid Antigen Test Nasal. The relative sensitivity was 90.6 % (Ct value ≤ 30; 95 % CI: 75.0 % - 98.0 %) for professionally collected samples, and 84.4 % (Ct value ≤ 30; 95 % CI: 67.2 % - 94.7 %) for self-collected samples. For patients for whom days post symptom onset was known, and was 0-5 days, the relative sensitivity in comparison to RT-PCR was 88.9 % (CI: 70.8 % - 97.7 %) for professionally collected nasal samples and 85.7 % (CI: 67.3 % - 96.0 %) for self-collected nasal samples.
The relative specificity in comparison to RT-PCR was 98.6 % (CI: 94.9 % - 99.8 %) for professionally collected nasal samples and 99.2 % (CI: 97.1 % - 99.9 %) for self-collected nasal samples.

Summary of sample characteristics and performances:

	Overall	HCP-collection	Self-collection
N	468	179	289
Asymptomatic, n/N (%)	14/468 (3.0 %)	7/179 (3.9 %)	7/289 (2.4 %)
Symptomatic, n/N (%)	454/468 (97.0 %)	172/179 (96.1 %)	282/289 (97.6 %)
DPSO, median (range)	4 (0 - 14)	4 (1 - 10)	4 (0 - 14)
PCR positive, n/N (%)	80/468 (17.1 %)	41/179 (22.9 %)	39/289 (13.5 %)
PCR positive symptomatic, n/N (%)	78/80 (97.5 %)	39/41 (95.1 %)	39/39 (100 %)
PCR positive asymptomatic, n/N (%)	2/80 (2.5 %)	2/41 (4.9 %)	0/39 (0 %)
PCR negative, n/N (%)	388/468 (82.9 %)	138/179 (77.1 %)	250/289 (86.5 %)
PCR sample type	Combined OP/NP		

Relative sensitivity, % (95% CI), N	**Professional collection**	**Self-collection**
Ct[a] ≤ 24	100 % (CI: 78.2 % - 100 %), 15	95.7 % (CI: 78.1 % - 99.9 %), 23
Ct[a] ≤ 27	92.6 % (CI: 75.7 % - 99.1 %), 27	92.9 % (CI: 76.5 % - 99.1 %), 28
Ct[a] ≤ 30	**90.6 % (CI: 75.0 % - 98.0 %), 32**	**84.4 % (CI: 67.2 % - 94.7 %), 32**
Ct[a] ≤ 33	88.2 % (CI: 72.5 % - 96.7 %), 34	78.4 % (CI: 61.8 % - 90.2 %), 37
All Ct values	80.5 % (CI: 65.1 % - 91.2 %), 41	74.4 % (CI: 57.9 % - 87.0 %), 39

a) for samples run on **cobas** the Target 2 (E gene) Ct values were used.

Relative specificity, % (95% CI), N	**Professional collection**	**Self-collection**
All Ct values	98.6 % (CI: 94.9 % - 99.8 %), 138	99.2% (CI: 97.1% - 99.9%), 250

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 nasal swab confirmed with PCR. LoD is determined as 9.25 X $10^{1.2}$ $TCID_{50}$/mL for direct nasal swab by testing serially diluted mock positive specimens.

2. Cross-reactivity & microbial interference:
There was no cross-reactivity and interference with the following microbes at indicated concentrations:
Human coronavirus 229E (1 X $10^{5.5}$ $TCID_{50}$/mL), Human coronavirus OC43 (1 X $10^{7.77}$ $TCID_{50}$/mL), Human coronavirus NL63 (1 X $10^{5.07}$ $TCID_{50}$/mL), MERS-coronavirus (4.17 X 10^5 $TCID_{50}$/mL), Adenovirus Type1 (2.57 X 10^8 $TCID_{50}$/mL), Adenovirus Type2 (1.15 X 10^7 $TCID_{50}$/mL), Adenovirus Type5 (1 X $10^{7.53}$ $TCID_{50}$/mL), Adenovirus Type6 (1 X $10^{7.29}$ $TCID_{50}$/mL), Adenovirus Type7A (1 X $10^{5.15}$ $TCID_{50}$/mL), Adenovirus Type11 (1 X $10^{7.29}$ $TCID_{50}$/mL), Adenovirus Type14 (1 X $10^{5.39}$ $TCID_{50}$/mL), Adenovirus Type40 (1 X $10^{6.58}$ $TCID_{50}$/mL), Human Metapneumovirus3 type B1 (1 X $10^{6.34}$ $TCID_{50}$/mL), Human Metapneumovirus16 type A1 (1 X $10^{6.98}$ $TCID_{50}$/mL), Parainfluenza virus 1 (1 X $10^{8.49}$ $TCID_{50}$/mL), Parainfluenza virus 2 (1 X $10^{6.10}$ $TCID_{50}$/mL), Parainfluenza virus 3 (1 X $10^{6.82}$ $TCID_{50}$/mL), Parainfluenza virus 4A (1 X $10^{6.58}$$TCID_{50}$/mL), Influenza A H1N1 pdm/Michigan/45/15 (1 X $10^{6.10}$ $TCID_{50}$/mL), Influenza A H1N1 Brisbane/59/07 (1 X $10^{5.86}$ $TCID_{50}$/mL), Influenza A H3N2 Singapore/INFIMH-16-0019/16 (4.68 X 10^4 $TCID_{50}$/mL), Influenza A H3N2 South Australia/55/14 (1 X $10^{5.07}$ $TCID_{50}$/mL), Influenza A H3N2 Hong Kong/8/68 (1 X $10^{5.70}$ $TCID_{50}$/mL), Influenza A H3N2 Victoria/361/11 (1 X $10^{5.15}$ $TCID_{50}$/mL), Influenza B Massachusetts/2/12 (1 X $10^{5.39}$ $TCID_{50}$/mL), Influenza B Malaysia/2506/04 (1 X $10^{5.07}$ $TCID_{50}$/mL), Influenza B Lee/40 (1 X $10^{5.39}$ $TCID_{50}$/mL), Influenza B Yamagata/16/88 (1 X $10^{5.39}$ $TCID_{50}$/mL), Influenza B Victoria/2/87 (1.86 X 10^4 $TCID_{50}$/mL), Influenza B Texas/6/11 (1 X $10^{6.58}$ $TCID_{50}$/mL), Influenza B Colorado/6/17 (4.68 X 10^4 $TCID_{50}$/mL), Influenza B Florida/02/06 (3.8 X 10^6 $TCID_{50}$/mL), Enterovirus type 68 09/2014 Isolate 4 (3.55 X 10^5 $TCID_{50}$/mL), Respiratory syncytial virus A (1 X $10^{6.58}$ $TCID_{50}$/mL), Respiratory syncytial virus B (5.01 X 10^5 $TCID_{50}$/mL), Rhinovirus 1A (1 X $10^{5.55}$ $TCID_{50}$/mL), Rhinovirus A16 (1 X $10^{6.1}$ $TCID_{50}$/mL), Rhinovirus B42 (1.41 X 10^5 $TCID_{50}$/mL), Haemophilus influenzae (NCCP 13815) (2.54 X 10^7 CFU/mL), Haemophilus influenzae (NCCP 13819) (3.39 X 10^7 CFU/mL), Haemophilus influenzae (NCCP 14581) (4.10 X 10^7 CFU/mL), Haemophilus influenzae (NCCP 14582) (1.06 X 10^7 CFU/mL), Streptococcus pneumoniae type1 (KCCM 41560) (1.54 X 10^6 CFU/mL), Streptococcus pneumoniae type2 (KCCM 40410) (1.04 X 10^7 CFU/mL), Streptococcus pneumoniae type3 (KCCM 41569) (1.34 X 10^7 CFU/mL), Streptococcus pneumoniae type5 (KCCM 41570) (1.24 X 10^7 CFU/mL), Streptococcus pyogenes (ATCC 12344) (3.22 X 10^7 CFU/mL), Candida albicans (ATCC 10231) (1.78 X 10^6 CFU/mL), Bordetella pertussis (NCCP 13671) (6.24 X 10^7 CFU/mL), Mycoplasma pneumoniae (ATCC 15531) (2.48 X 10^9 CFU/mL), Chlamydia pneumoniae (ATCC VR-2282) (9.1 X 10^7 IFU/mL), Legionella pneumophila (ATCC 33155) (1.9 X 10^8 CFU/mL), Staphylococcus aureus (NCCP 14647) (1.00 X 10^9 CFU/mL), Staphylococcus epidermidis (KCCM 35494) (6.22 X 10^8 CFU/mL).

Cross-reactivity was observed for SARS-CoV.

Note: Human coronavirus HKU1, *Pneumocystis jirovecii* (PJP) and *Mycobacterium tuberculosis* have not been tested. There can be cross-reaction with human coronavirus HKU1, PJP or TB, even though the percentage identity of the nucleocapsid protein sequence of HKU1, and proteins of PJP and TB with the nucleocapsid protein sequence of SARS-CoV-2 was 31.6 %, 12.3 % and 13.0 %, respectively, which is considered as low homology.

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) (1:10 dilution), 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), Whole Blood (4 %), Mucin (0.5 %).

4. High-dose hook effect:
SARS-CoV-2 cultured virus was spiked into specimens. SARS-CoV-2 cultured virus did not show hook effect up to 1 X $10^{6.2}$ $TCID_{50}$/mL.

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

1 Coronaviruses. European Centre for Disease Prevention and Control. https://www.ecdc.europa.eu/en/covid-19/latest-evidence/coronaviruses. Accessed 6 Jan 2021.

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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

5 WHO. https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020. Accessed 6 Jan 2021.

6 WHO. https://www.who.int/publications-detail-redirect/diagnostic-testing-for-sars-cov-2. Accessed 6 Jan 2021.

7 Centers for Disease Control and Prevention. https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html. Accessed 6 Jan 2021.

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

Additions, deletions or changes are indicated by a change bar in the margin.

CE

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