134101001K04:50 tests/kit
134101001K03:25 tests/kit
134101001K02: 5 tests/kit
134101001K01: 1 test/kit

RapiSafe™ SARS-CoV-2 Antigen Rapid Test (Colloidal Gold)

INTENDED USE

The kit is a lateral flow immunoassay for the qualitative detection of SARS-CoV-2 nucleocapsid protein (SARS-CoV-2 Ag) in nasopharyngeal and oropharyngeal samples.

SUMMARY

The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) causes an epidemic of acute respiratory syndrome in humans. SARS-CoV-2 is a single-stranded RNA virus, it has an envelope, particles are round or oval, often polymorphic, and the diameter is 60-140nm. SARS-CoV-2 encodes four structural proteins: spike, envelope, membrane, and nucleocapsid. Genetic sequencing of the virus suggests that it is a betacoronavirus closely linked to the SARS virus. SARS-CoV-2 is mainly transmitted through respiratory droplets and can also be transmitted through contact. The sources of infection are mainly patients with novel coronavirus or asymptomatic infected by the novel coronavirus.

Upper respiratory specimen, such as nasopharyngeal swab and oropharyngeal swab, are commonly used for diagnostic testing. Standard confirmation of acute SARS-CoV-2 infections is based on the detection of unique viral sequences by nucleic acid amplification tests (NAATs), such as real-time reverse-transcription polymerase chain reaction (rRT-PCR). The assays' targets include regions on the E, RdRP, N and S genes. Antigen is generally detectable in nasopharyngeal swabs during the acute phase of SARS-CoV-2 infection. Antigen-detection diagnostic tests are designed to directly detect SARS-CoV-2 proteins produced by replicating virus in respiratory secretions and have been developed as both laboratory-based tests, and for near-patient use, socalled rapid diagnostic tests, or RDTs[1].

TEST PRINCIPLE

Sandwich colloidal gold immunochromatography.

The test card is composed of sample pad, colloidal gold pad, nitrocellulose membrane, absorbent paper, PVC base plate and plastic card. A mouse anti-SARS-CoV-2 nucleocapsid protein monoclonal antibody with colloidal gold particle labeling was solidified on the colloidal gold pad. There are two pre-coated lines on the surface of nitrocellulose membrane: a Control line(C line) and a Test line (T line). Both the C line and T line in the result window are not visible before applying any samples. A mouse anti-SARS-CoV-2 nucleocapsid protein monoclonal antibody is coated on the T line region and a goat anti-mouse IgG polyclonal antibody is coated on the C line region.

During the test, the SARS-CoV-2 antigen in the sample flows through the sample pad and binds with the mouse anti-SARS-CoV-2 nucleocapsid protein monoclonal antibody labeled with colloidal gold particles on the gold pad to form immuno-complexs. This complex migrates on the nitrocellulose membrane via capillary action to the T line, where it is captured by another mouse anti-SARS-CoV-2 nucleocapsid protein monoclonal antibody. A colored T line becomes visible in the result window if SARS-CoV-2 antigens are present in the sample. The intensity of the colored T line varies depending upon the amount of SARS-CoV-2 antigen present in the sample.

The remaining unreacted gold labeled antibodies continue to migrate to C line through capillary action on the nitrocellulose membrane, and combine with the goat anti‑mouse IgG polyclonal antibody on C line to form immuno-complexes, thus producing visible color bands at the position of C line.

REAGENTS

Kit Contents

Component	1 test/kit	5 tests/kit	25 tests/kit	50 tests/kit
Test Card	1	5	25	50
Sample Extraction Tube	1	5	25	50
Sample Extraction Solution*	1×0.5 mL	5×0.5 mL	1×15 mL	2×15 mL
Information Card Sticker	1	5	25	50
Sterile Swab	1	5	25	50
Biosafety Bag	1	5	25	50
Test Card is packaged individually in a sealed pouch with desiccant. *Sample Extraction Solution has been pre-packed in the Sample Extraction Tube for 1 test/kit and 5 tests/kit. Sample Extraction Solution contains Tris-HCl buffer, sodium chloride, surfactant, BSA and preservatives (ProClin 300, 0.02%).				

Warnings and Precautions

- For *in vitro* diagnostic use.
- For professional use only.
- Do not reuse the test card.
- Exercise the normal precautions required for handling all laboratory reagents.
- Personal protective measures should be taken to prevent any part of the human body from contacting samples, and reagents, and should comply with local operating requirements for the assay. Do not use kit beyond the expiration date indicated on the label.
- Leave test card sealed in its foil pouch until just before use. Do not use if the foil pouch is damaged or open.
- Do not mix components from different kit lots.
- Ensure all test components are equilibrated to room temperature before use.
- Do not touch the sample pad and nitrocellulose membrane on the test card.
- Do not touch swab tip when handling the swab sample.
- Do not read the test result after 30 minutes.
- Samples are handled immediately after collection, do not store the swab in the original paper packaging.
- Proper sample collection and handling are essential for correct results.
- Invalid results can occur when an insufficient or excessive volume of samples is added to the test card.
- 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.
- This product contains ProClin 300. ProClin 300 contains methylisothiazolinone, which may cause skin irritation. In case of contact with the skin, please rinse with plenty of water. If skin irritation or rash appears, please seek medical advice immediately.

Note: If any serious incident has occurred in relation to the device, please report to Shenzhen New Industries Biomedical Engineering Co., Ltd. (Snibe) or our authorized representative and the competent authority of the Member State in which you are established.

Storage and Stability

- Do not freeze the kit.
- Protect from direct sunlight.
- Unopened at 2-30°C is stable until the stated expiration date.
- The test card should be used within 1 hour after taking out from the foil pouch.

▌SPECIMEN COLLECTION AND PREPARATION

- Use appropriate precautions in the collection, handling, and storage of patient samples, refer to the CDC Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens for COVID-19 at https://www.cdc.gov/coronavirus/2019- nCoV/lab/guidelines-clinical-specimens.html, and the WHO's Interim guidance for Laboratory testing for 2019 novel coronavirus (2019-nCoV) in suspected human cases at https://www.who.int/publications/i/item/10665-331501, as amended and supplemented. Refer to the WHO website for additional publications.
- Avoid splashing or forming aerosol, as droplets are a means of transmission of SARS-CoV-2 virus.
- Please pay attention to the risk of infection during sample collection and preparation.
- All samples, even after the inactivation procedure, must be considered as potentially able to transmit infectious agents; accordingly, samples 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. Any materials for reuse must be appropriately sterilized in compliance with the local laws and guidelines. Check the effectiveness of the sterilization/decontamination cycle.
- To prevent cross contamination, do not reuse the sample extraction tube tips, pipettes or pipette tips.
- Only the specimens listed below were tested and found acceptable.

Dry nasopharyngeal swab and oropharyngeal swab.

Nasopharyngeal swab and oropharyngeal swab are transported in Universal Transport Media (Copan, UTM) or Viral Transport Media (MANTACC, VTM) *.

* UTM and VTM from other manufacturers have not yet been verified. The UTM and VTM from various manufacturers may contain differing materials which could affect the test results in some cases. Follow UTM and VTM manufacturers' instructions carefully when doing sample collection.

Pre-treating Procedure for Swab in UTM or VTM

- Collect the sample by nasopharyngeal swab and oropharyngeal swab transported in UTM/VTM.
- Ensure the clinical samples and UTM/VTM are equilibrated to room temperature before use.
- Pipette at least 0.6 mL of the sample eluted in UTM/VTM into sample extraction tube*. To obtain accurate results, avoid mucoid substances when pipetting sample from the above UTM/VTM.

*500 µL sample extraction solution has been pre-packed in the sample extraction tube.

Pre-treating Procedure for Dry Swab Use Pre-aliquoted Sample Extraction Solution (REF: 134101001K01, 134101001K02)

- Collect nasopharyngeal swab and oropharyngeal swab samples according to clinical laboratory standard methods.
- Unscrew the blue cover of the pre-filled tube containing the sample extraction solution, place and soak the nasopharyngeal swab or oropharyngeal swab in liquid.
- Squeeze the lower bottom of the tube, while rotate the swab at least 5 times and plunge the swab up and down 5 times. Be careful not to spill the liquid.
- Leave the swab in the tube at room temperature for 5-6 minutes.
- Plunge the swab up and down while squeezing the sides of the tube to extract the liquid from the swab, and tightly sealed the tube with the blue cap. Dispose of the used swab in the biohazardous waste collection.

Pre-treating Procedure for Dry Swab Use Sample Extraction Solution (REF: 134101001K03, 134101001K04)

- Collect nasopharyngeal swab and oropharyngeal swab samples according to clinical laboratory standard methods.
- Prepare a sample extraction tube, add the sample extraction solution droplet to the 500 µL scale line of the sample extraction tube or transfer 500 µL sample extraction solution to the sample extraction tube using a pipette, place and soak the nasopharyngeal swab or oropharyngeal swab in liquid.
- Rotate the swab in the liquid at least 5 times, and plunge the swab up and down 5 times. Be careful not to spill the liquid.
- Leave the swab in the tube at room temperature for 5-6 minutes.
- Plunge the swab up and down while squeezing the sides of the tube to extract the liquid from the swab, and tightly sealed the tube with the blue cap. Dispose of the used swab in the biohazardous waste collection.

Preparation for Analysis

- Carefully read the instructions for using the SARS-CoV-2 Antigen Rapid Test (Colloidal Gold).
- Prior to starting the procedure, test card and reagent must be equilibrated to room temperature.
- Check the expiry date on the back of the foil pouch. Do not use the test card, if the expiry date has passed.
- Open the foil pouch and remove the test card. Use the test immediately after opening the pouch.

Specimen Storage

- Samples should be tested as soon as possible after the completion of the pre-treating procedure. If immediate testing is not possible, pre-treating samples can be stored at room temperature up to 1 hour or 2-8°C up to 4 hours.
- The sample from UTM/VTM can be stored at room temperature up to 8 hours or 2-8°C up to 12 hours or at -70°C for 2 months. Frozen specimens subjected to up to 3 freeze/thaw cycles have been evaluated.

Specimen Shipping

- Package and label specimens in compliance with applicable local regulations covering the transport of clinical specimens and infectious substances.
- Do not exceed the storage limitations listed above.

▌PROCEDURE

Materials Provided

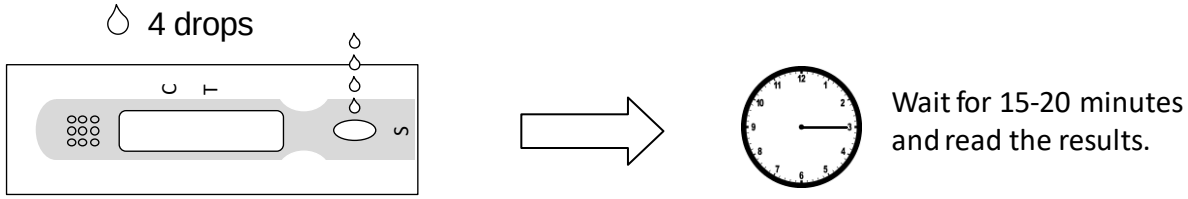
SARS-CoV-2 Antigen Rapid Test (Colloidal Gold).

Materials Required (But Not Provided)

- Personal protective equipment per local recommendations or requirements.
- Clock, timer or stopwatch

Assay Procedure

- Take out a test card from the packaging bag by tearing at the notch and place it on a level surface.
- Break off the column above the blue cover of the sample extraction tube.
- Add 4 drops of extracted sample at a 90° angle to the sample well of the test card.
- Wait for 15-20 minutes and read the results.
- After the test, put the medical wastes into the biosafety bag.

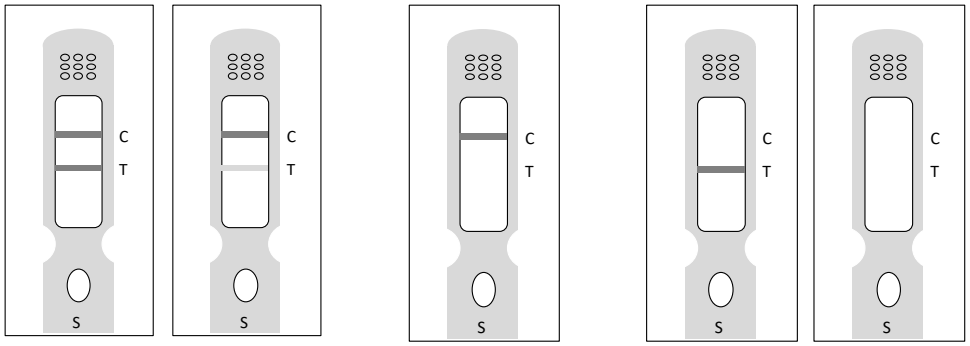


Quality Control

- A procedural control is included in the test. A colored line appearing in the C line region is considered an internal procedural control. It confirms sufficient specimen volume, adequate capillary action and correct procedural technique.

▌Reading and interpreting 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 C line. Even if the C line is faint or not uniform, the test should be considered to be performed properly.
- Positive result: Colored lines appeare in the T line and C line region. Even if the T line is very faint or not uniform the test result should be interpreted as a positive result.
- Negative result: A colored line only appears in the C line region, but the T line region is not visible.
- Invalid result: If no C line is visible, no matter whether the T line is visible or not, the test result should be considered as invalid. It is recommended to select a new kit to test, if the C line still does not show a color, please contact with Snibe or our authorized distributor.



Positive Negative Invalid

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 nasopharyngeal swab and oropharyngeal swab.
- 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.
- Avoid testing under strong ventilation conditions to ensure adequate sample migration.
- A negative result may occur if the concentration of antigen in a sample is below the detection limit of the test.
- The following situations can lead to unreliable results and false negatives: 1) Sample is improperly collected or handled. 2) Insufficient or excessive volume of samples is added to the test card. 3) Swabs in the sample extraction tube are not rotated, plunged or squeezed. 4) Swabs are stored in their original paper packaging after specimen collection.
- 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 infection.

SPECIFIC PERFORMANCE CHARACTERISTICS

Representative performance data are provided in this section. Results obtained in individual laboratories may vary.

Precision

Precision was determined using the assay, 4 pooled positive oropharyngeal swab samples and 1 negative oropharyngeal swab sample in a protocol (EP05-A3) of the CLSI (Clinical and Laboratory Standards Institute): three users , three lots of reagent on three days (n = 27). The data is used to calculate the positive and negative coincidence rate. For the SARS-CoV-2 Antigen Rapid Test (Colloidal Gold), the positive and negative coincidence rate was 100%.

Sample	Operator A		Operator B		Operator C		Total	
	% Positive	95% CI	% Positive	95% CI	% Positive	95% CI	% Positive	95% CI
S1 (Positive)	100% (27/27)	(87.5%, 100%)	100% (27/27)	(87.5%, 100%)	100% (27/27)	(87.5%, 100%)	100% (81/81)	(95.5%, 100%)
S2 (Positive)	100% (27/27)	(87.5%, 100%)	100% (27/27)	(87.5%, 100%)	100% (27/27)	(87.5%, 100%)	100% (81/81)	(95.5%, 100%)
S3 (Positive)	100% (27/27)	(87.5%, 100%)	100% (27/27)	(87.5%, 100%)	100% (27/27)	(87.5%, 100%)	100% (81/81)	(95.5%, 100%)
S4 (Positive)	100% (27/27)	(87.5%, 100%)	100% (27/27)	(87.5%, 100%)	100% (27/27)	(87.5%, 100%)	100% (81/81)	(95.5%, 100%)
S5 (Negative)	0% (0/27)	(0.0%, 12.5%)	0% (0/27)	(0.0%, 12.5%)	0% (0/27)	(0.0%, 12.5%)	0% (0/81)	(0.0%, 4.5%)

Analytical Sensitivity

Limit of Detection (LoD) = 2×10^2 $TCID_{50}$/mL.

Interference

The following substances, naturally present in respiratory specimens or that may be artificially introduced into the samples of nasopharyngeal and oropharyngeal, were evaluated with the SARS-CoV-2 Antigen Rapid Test (Colloidal Gold) at the concentrations listed below and were found not to affect test performance.

Substance	Active Ingredient	Concentration	Substance	Active Ingredient	Concentration
Endogenous	Mucin	2% (w/v)	Anti-viral Drug 1	Oseltamivir Phosphate	10 mg/mL
	Whole Blood	1% (v/v)	Anti-viral Drug 2	Zanamivir	5 mg/mL
OTC Nasal Drops	Phenylephrine	15% (v/v)	Anti-viral Drug 3	Ribavirin	1 mg/mL
OTC Nasal Gel	Sodium Chloride	5% (v/v)	Anti-inflammatory drug 1	Acetaminophen	200 μmol/L
OTC Nasal Spray 1	Cromolyn	15% (v/v)	Anti-inflammatory drug 2	Acetylsalicylic acid	3.7 mmol/L
OTC Nasal Spray 2	Oxymetazoline	15% (v/v)	Anti-inflammatory drug 3	Ibuprofen	2.5 mmol/L
OTC Nasal Spray 3	Fluconazole	5% (w/v)	Antibiotic 1	Erythromycin	81.6 μmol/L
Throat Lozenge 1	Menthol	0.15% (w/v)	Antibiotic 2	Ciprofloxacin	31 μmol/L
Throat Lozenge 2	Benzocaine	0.15% (w/v)	Antibiotic 3	Tobramycin	5 μg/mL
OTC Homeopathic Nasal Spray	Fluticasone Propionate	5% (v/v)	Antibiotic 4	Mupirocin	10 mg/mL
Sore Throat Phenol Spray	Phenol	15% (v/v)	-	-	-

Cross-Reactivity

The cross-reactivity study for the SARS-CoV-2 Antigen Rapid Test (Colloidal Gold) was designed to evaluate potential cross reactants that may be present in the samples of nasopharyngeal and oropharyngeal. The results are listed in the following table:

Potential cross reacting substance	Concentration of potentially cross reacting substance	Potential cross reacting substance	Concentration of potentially cross reacting substance
MERS	4×10^4 $TCID_{50}$/mL	Rhinovirus	1×10^5 $TCID_{50}$/mL
HCoV-HKU1	1×10^5 $TCID_{50}$/mL	Enterovirus	1×10^4 $TCID_{50}$/mL
HCoV-229E	1×10^5 $TCID_{50}$/mL	Metapneumovirus	1×10^5 $TCID_{50}$/mL
HCoV-OC43	1×10^5 $TCID_{50}$/mL	Measles virus	1×10^5 $TCID_{50}$/mL

HCoV-NL63	1×10^5 $TCID_{50}$/mL	Mumps virus	1×10^5 $TCID_{50}$/mL
Influenza A H1N1	3×10^5 $TCID_{50}$/mL	Mycobacterium tuberculosis	1×10^6 cell/mL
Influenza A H3N2	3×10^5 $TCID_{50}$/mL	Mycoplasma pneumoniae	1×10^6 cell/mL
Influenza B	3×10^5 $TCID_{50}$/mL	Chlamydia pneumoniae	1×10^6 cell/mL
Parainfluenza virus Type 1	1×10^5 $TCID_{50}$/mL	Haemophilus influenzae	1×10^6 cell/mL
Parainfluenza virus Type 2	1×10^5 $TCID_{50}$/mL	Streptococcus pneumoniae	1×10^6 cell/mL
Parainfluenza virus Type 3	1×10^5 $TCID_{50}$/mL	Legionella pneumophila	1×10^6 cell/mL
Parainfluenza virus Type 4	1×10^5 $TCID_{50}$/mL	Staphylococcus aureus	1×10^6 cell/mL
Adenovirus	1×10^5 $TCID_{50}$/mL	Bordetella pertussis	1×10^6 cell/mL
Respiratory syncytial virus	1×10^5 $TCID_{50}$/mL	Candida albicans	1×10^6 cell/mL

Verification of mutants

The matched antibodies used in the SARS-CoV-2 Antigen Rapid Test (Colloidal Gold) avoid the major Nucleocapsid protein mutation sites, so the kit can detect the major virus mutants that shown in the table below.

WHO label	Pango lineage	Mutation sites of N protein	Earliest documented samples
Alpha	B.1.1.7	D3L, S235F	United Kingdom, Sep-2020
Beta	B.1.351	T205I	South Africa, May-2020
Gamma	P.1	P80R	Brazil, Nov-2020
Delta	B.1.617.2	R203M, D377Y	India, Oct-2020
Kappa	B.1.617.1	D63G, R203M, D377Y	India, Oct-2020

Whether the clinical sensitivity and clinical specificity will be affected by mutation needs further study.

High-Dose Hook

No high-dose hook effect was seen for SARS-CoV-2 Ag concentrations up to 2×10^6 $TCID_{50}$/mL.

Clinical Sensitivity

The clinical sensitivity of the SARS-CoV-2 Ag assay was determined by testing 130 samples confirmed COVID-19 infected specimens by RT-PCR.

Days Post Onset of Symptoms	Sample type	N of samples	Reactive	Sensitivity	95% CI
0-7	Nasopharyngeal swab	60	58	96.7%	88.6%~99.1%
	oropharyngeal swab	70	68	97.1%	90.2%~99.2%
	total	130	126	96.9%	92.4%~98.8%

The positive rate of SARS-CoV-2 Ag may be affected by the infection period of the test subject in different studies.

Clinical Specificity

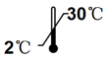
The clinical specificity of the SARS-CoV-2 Ag assay was determined by testing 240 samples from subjects negative for SARS-CoV-2.

Sample type	N of samples	Non-reactive	Specificity	95% CI
Nasopharyngeal swab	112	111	99.1%	95.1%~99.8%
oropharyngeal swab	128	127	99.2%	95.7%~99.9%
total	240	238	99.2%	97.0%~99.8%

REFERENCES

1. WHO. Antigen-detection in the diagnosis of SARS-CoV-2 infection using rapid immunoassays. Interim guidance 11 September 2020.

SYMBOLS EXPLANATIONS

	Consult instructions for use		Manufacturer
	Temperature limit (Store at 2-30°C)		Use-by date
	Contains sufficient for <n> tests		Keep away from sunlight
IVD	*In vitro* diagnostic medical device	EC REP	Authorized representative in the European Community
REF	Catalogue number	LOT	Batch code
CE	CE marking		Keep dry
	Do not use if package is damaged		Do not reuse

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