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# COVID-VIRO ALL IN DUO®

## Nasal test kit COVID-19/Influenza A/B all in one

**Réf : TR-COG-002**

Instructions for use

Read the instructions for use completely before performing the test.

The instructions must be followed carefully

## INTENDED USE

**COVID-VIRO ALL IN DUO®** is a rapid test, specially designed and secured for use in children or in adults and allowing the detection of the N protein of SARS-CoV-2, Influenza A, Influenza B in nasal secretions.

**COVID-VIRO ALL IN DUO®** is a rapid test that assists in the diagnosis of SARS-CoV-2, Influenza A and Influenza B infections.

**COVID-VIRO ALL IN DUO®** is a test for professional use only.

**COVID-VIRO ALL IN DUO®** detects SARS-CoV-2 and new variants in which the synthesis of nucleoprotein N is not affected (alpha, beta, gamma, delta and omicron variants).

## INTRODUCTION

SARS-CoV-2 was identified in 2019, it belongs to the β-coronavirus familly. It is the pathogen causing an emerging atypical pneumonia, coronavirus disease 2019 (Covid-19).

Several SARS-CoV-2 variants, called alpha, beta, gamma, delta and omicron have been identified by viral genome sequencing. Their RNAs have multiple mutations and deletions resulting in deletions or amino acid changes in the S (Spike) protein.

Currently, patients infected with SARS-CoV-2 are the main source of transmission: infected persons, who are asymptomatic, can also be a source of infection. Based on the current epidemiological survey, the incubation period can range from 1 to 14 days but is usually 3 to 7 days.

The main symptoms are fever or the feeling of fever and cough. Sudden loss of smell, without nasal obstruction and total loss of taste are also symptoms that have been observed in patients. In people with more severe forms, breathing difficulties are present, which can lead to hospitalisation in intensive care and death.

Influenza is an acute, highly contagious viral infection of the respiratory tract. The agents responsible for the infection are immunologically divergent single-stranded RNA viruses, called influenza viruses. There are three types of influenza virus: A, B and C. Type A viruses are the most common and are associated with the most severe epidemics, while type B infection is generally milder. Type C viruses have never been associated with a major epidemic of human disease. Type A and B viruses can circulate simultaneously, but usually one type is dominant in a given season and in a particular epidemic area. The disease is easily transmitted by coughing and sneezing droplets containing virus. Influenza epidemics normally occur each year during the autumn and winter seasons.

**COVID-VIRO ALL IN DUO®** has been designed to detect the SARS-CoV-2 Nucleocapsid Protein (N) as well as specific target antigens of Influenza A and Influenza B.

**COVID-VIRO ALL IN DUO®** detects alpha, beta, gamma, delta and omicron variants with the same performance as other known SARS-CoV-2 strains. Mutations in Spike protein synthesis do not affect test performance. The nucleocapsid (N) protein of SARS-CoV-2 is usually detectable in upper respiratory tract specimens during the acute phase of infection.

## PRINCIPLE

**COVID-VIRO ALL IN DUO®** is a dual lateral flow immunochromatographic test that uses highly sensitive monoclonal antibodies to detect specific target antigens for each virus (SARS-CoV-2, Influenza A and Influenza B) in a nasal sample.

The test uses monoclonal antibodies directed against target antigens for each virus and fixed at the test site (T) on a nitrocellulose strip. A monoclonal antibody directed against target antigens for each virus and labelled with colloidal gold is used as a lyophilised conjugate.

In the test, the antigens in the sample interact with the antigen-specific monoclonal antibodies conjugated to the colour particles to form a coloured antibody-antigen complex.

This complex migrates by capillary action across the membrane to the test line (T) where it is captured by the antigen specific monoclonal antibodies bound to the membrane.

A coloured test line will appear in the results window (T) if antigens for any of the viruses are present in the sample. The intensity of the coloured test line will vary according to the amount of antigen present in the sample. If no antigen is present in the sample, no colour will appear on the test line (T). The control line is used as a procedural control and should always appear in the control area (C) if the test procedure is performed correctly.

## MATERIALS

**Materials Provided**

- 10 Individually packed tests
- Package insert

**Materials Required but Not provided**

- Clock, timer or stopwatch

## PRECAUTIONS

- The test device should remain in the sealed pouch until use.
- Do not use the kit after the expiry date, do not use the kit with a hole or damage in the bag.
- Incorrect results may be obtained if the kit is stored incorrectly.
- The kit is for single use only. It should not be removed from the bag until just before testing (to avoid cross-contamination).
- Avoid skin or eye contact with the pad in the dosette before, during or after the test. If the solution comes into contact with the skin or eyes, rinse thoroughly with water.
- For accurate results, do not use samples that contain blood or are too viscous.
- Wear appropriate protective clothing, gloves and eye/face protection when handling the contents of this kit. The used kit should be disposed of in accordance with local regulations.

## STORAGE AND STABILITY

- Store The **COVID-VIRO ALL IN DUO®** Test Kit at 2~30℃ when not in use.
- **DO NOT FREEZE**.
- Kit contents are stable until the expiration dates marked on their outer packaging and containers.

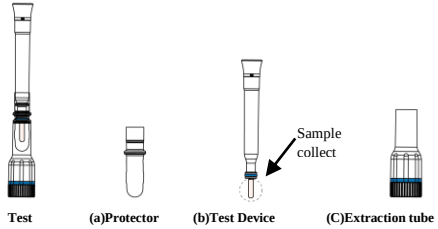
## TEST PROCEDURE

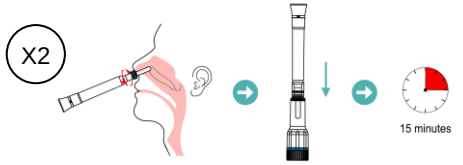
Bring devices, reagents and specimens and/or controls to room temperature (15~30°C) before use.

1. Remove the test from its packing. Label the device with the patient's identification. For best results, the assay should be performed within one hours.
2. 1) Take the test device out of the extraction tube.
   2) Remove the protector.
3. Gently insert the sample collector until resistance is met (about 1-2 cm into the nostril).
4. Rotate the collector five times against the nasal wall and remove from the nostril.
5. Repeat the sample collection procedure for the other nostril to ensure that sufficient specimen be collected from both nasal cavities.

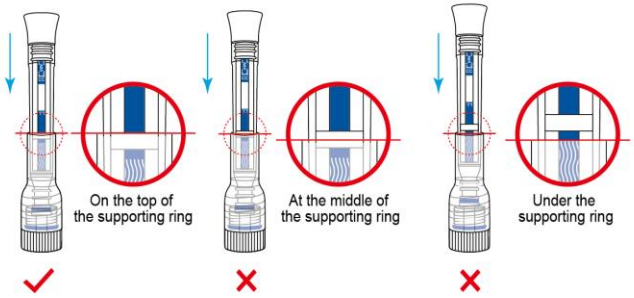
**Note: 1. It is important to obtain as much secretion as possible.**
**2. Do not insert the collector any deeper if you feel strong resistance.**

6. Place the test device vertically into the extraction tube until the top edge of the extraction tube reach the top of the supporting ring.
7. Read the results at 15 minutes.



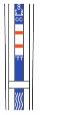




**Note:**
**When placing the test device vertically in the extraction tube, the edge of the extraction tube must reach the top of the support ring. Failure to do so may result in migration failure, resulting in an incorrect or invalid result.**

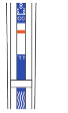



## RESULT INTERPRETATION

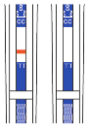
**For COVID-19 test:**



**POSITIVE: Two colored bands appear on the membrane.** One band appears in the control region (C) and another band appears in the test region (T).



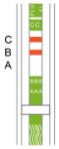
**NEGATIVE: Only one colored band appears, in the control region (C).** No apparent colored band appears in the test region (T).



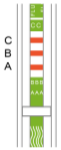
**INVALID: Control band fails to appear.** Results from any test which has not produced a control band at the specified read time must be discarded. Please review the procedure and repeat with a new test. If the problem persists, discontinue using the kit immediately and contact your local distributor.

**For Influenza A/B test:**


**INFLUENZA A POSITIVE:** One colored band appears in the control region (C), and another colored band in the A region (A).

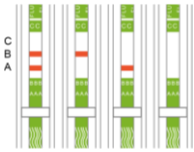



**INFLUENZA B POSITIVE:** One colored band appears in the control region (C), and another colored band in the B region (B).




**INFLUENZA A+B POSITIVE:** One colored band appears in the control region (C), and two other colored bands appear in both A region (A) and B region (B).
**NOTE:** Co-infection with influenza A and B is rare. A clinical specimen that generates positive results for both A and B should be considered an invalid result, and another test should be performed. If the test is again positive for both influenza A and B, the specimen should be re-tested by another method prior to reporting of results.


**NEGATIVE:** Only one colored band appears in the control region (C), and band appears neither in the A region (A) nor B region (B).




**INVALID:** No colored band appears in the control region (C), whether a test band(s) is present or not. Repeat invalid tests with a new sample, new test device and reagent. Insufficient sample volume, inaccurate operating procedure or expired tests may yield an invalid result. Contact your local distributor if the problem continues.

**NOTE:**

**1.** The color intensity in the test region(s) may vary depending on the concentration of analytes present in the specimen. Note that this is a qualitative test only, and cannot determine the concentration of analytes in the specimen.

## QUALITY CONTROL

**Internal Procedural Controls**

The **COVID-VIRO ALL IN DUO®** Test Kit has built-in (procedural) controls. Each test has an internal standard zone to ensure proper sample flow. The user should confirm that the colored band located at the "C" region is present before reading the result.

## LIMITATIONS OF THE TEST

1. The **COVID-VIRO ALL IN DUO®** Test Kit is for professional *in vitro* diagnostic use, and should only be used for the qualitative detection of viral antigens specific for SARS-CoV-2, Influenza A virus, and Influenza B virus. The intensity of color in a positive band should not be evaluated as "quantitative or semi-quantitative".
2. Both viable and nonviable viruses are detectable with the kit.
3. As with all diagnostic tests, a definitive clinical diagnosis should not be based on the results of a single test, but should only be made by the physician after all clinical and laboratory findings have been evaluated.
4. Failure to follow the TEST PROCEDURE and RESULT INTERPRETATION may adversely affect test performance and/or invalidate the test result.
5. Results obtained with this assay, particularly in the case of weak test lines that are difficult to interpret, should be used in conjunction with other clinical information available to the physician.
6. Negative results do not preclude viral infections and should be confirmed via molecular assay.

## PERFORMANCE CHARACTERISTICS

**Analytical Sensitivity:**

The limit of detection(LOD) of **COVID-VIRO ALL IN DUO®** Test Kit, defined as the concentration of influenza virus and SARS-CoV-2 virus that produces positive **COVID-VIRO ALL IN DUO®** Test Kit results approximately 95% of the time, was identified by evaluating different concentrations of inactivated Flu A(H3N2, H1N1), inactivated Flu B(Victoria, Yamagata) and inactivated SARS-CoV-2 in the **COVID-VIRO ALL IN DUO®** Test Kit.

20 tests were run at each concentration. The results identify a concentration of $1.0\times10^4$ $TCID_{50}$/ml as the LOD for Flu A (H3N2), $4.3\times10^4$ $TCID_{50}$ as the LOD for Flu A (H1N1), $2.2\times10^5$ $TCID_{50}$ for Flu B (Victoria), $2.5\times10^5$ $TCID_{50}$ for Flu B (Yamagata) and $1\times10^{2.4}$ $TCID_{50}$/mL as the LOD for SARS-CoV-2.

**Clinical Evaluation:**

For COVID-19 antigen detection:

A total of 612 specimens collected were evaluated in the **COVID-VIRO ALL IN DUO®** Test Kit and compared to RT-PCR. No differences in test performance were observed based on patient age or gender. 107 specimens were found to be positive by RT-PCR and 505 specimens were found to be negative by RT-PCR. These specimens were tested with the **COVID-VIRO ALL IN DUO®** Test Kit. The results are shown in Table 1.

Table 1: COVID-19 Antigen Test vs. RT-PCR

| | | RT-PCR | | Total |
|---|---|---|---|---|
| | | Positive | Negative | |
| COVID-19-Antigen-Test | **Positive** | 101 | 0 | 101 |
| | **Negative** | 6 | 505 | 511 |
| | **Total** | 107 | 505 | 612 |

Relative Sensitivity: 94.39 % (88.3 – 97.4%)*
Relative Specificity: 100 % (99.2 - 100%)*
Total agreement: 99 %
*95% Confidence Interval

**For Influenza A/B antigen detection:**

A total of 450 specimens collected were evaluated in the **COVID-VIRO ALL IN DUO®** Test Kit and compared to RT-PCR.

For all specimens evaluated, the overall sensitivity of the **COVID-VIRO ALL IN DUO®** Test Kit when compared to RT-PCR was 95.9% (70/73) for influenza A and 94.4% (51/54) for influenza B. The overall specificity was 99.5% (375/377) for influenza A and 99.7% (395/396) for influenza B. The results are shown in Table 2 and Table 3.

Table 2: Influenza A antigen test VS RT-PCR

| | | RT-PCR | | Total |
|---|---|---|---|---|
| | | Positive | Negative | |
| Influenza A/B Rapid Test | **Influenza A+** | 70 | 2 | 72 |
| | **Influenza A-** | 3 | 375 | 378 |
| | **Total** | 73 | 377 | 450 |

Positive agreement: 95.9 % (88.6%~98.6%) *
Negative agreement: 99.5 % (98.1%~99.9%) *
Total agreement: 98.9 % (97.4%~99.5%) *
*95% Confidence Interval

Table 3: Influenza B antigen test VS RT-PCR

| | | RT-PCR | | Total |
|---|---|---|---|---|
| | | Positive | Positive | |
| Influenza A/B Rapid Test | **Influenza B+** | 51 | 1 | 52 |
| | **Influenza B-** | 3 | 395 | 398 |
| | **Total** | 54 | 396 | 450 |

Positive agreement: 94.4 % (84.9%~98.1%) *
Negative agreement: 99.7 % (98.6%~100.0%) *
Total agreement: 99.1 % (97.7%~99.7%) *
*95% Confidence Interval

**Cross Reactivity:**

Cross reactivity with the following organisms has been studied. Samples positive for the following organisms were found negative when tested with the **COVID-VIRO ALL IN DUO®** Test Kit.

| | | |
|---|---|---|
| HCoV-229E | *Bordetellapara pertussis* | Adenovirus 1 |
| HCoV-OC43 | *Bordetella pertussis* | Adenovirus 2 |
| HCoV-NL63 | *Candida albicans* | Adenovirus 3 |
| MERS-coronavirus | *Chlamydia pneumoniae* | Adenovirus 4 |
| SARS-coronavirus | *Group C Streptococcus* | Adenovirus 5 |
| Human metapneumovirus | *Haemophilus influenzae* | Adenovirus 7 |
| Norovirus | *Legionella pneumophila* | Adenovirus 55 |
| Parainfluenza virus 1 | *Mycoplasma pneumoniae* | Epstein-Barr virus |
| Parainfluenza virus 2 | *Mycobacterium tuberculosis* | Enterovirus EV70 |
| Parainfluenza virus 3 | *Staphylococcus aureus* | Enterovirus EV71 |
| Parainfluenza virus 4 | *Staphylococcus epidermidis* | Enterovirus A16 |
| Respiratory syncytial virus | *Streptococcus agalactiae* | Enterovirus A24 |
| Respiratory syncytial virus | *Streptococcus pneumoniae* | Enterovirus B1 |
| Rhinovirus A30 | *Streptococcus pyogenes* | Echovirus 6 |
| Rhinovirus B52 | | |

**Interfering Substances**

The following substances, naturally present in respiratory specimens or that may be artificially introduced into the respiratory tract, were evaluated at the concentrations listed below. None of them were found to affect test performance of the kit.

| Substance | Concentration | Substance | Concentration |
|---|---|---|---|
| 3 OTC nasal sprays | 10% | Guaiacol glyceryl ether | 20mg/mL |
| 3 OTC mouth washes | 10% | Mucin | 1% |
| 3 OTC throat drops | 10% | Whole blood | 4% |
| 4-acetamidophenol | 10 mg/mL | Mupirocin | 250µg/mL |
| Acetylsalicylic acid | 10 mg/mL | Oxymetazoline | 25µg/mL |
| Albuterol | 10 mg/mL | Phenylephrine | 10 mg/mL |
| Chlorpheniramine | 5 mg/mL | Phenylpropanolamine | 1mg/mL |
| Dexamethasone | 50µg/mL | Zanamivir | 10mg/mL |
| Dextromethorphan | 10µg/mL | Adamantanamine | 500 ng/mL |
| Diphenhydramine | 5 mg/mL | Oseltamivir phosphate | 10mg/mL |
| Doxylamine succinate | 1 mg/mL | Tobramycin | 10mg/mL |
| Flunisolide | 25µg/mL | Triamcinolone | 14mg/mL |

## LITERATURE REFERENCES


**1.** Forni, D., Cagliani, R., Clerici, M. & Sironi, M. Molecular evolution of human coronavirus genomes. Trends Microbiol. 25, 35–48 (2017).

**2.** Kan, B. et al. Molecular evolution analysis and geographic investigation of severe acute respiratory syndrome coronavirus-like virus in palm civets at an animal market and on farms. J. Virol. 79, 11892–11900 (2005).

**3.** Ithete, N. L. et al. Close relative of human Middle East respiratory syndrome coronavirus in bat, South Africa. Emerg. Infect. Dis. 19, 1697–1699 (2013).


## GLOSSARY OF SYMBOLS

| | | | |
|---|---|---|---|
| | Read the instructions for use | | Expiry date |
| IVD | For *in vitro* diagnostic use only | LOT | Batch number |
| 2°C 30°C | Store between 2 and 30°C | Σ | Number of tests per kit |
| | Manufacturer | REF | Reference |
| | Do not reuse | CE | CE marking |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