COVID-19 Ag Respi-Strip

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IFU-5723/TB/V03

***In vitro* rapid diagnostic test for the detection of SARS-CoV-2 antigen in nasopharyngeal secretions**

FOR IN VITRO USE **EN**

FOR PROFESSIONAL USE ONLY

Reference: C-1023: 25 tests per kit, buffer, 25 Test tubes and stoppers
C-1323: 250 tests per kit, buffer

(EN) For Instructions For Use in your language : (FR) Pour obtenir les notices dans la langue de votre choix : (ES) Para las instrucciones de uso en su idioma : (PT) Para Instruçoes de Uso na sua lingua : (IT) Per le Istruzioni di Uso nella sua lingua : (DE) Für Gebrauchsanleitungen in Ihrer Sprache : (NL) Voor Gebruiksaanwijzing in uw eigen taal:
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I. INTRODUCTION

The Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) responsible for the Coronavirus disease 2019 (COVID-19) first emerged in December 2019 in China. The emergence of the new SARS-CoV-2 coronavirus and its rapid dissemination in all continents has led to high concern at the local and international health authorities level, in the scientific community and in the media and population. As of 11 March 2020, the SARS-CoV-2 has spread worldwide to more than 116 countries with over 118322 COVID-19 confirmed cases and 4292 fatalities leading the WHO to declare the disease as a pandemy. SARS-CoV-2 cause diseases of the respiratory tract leading to severe pneumonia in fragile patients, with most of the fatal cases in the elderly population.

In the absence of vaccine and specific treatment, the containment of the epidemics rely mainly on rapid identification and isolation of COVID-19 patients. This strategy is based on the availability of rapid diagnostic test to be performed on any suspect patient presenting specific symptoms. Noteworthy is the reporting of asymptomatic carriage of the virus in 1% of infected people and possible prolonged shedding after recovery which may hamper proper control of the epidemic, making the availability of diagnostic tests even more crucial. Development of point of care testings was recommended by a WHO experts panel on February 11-12, 2020 (COVID 19 Public health emergency of international concern. Global research and innovation forum: towards a research roadmap).

Serological antibody-detection assays do not fulfil the requirement of the detection early after infection as the average incubation period of 3-5 days is too short for development of an immune response. The detection of the antigen are the most suitable tests for detection of the early infection.

II. PRINCIPLE OF THE TEST

This test is ready to use and is based on a membrane technology with colloidal gold nanoparticles. A nitrocellulose membrane is sensitized with monoclonal antibodies directed against SARS-CoV and SARS-CoV-2 highly conserved nucleoprotein antigen. Another monoclonal antibody is conjugated to colloidal gold nanoparticles. The conjugate is immobilized on a membrane.

This test is aimed to the detection of SARS-CoV-2 either in nasopharyngeal secretions or in culture supernatant after several days to reach a better sensitivity.

When the NPS (nasopharyngeal secretions) or culture extracted solution comes into contact with the strip, the solubilised conjugate migrates with the sample by passive diffusion and the conjugate and sample material come into contact with the anti-SARS antibody adsorbed onto the nitrocellulose strip. If the sample contains SARS-CoV-2, the conjugate–SARS-CoV complex will remain bound to the anti-SARS-CoV-2 antibody immobilized onto the nitrocellulose. The result is visible within 15 minutes in the form of a red line that develops on the strip. The solution continues to migrate to encounter a control reagent that binds a control conjugate, thereby producing a second red line.

III. REAGENTS AND MATERIALS

1. COVID-19 Ag Respi-Strip (25 or 250)
The strips come in a bottle with a desiccant.

2. LY-S dilution buffer (3,5 mL or 15 mL)
Saline solution buffered to pH 7.5 containing Tris, EDTA, NaN_3 (<0.1%), a detergent and blocking proteins.

3. Materials supplied with item C-1023
The tubes and stoppers (25) come in zip-locked plastic bags

4. Instruction for use (1)
Materials to be ordered separately:
- Negative control (Ref.: CTR-1000)

IV. SPECIAL PRECAUTIONS

- All operations linked to the use of the test must be performed in accordance with Good Laboratory Practices (GLP).
- All reagents are for *in vitro* diagnostic use only.
- Avoid touching nitrocellulose with your fingers.
- Wear gloves, mask FFP2 or FFP3, lab glasses when handling samples. Or run the test under a Laminar Air Flow cabinet
- Never use reagents from another kit.
- If strips are stored in a container, the container must be resealed as soon as the necessary number of strips for the operation has been removed as the strips are sensitive to humidity. Make sure that the desiccant bag is present.
- Green lines indicate immunoreagents adsorption sites. Green colour disappears during the test.
- Reagents' quality cannot be guaranteed beyond their shelf-life dates or if reagents are not stored under required conditions as indicated in the insert.
- To avoid diluting the colloidal gold conjugate in the solution, take care not to immerse the strip above the line indicated under the arrows printed on the sticker.

V. WASTE DISPOSAL

- Dispose of gloves, swabs, closed test tubes and used devices in accordance with GLP and biosecurity legislation (ref. C).
- Each user is responsible for the management of any waste produced, and must ensure that it is disposed of in accordance with the applicable legislation.

VI. STORAGE

- An unopened kit may be kept at between 4 and 30°C and used until the shelf-life date indicated on the packaging.
- The strips remain stable for 15 weeks (in the closed container) after bottle opening if they are kept at between 4 and 30°C and in a dry environment.
- Avoid freezing strips and buffer.

VII. SPECIMEN HANDLING AND COLLECTION

Specimens to be tested should be obtained and handled by standard methods for the collection of nasopharyngeal aspirates, nasopharyngeal washes or nasal/nasopharyngeal swabs. Sample must be liquid to allow migration in the tests.

Specimens must be tested as soon as possible after collection, even if stored at 2-8°C, as any delay may result in a low signal intensity possibly leading to false negative results. If not immediately used, samples must be stored frozen at -20°C for long periods.

Coris BioConcept recommends using the Flocked Swabs of Copan Flock Technologies in order to guarantee the same performances as when nasopharyngeal washes or aspirates are used. The efficiency of other brands of swabs has not been established with our respiratory kits.

Make sure that the specimens are not treated with solutions containing formaldehyde or its derivatives.

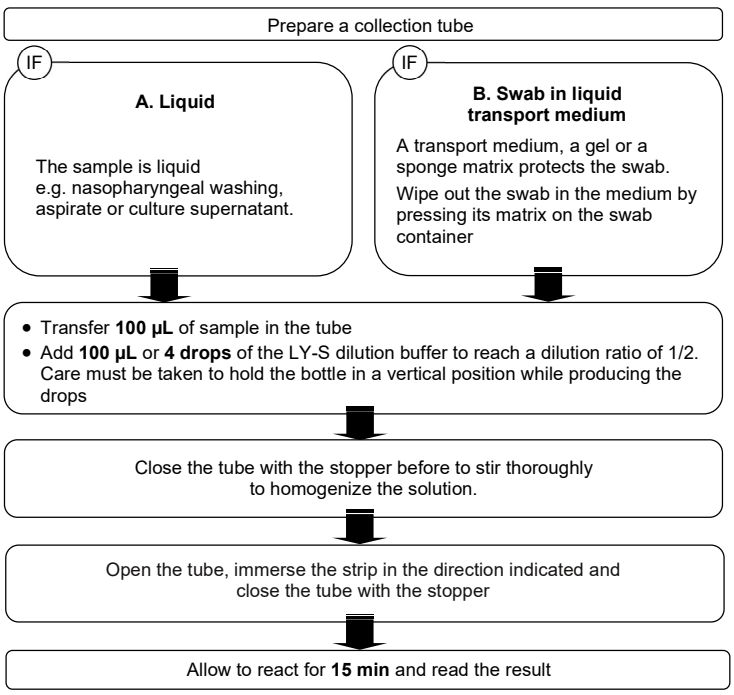
VIII. PROCEDURE

PREPARATIONS OF THE TEST:
Allow kit components, in unopened packaging, and specimens to reach room temperature (15-30°C) before performing a test.

Once opened, run the test immediately. Indicate the patient's name or specimen number on the tube. Place the marked test tubes in a rack.

SPECIMEN PREPARATION PROCEDURE:
Performance claims with regard to samples types other than Nasopharyngeal Secretions have not been established. We recommend the use of fresh NPS for optimal test performance.

For item C-1323, in order to perform the test properly, use only test tubes complying with the following specifications: maximum internal diameter of 14mm and minimum height of 70mm. A greater height is required if you wish to close the tube with a stopper.



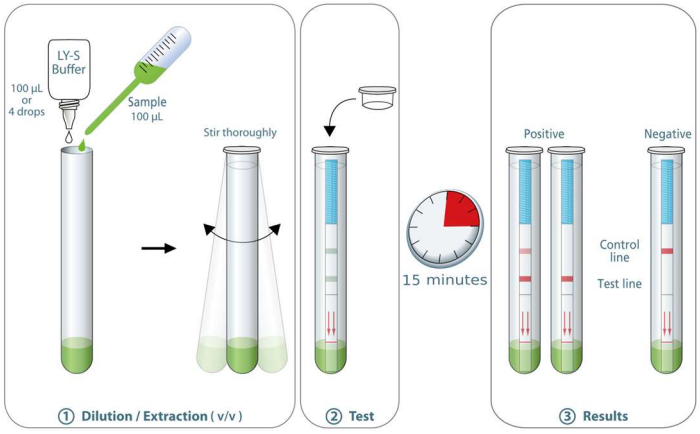
Positive results may be reported sooner the moment the test and control lines become visible.

Do not take the appearance of new lines into account after the reaction time is passed. The result must be read on still wet strip.

After reading, discard the tube with the strip according to biosecurity requirements.

IX. INTERPRETING RESULTS

The results are to be interpreted as follows:



Negative test result: a reddish-purple line appears at the Control line (C) position (upper line). No other band is present.

Positive test result: a visible reddish-purple band appears at the Test line position (T). Intensity of the test line may vary according to the quantity of antigens found in the sample. Any reddish-purple line (T), even weak, should be considered as a positive result. In addition, a reddish-purple band at the Control line (C) appears or not (see caution).

Invalid test result: The absence of a Control line indicates a failure in the test procedure (unless with positive result, see caution). Any reddish-purple line (C), even weak, should be considered as valid.

Caution: The control line indicates that the migration occurred up to the top of the strip. It validates a negative result. In case of a positive result, the control line may not appear. Nevertheless if the test line is positive it should be regarded as a real positive.

Note: during the drying process, a very faint shadow may appear at the Test line position. It should not be regarded as a positive result.

X. QUALITY CONTROL

In accordance with Good Laboratory Practices, we recommend checking the test's performance regularly according to the laboratory's requirements.

XI. PERFORMANCE

A. Detection Limit:

The detection limit was determined with a quantified SARS-CoV-2 virus and has been evaluated at $5x10^3$ pfu/mL.

B. Sensitivity - Specificity:

The kit was validated (two Reference Hospitals) in comparison with RT-PCR on a total of 231 nasopharyngeal swab specimens. The following results were obtained:

Evaluation #1

qRT-PCR / Coris BioConcept	Positive	Negative	Total
Positive	18	0	18
Negative	12	69	81
Total	30	69	99

95 % Confidence Interval[1]

Sensitivity:	60 % (40.7 to 76.8 %)
Sensitivity threshold	85.7 % on samples with Ct < 25 (62.6 to 96.2 %)
Specificity:	100 % (93.4 to 100%)
Positive Predictive value:	100 % (78.1 to 100%)
Negative predictive value:	85.2 % (75.2 to 91.8 %)
Agreement:	87.9 % (87/99)

Evaluation #2

RT-PCR / Coris BioConcept	Positive	Negative	Total
Positive	44	1	45
Negative	29	58	87
Total	73	59	132

95 % Confidence Interval[1]

Sensitivity:	60.3 % (48.1 to 71.3 %)
Sensitivity threshold	76.7 % on samples with Ct < 25 (61 to 87.7 %)
Specificity:	98.3 % (89.7 to 99.9 %)
Positive Predictive value:	97.8 % (86.8 to 99.9 %)
Negative predictive value:	66.7 % (55.7 to 76.2 %)
Agreement:	77.3 % (102/132)

C. Repeatability and reproducibility

To check intra-batch accuracy (repeatability), the same positive samples and a buffer solution were processed 15 times on kits of the same production batch in the same experimental conditions. All observed results were confirmed as expected.

To check inter-batch accuracy (reproducibility), some samples (positive and buffer) were processed on kits from three different production batches. All results were confirmed as expected.

D. Interference:

Cross-reactivity to samples positive for the following pathogens was tested and found to be negative: Influenza A, Influenza B, Respiratory Syncitial Virus (RSV), Adenovirus, Rhinovirus, Parainfluenza virus, Metapneumovirus, Enterovirus, Coronaviruses (HKU1, 229E, OC43, NL63), *Streptococcus pneumoniae, Streptococcus pyogenes, Haemophilus influenzae, Pseudomonas aeruginosa, Acinetobacter baumanii, Nocardia asteroides, Moraxella catarrhalis, Legionella pneumophila*, *Mycoplasma pneumoniae*, *Klebsiella pneumoniae*, *Aspergillus niger.*

Tests for cross-reactivity has been tested on *Staphylococcus aureus* and found positive at high bacteria concentrations (10^9 cfu/mL). No false-positive results were obtained when testing naso-pharyngeal sample from known *S. aureus* infected patients (n = 15).

As expected, COVID-19 Ag Respi-Strip test detects both SARS-CoV and SARS-CoV-2 viruses.

XII. LIMITS OF THE KIT

The test is qualitative and cannot predict the quantity of antigens present in the sample. Clinical presentation and other test results must be taken into consideration to establish diagnosis.

A positive test does not rule out the possibility that other pathogens may be present.

Kit test is an acute-phase screening test. Specimens that are collected after this phase may contain antigen titres below the reagent's sensitivity threshold. If a sample is given a negative result despite the observed symptoms, any other relevant test should be run to check the sample.

XIII. TECHNICAL PROBLEMS / COMPLAINTS

If you encounter a technical problem or if performances do not correspond with those indicated in this package insert:

1. Record the kit batch number
2. If possible, keep the clinical sample in the freezer during the complaint management
3. Contact Coris BioConcept (client.care@corisbio.com) or your local distributor

XIV. BIBLIOGRAPHIC REFERENCES

A. **Na Zhu, Dingyu Zhang, et.al.** ; *A Novel Coronavirus from Patients with Pneumonia in China, 2019;* N Engl J Med. 2020 Feb 20;382(8):727-733. doi: 10.1056/NEJMoa2001017. Epub 2020 Jan 24.

B. **Chan J. F.-W., Kok K.-H., et al. :** *Genomic characterization of the 2019 novel human-pathogenic coronavirus isolated from a patient with atypical pneumonia after visiting Wuhan.*; EMI 2020, doi.org/10.1080/22221751.2020.1719902.

C. **Belgian biosecurity legislation** https://www.biosecurite.be/content/utilisation-confinee-dogm-et-pathogenes

Last update: 08 APRIL 2020

REF	Catalogue number		Manufacturer
IVD	In vitro diagnostic medical device		Temperature limits
Σ	Contains sufficient for <n> tests	LOT	Batch code
	Consult instructions for use		Do not reuse
	Keep dry		Use by
DIL SPE	Diluent specimen	CONT NaN_3	Contains Sodium azide