BioMedomics™ INFECTIOUS DISEASE

CoV-SCAN

Rapid Antigen Test

Instructions For Use

REF: 50-001 PN: 50-001-01.CE

Intended Use |

The BioMedomics CoV-SCAN Rapid Antigen Test (CoV-SCAN) is a lateral flow immunochromatographic assay intended for the qualitative detection of the nucleocapsid protein (N-protein) antigen from SARS-CoV-2 in nasal swab specimens directly collected from individuals, two (2) years old and older, who are suspected of COVID-19 by a healthcare provider within the first five (5) days of symptom onset.

CoV-SCAN is intended to be performed at the point-of-care in non-laboratory settings, Point-of-Care (POC), by minimally-trained operators.

Results are for the identification of SARS-CoV-2 N-protein antigen. Antigen is generally detectable in nasal swabs specimens during the acute phase of infection. Positive results indicate the presence of viral antigens, but clinical correlation with patient history and other diagnostic information is necessary to determine infection status. Positive results do not rule out bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause of disease.

Negative results should be treated as presumptive. Negative results do not rule out a SARS-CoV-2 infection and should not be used as the sole basis for treatment or patient management decisions, including infection control decisions. Negative results should be considered in the context of a patient's recent exposures, history, and the presence of clinical signs and symptoms consistent with COVID-19, and confirmed with a molecular assay, if necessary, for patient management.

CoV-SCAN is intended for use by medical professionals or trained operators who are proficient in performing tests and trained clinical laboratory personnel or individuals trained in point-of-care settings.

Summary and Explanation of the Test |

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is a novel beta coronavirus and is the causative agent of Coronavirus Disease 2019 (COVID-19) and the pandemic. SARS-CoV-2 is mainly transmitted through droplets and contact routes, and people who are infected with SARS-CoV-2 may express signs and symptoms of acute respiratory illness, such as fever, cough, shortness of breath, etc., but can also be asymptomatic.[1-2]

The median incubation time is estimated to be 5.1 days with symptoms expected to be present within twelve (12) days of infection. Symptomatic, pre-symptomatic and asymptomatic SARS-CoV-2 carriers all can be potential sources for viral transmission.

Test Principle |

CoV-SCAN is a lateral flow immunochromatographic assay for the detection of extracted nucleocapsid protein (N-protein) antigens specific to SARS-CoV-2 in nasal swab specimens directly collected from individuals who are suspected of COVID-19 by a healthcare provider within the first five (5) days of symptom onset.

Nasal swab specimens require a sample preparation step (extraction) in which the sample is eluted into the lysis buffer solution. Extracted sample is added to the sample well of the test cassette to initiate the test. When the sample migrates in the test strip, SARS-CoV-2 viral antigens bind to anti-SARS-CoV-2 N-protein antibodies conjugated to indicator and capture particles in the test strip, forming an immune complex. The immune complex is then captured by the test line on the nitrocellulose membrane as it migrates through the strip.

Test results are interpreted at fifteen (15) minutes after sample addition. The presence of two (2) colored lines in the control line region (C-Line) and test line region (T-line) indicates the sample is SARS-CoV-2 positive. The presence of one (1) colored line, C-line, indicates the sample is SARS-CoV-2 negative. The absence of the C-line indicates an invalid test, and the sample must be retested.

CoV-SCAN is designed to detect the N-protein antigen of SARS-CoV-2 using a novel double antibody sandwich assay format. It uses a panel of antibodies, targeting multiple antigenic sites on SARS-CoV-2 N-protein antigen, that can detect many new variants of concern at equivalent (or up to eight-fold) improved sensitivity compared to original isolate.

Chemically-inactivated virus was serially diluted in nasal swab matrix (confirmed COVID-19 negative by RT-PCR method) and applied to cassettes in singlet. Each cassette was read by three (3) separate human readers after fifteen (15) minutes after sample addition. The concentrations at which all three (3) operators interpreted the test as positive are indicated in the table below.

Variant of concern	Concentration on swab ($TCID_{50}$/swab)
WA1 (Original isolate)	12.5
P.1 (Gamma)	12.5
B.1.1.7 (Alpha)	12.5
B.1.351 (Beta)	12.5
B.1.526 (New York)	3.125
B.1.427 (California, variant-1)	1.5625
B.1.429 (California, variant-2)	3.125
R.1 (New Jersey)	1.5625
B.1.617.1 (Delta, variant-1)	3.125
B.1.617.2 (Delta, variant-2)	6.25

Table 1. Sensitivity of CoV-SCAN to SARS-CoV-2 variants

Contents of the Kit |

One test kit contains:

1 Test Cassette | 1 Bottle of Lysis Buffer (12 mL) | 1 Instructions for Use | 1 Extraction tube | 1 Dropper | 1 Sterile Swab | 1 Quick Reference Instructions

The following materials are required but not provided within the CoV-SCAN kit:

- COVID-19 Antigen External Control Kit (PN 55-001-02) which contains Positive and negative control swabs (available from BioMedomics)
- Gloves
- Timer/clock/stopwatch

Active Components |

- Test cassette: gold conjugate, test line, and control line contains a panel of antibodies, targeting multiple antigenic sites on SARS-CoV-2 N-protein antigen to detect the N-protein antigen of SARS-CoV-2 using a novel double antibody sandwich assay format.
- Lysis buffer: buffered detergent solution.

Warnings and Precautions |

- For human *in vitro* diagnostic use only.
- The performance of this device has not been assessed in a population

vaccinated against COVID-19.

- The following CoV-SCAN Rapid Antigen Test components (test cassettes, extraction tubes, droppers and sterile swabs) are for single-patient use. Do not reuse single-use components.
- Universal precautions should be observed when handling patient specimens or contaminated medical devices.
- Always wear personal protective equipment (PPE) when working with patient specimens and contaminated devices. PPE includes gloves, gown, mask, goggles or face shield.
- Discard any medical waste in accordance with all applicable local, state and national laws.
- Do not use test cassette, buffer solution, or any other kit components if the pouch is damaged or the seal is broken.
- Do not use test cassette, buffer solution, or any kit component beyond the indicated expiration date.
- These Instructions for Use must be read completely before performing the test. Failure to follow directions in these instructions may yield inaccurate test results.

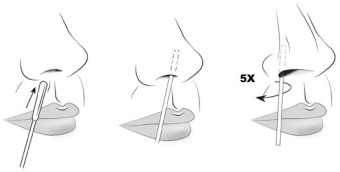
Storage Instructions |

The test kit should be stored away from direct light at room temperature (2°C to 30°C) and not beyond the expiration date on the label.

After opening the sealed cassette pouch, the test cassette should be used immediately.

Sample Requirements |

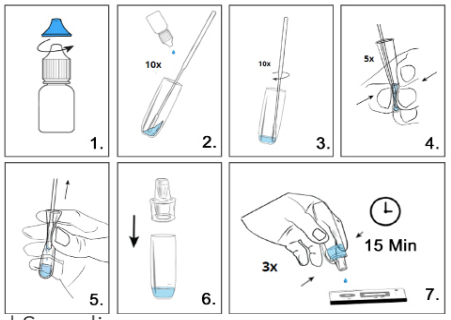
Lay out necessary materials on a clean, flat surface: test cassette, extraction tube, lysis buffer, dropper and swab.



- Insert tip of swab inside the nostril (less than 1 inch into nostril for adults and less than ½ inch for children). Firmly sample the nasal wall by rotating the swab in a circular path against the wall 5 times. Repeat on the other nostril. Take approximately 10-15 seconds per nostril.
- Remove the swab.
- Sample should be treated with Lysis Buffer provided in this kit as soon as possible after collection. If the sample cannot be processed immediately, it should be stored immediately in a dry, sterilized and strictly sealed plastic tube. It can be stored at 2°C-8°C for twenty-four (24) hours. Alternatively, the sample can be stored at up to 30°C for up to four (4) hours prior to processing.

Test Procedure |

Note: One test cassette can only be used to test one nasal swab specimen. Do not open pouch until ready to use.



1 | Sampling:

- Place nasal swab specimen vertically into the extraction tube, remove the colored tip of the lysis buffer bottle, and add about ten (10) drops of lysis buffer into the tube. Replace colored tip on lysis buffer bottle. Tilt the tube to soak the swab in lysis buffer solution (Step 1-2).
- Swirl the swab against the inner tube wall about ten (10) times and squeeze the swab from the outer tube wall five (5) times to completely dissolve the sample in the solution (Step 3-4).
- Apply pressure to squeeze the fluid out of the swab as you pull it out of the extraction tube. Discard the swab (Step 5).
- Push the dropper cap onto the extraction tube. Press down firmly to ensure a secure fit (Step 6).

2 | Testing:

- Invert the extraction tube and squeeze three (3) drops of liquid next to the letter "S" on the test cassette (Step 7).

3 | Read Results:

- Results should be read between fifteen to twenty (15-20) minutes after addition of liquid to the test cassette.
- Results observed later than twenty (20) minutes after liquid addition to the test cassette are invalid.

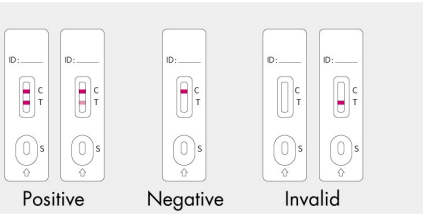
Test Method Limitations |

Proper sample collection is critical for optimal test performance. Failure to follow the collection and sampling requirements may give inaccurate results.

Results from antigen testing should not be used as the sole basis to diagnose or exclude SARS-CoV-2 infection or to inform infection status. Results should be used in combination with clinical observations and other testing methods.

Display of Results/Expected Values |

A total of two detection lines are possible, with the C-line appearing when sample has flowed through the cassette and the test performed correctly.



1. Invalid Result: If no lines appear OR only the T-line appears, then the test is invalid. Repeat the test with a new test cassette.
2. Negative Result: If only the C-line appears and the T-line is not visible, then the sample contains no N-protein antigens, or the antigen concentration is less than the limit of detection; in such a case, the result is negative. Negative results do not rule out SARS-CoV-2 infection, particularly in those who have been in contact with the virus. Follow-up testing with a molecular diagnostic test should be considered to rule out infection in these individuals. Negative results may be caused by low concentrations of the SARS-CoV-2 N-protein antigens in the sample and therefore cannot completely rule out the possibility of infection.
3. Positive Result: If both the C-line and the T-line appear, then the novel coronavirus has been detected and the result is positive. Result should be determined by whether the T-line is present, regardless of its intensity.

Quality Control Procedure |

- Each test cassette has a built-in control. A red C-line can be considered an internal positive procedural control. The C-line will appear if the test procedure has been performed correctly. If the C-line does not appear, the result is invalid and a new test must be performed with a new test cassette. If the problem persists, please contact

your local vendor or BioMedomics for technical support.

- External control swabs may also be used to demonstrate that the reagents and assay procedure perform properly. It is recommended that positive and negative external controls be run for each new shipment or new lot of CoV-SCAN kits, each new operator or as required by local quality/regulation. External controls are available separately and may be ordered from BioMedomics (PN 55-001-02). Follow the Instructions for Use supplied with the external controls.

Performance Characteristics |

Clinical Performance - Nasal Swab:

The clinical performance characteristics of CoV-SCAN using nasal swab specimens were evaluated in a prospective study conducted at Columbia University Irving Medical Center (CUIMC) between January 2021 and February 2021 against an FDA Emergency Use Authorized RT--PCR molecular assay as a comparator method.

To be enrolled in the study, patients must be > 2 years old and had to be presenting at the participating study centers with COVID-19-like symptoms and meet inclusion/exclusion criteria. All patients presented with a fever or at least two (2) symptoms of COVID-19 infection. The patients presenting the COVID-19-like symptoms within five (5) days of symptom onset at the study sites were enrolled. The mean age of the analytic sample was 52.4 (range 9.7 to 89.7) and 40/ 70 (57%) were female. Mean duration from symptom onset to enrollment and specimen collection was 2.3 days.

Two nasal swabs were collected from each participant with the order of collection varied for performance of CoV-SCAN or comparator RT-PCR. Each swab was collected using the same process, by slowly rolling the swab in each nostril 5 times. The swabs were tested directly on CoV-SCAN and the comparator RT-PCR method to demonstrate agreement.

The performance of CoV-SCAN compared to the RT-PCR comparator method on paired anterior nasal swab specimens from seventy (70) participants with COVID-19 symptoms are presented in the table below:

	Cepheid Xpert Xpress (Xpert Xpress SARS-CoV-2/ Flu/RSV)		
CoV-SCAN	Positive	Negative	Total
Positive	33	0	33
Negative	6	31	37
Total	39	31	70
PPA (95% CI)	84.6% (69.5%-94.1%)		
NPA (95% CI)	100% (88.8%-100%)		

Table 2. Positive percent agreement and negative percent agreement of CoV-SCAN and RT-PCR results (n=70)

CoV-SCAN was positive for 1/6 (16.6%) of samples with a RT-PCR CT value > 30.0. CoV-SCAN was positive for 7/8 (87.5%) of samples with CT values > 25.0 and < 30.0, and 32/33 (96.9%) of samples with CT values < 30.0.

The data were further refined by patient age and days since symptoms onset in the tables below:

	CoV-SCAN		
Age Group	Total (n=70)	Positive (n=33)	Prevalence
<5 Years of Age	0	0	--
6-21 Years of Age	5	3	60%
22-59 Years of Age	43	15	35%
> 60 Years of Age	22	15	68%

Table 3. Patient demographics (Age)

Days since symptoms onset	**Cumulative RT-PCR + (n=39)**	**Cumulative CoV-SCAN positive (n=33)**	**PPA**	**95% CI**
0-1 days	13	12	92.3%	64.0-99.8%
2-3 days	19	15	78.9%	54.5-94.0%
4-5 days	7	6	85.7%	42.1-99.6%

Table 4: Patient demographics (days since symptom onset)

Limit of Detection (LoD):

CoV-SCAN LoD was evaluated by using different concentrations of heat-inactivated SARS-CoV-2 isolate USAWA1/2020 (NR-52286). To prepare positive samples, the strain was spiked into the pooled COVID-19 negative nasal swab fluid obtained from multiple healthy volunteers eluted in VTM and confirmed as SARS-CoV-2 negative by RT-PCR. The estimated LoD found from the initial two-fold (2X) serial dilution test was confirmed by testing twenty (20) replicates. The confirmed LoD for direct swab was 1.25 x 10^3 $TCID_{50}$/ml.

LoD Confirmation Results			
Sample Type	**LoD Concentration**	**Number Positive/ Total**	**%Detected**
Heat inactivated SARS-CoV-2	1250 $TCID_{50}$/ml	20/20	100%

Table 5. LoD confirmation results

Cross-Reactivity (Analytical Specificity) and Microbial Interference |

Cross-reactivity and potential interference of CoV-SCAN was evaluated by testing pooled COVID-19 negative nasal swab fluid and commercial and pathogenic microbes (16 viruses, 8 bacteria and 1 yeast) that may be present in the nasal cavity. Each of the microbes was tested in triplicate in the presence/ absence of heat-inactivated SARS-CoV-2 at approximately 2.4 X LoD. No cross-reactivity or interference was observed with any of the following microbes when tested at the concentrations listed.

Microbes	**Concentration**
SARS-coronavirus	2 x 10^5 PFU/ml
MERS-coronavirus	2 x 10^5 PFU/ml
Human coronavirus 229E	2 x 10^5 PFU/ml
Human coronavirus OC43	2 x 10^5 PFU/ml
Human coronavirus NL63	2 x 10^5 PFU/ml
Adenovirus 10	2 x 10^5 PFU/ml
Human Metapneumovirus (hMPV)	2 x 10^5 PFU/ml
Parainfluenza 1	2 x 10^5 PFU/ml
Parainfluenza 2	2 x 10^5 PFU/ml
Parainfluenza 3	2 x 10^5 PFU/ml
Parainfluenza 4b	2 x 10^5 PFU/ml
Influenza A	2 x 10^5 PFU/ml
Influenza B	2 x 10^5 PFU/ml
Enterovirus	2 x 10^5 PFU/ml
Respiratory Syncytial Virus	2 x 10^5 PFU/ml
Human rhinovirus 16	2 x 10^5 PFU/ml
Haemophilus influenzae	2 x 10^6 CFU/ml
S. pneumoniae	2 x10^6 CFU/ml
S. pyogenes	2 x10^6 CFU/ml
B. pertussis	2 x10^6 CFU/ml
Mycoplasma pneumoniae	2 x10^6 CFU/ml
Chlamydia pneumoniae	2 x10^6 IFU/ml
Legionella pneumophila	2 x10^6 CFU/ml
Staphylococcus aureus	2 x10^6 CFU/ml
Staphylococcus epidermidis	1x10^6 CFU/ml
Candida albicans	2 x10^6 CFU/ml
Pooled normal human nasal wash	10 individuals

Table 6. Microbial interference

To estimate the likelihood of cross-reactivity with SARS-CoV-2 of organisms that were not available for wet testing, *In silico*-analysis using the Basic Local Alignment Search Tool (BLAST) managed by the National Center for Biotechnology Information (NCBI) was used to assess the degree of protein sequence homology. No significant homology was found for *Mycobacterium tuberculosis*, and *Pneumocystis jirovecii*, so no cross-reactivity or interference is anticipated. However, for human

coronavirus HKU1, 39.7% homology was observed for nucleocapsid protein from thirty-six (36) different accession numbers in Gene bank of NCBI, so cross-reactivity or interference cannot be ruled out.

High-Dose Hook Effect |

No high-dose hook effect was observed when CoV-SCAN was tested up to $2x10^5$ $TCID_{50}$/ml of heat-inactivated SARS--CoV-2.

Endogenous Interfering Substances |

To assess substances with the potential to interfere with the performance of CoV-SCAN, positive and negative samples were tested in triplicate in the presence of a total of fourteen (14) potentially interfering substances at the concentrations listed in the table below. In the positive samples, the heat-inactivated SARS-CoV-2 concentration was approximately 3 x LoD. In such cases CoV-SCAN did not yield any false negatives. Moreover, in the negative samples, CoV-SCAN did not produce any false positives for 13/14 of the compounds and concentrations listed below. Two (2) false positive occurred with 5% Zicam but not with 1% Zicam.

Potential interfering substance	**Results with either:** **Positive = HI SARS-CoV-2 at 3X LoD = 3750 TCID50/ml** **Negative = Covid-19-negative nasal fluid**			
	Posi-tive	Agree-ment	Nega-tive	Agree-ment
Naso Gel, 5% (v/v)	3/3	100 %	3/3	100%
CVS Phenylephrine Nasal Drops, 15% (v/v)	3/3	100 %	3/3	100%
Afrin, 15% (v/v)	3/3	100 %	3/3	100%
Nasal Crom, Cromolyn Nasal Spray, 15% (v/v)	3/3	100 %	3/3	100%
Zicam, 5% (v/v)	3/3	100 %	1/3	33%
Zicam, 1% (v/v)	3/3	100 %	3/3	100%
Homeopathic, Alkalol Nasal Fluid, 1:10 dilution	3/3	100 %	3/3	100%
Chloraseptic (Phenol) Sore Throat Spray, 15% (v/v)	3/3	100%	3/3	100%
Tobramycin, 4 ug/ml	3/3	100%	3/3	100%
Mupirocin, 10 mg/ml	3/3	100%	3/3	100%
Tamiflu (Oseltamivir Phosphate), 5 mg/ml	3/3	100%	3/3	100%
Fluticasone Propio-nate, 5% (v/v)	3/3	100%	3/3	100%
Chloraseptic lozenge, 1.5 mg/ml	3/3	100%	3/3	100%
Whole Blood, 4% (v/v)	3/3	100%	3/3	100%
Mucin, 0.5%	3/3	100%	3/3	100%
No Potential Interferent	3/3	100%	3/3	100%

Table 7. Potential interfering substance

Point of Care Use |

CoV-SCAN was utilized in a non-laboratory setting at near-patient or Point-of-Care (POC) testing environments to demonstrate that non-laboratory personnel can perform CoV-SCAN accurately in the intended use environment.

Testing was performed by five (5) operators with no laboratory experience and who were representative of the intended users. Operators only used the Quick Reference Instructions (QRI) for the test without any training provided.

The following table shows the results of minimally-trained operators running CoV-SCAN in a CLIA-waived setting in a blinded fashion.

	Cepheid Xpert Xpress (Xpert Xpress SARS-CoV-2/ Flu/RSV)		
CoV-SCAN	Positive	Negative	Total
Positive	27	0	27
Negative	4	30	34
Total	31	30	61
PPA (95% CI)	87.1% (70.2%-96.4%)		
NPA (95% CI)	100% (88.4%-100%)		

Table 8. POC testing-Concordance of CoV-SCAN and RT-PCR results (n=61)

Variants of concern detected include Alpha (B.1.1.7) and Delta (B.1.617.2, AY.2). Variants of interest detected: Iota (B.1.526) and Mu (B.1.621).

In addition, the robust use of CoV-SCAN for near patient or Point of Care (POC) testing was demonstrated by five (5) flex studies (data not shown).

Ordering Information |

BioMedomics CoV-SCAN Rapid Antigen Test Kit:

- REF: 50-001
- Part Number: 50-001-01.CE

BioMedomics COVID-19 Antigen External Control Kit

- REF: 55-001
- Part Number: 55-001-02

Technical Support |

For questions, or to report a problem, please call Technical Support at +1-919-890-3070 (Available Hours: Mon. to Fri.: 8 a.m. – 5 p.m. EST) or by email at techsupport@biomedomics.com.

References |

1. LY Wang, PR Chen, G W Zheng, et al. Research progress on novel coronavirus test methods. Modern Medicine and Clinic, 2020, 35(3): 411-416.

2. K Tugba, W Ralph, L Hakho. Molecular and Immunological Diagnostic Tests of COVID-19: Current Status and Challenges. IScience, 2020, 23 (8): Doi: 10.1016/j.isci.2020.101406

Do Not Re-use

Manufacturer

Use-by Date

in vitro diagnostic medical device

LOT Batch Code

Temperature limit

REF Catalogue Number

Contains sufficient for <n> tests

Do not use if package is damaged

Consult Instructions for use

STERILE EO Sterilized using ethylene oxide

EC REP Authorized representative of the European Community

PN Part Number

Do not re-sterilize

Scan for instructions in other languages (as available) or to access an electronic version of the Quick Reference Instructions (QRI)

BioMedomics, Inc.
1100 Perimeter Park Dr., Ste. 104
Morrisville, NC 27560, USA
+1-919-890-3070

EC REP MT Promedt Consulting GmbH
Altenhofstrasse 80
66386 St. Ingbert, Germany
+49-68-94-58 10 20

BioMedomics

www.BioMedomics.com | info@BioMedomics.com
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