CoviGnost AG+InfluGnost A+B test panel

RAPID CHROMATOGRAPHIC IMMUNOASSAY FOR QUALITATIVE DETECTION OF SARS-CoV-2 AND INFLUENZA A AND INFLUENZA B VIRUS ANTIGENS PRESENT IN HUMAN NASOPHARYNX

CE IVD

Product code:
COVIN020 - test panel, 1x20 tests
COVIN05 - test panel, 1x5 tests
COVIN01 - test panel, 1x1 test

INTENDED USE

CoviGnost AG+InfluGnost A+B test panel is a rapid chromatographic immunoassay for the qualitative detection of SARS-CoV-2, Influenza A and Influenza B virus antigens in nasopharyngeal swab specimens during the acute phase of infection.
Positive results indicate the presence of viral antigens, but the clinical correlation with patient history and other diagnostic information is necessary to determine infection status. Positive results do not rule out a bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause of the disease.
Negative results do not preclude SARS-CoV-2/ Influenza A+B infection and should not be used as the sole basis for treatment or patient management 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/ Influenza A+B.
The test is intended for professional clinical-laboratory use only.

SUMMARY

COVID-19 is an acute respiratory infectious human disease caused by novel coronavirus SARS-CoV-2 that belongs to the β genus. Currently, the patients infected by the novel coronavirus are the main source of infection; asymptomatic individuals can also be an infectious source. The main manifestations include fever, fatigue and dry cough. Nasal congestion, runny nose, sore throat, myalgia and diarrhea are found in a few cases.
Influenza (commonly known as 'flu') is a highly contagious, acute viral infection of the respiratory tract. It is a communicable disease easily transmitted through the coughing and sneezing of aerosolized droplets containing live virus particles. Influenza outbreaks occur each year during the fall and winter months. Type A viruses are typically more prevalent than type B viruses and are associated with the most serious influenza epidemics, while type B infections are usually milder.
The gold standard of laboratory diagnosis is a 14-day cell culture with one of a variety of cell lines that can support the growth of the influenza virus. Cell culture has limited clinical utility, as results are obtained too late in the clinical course for effective patient intervention. Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) is a newer method that is generally more sensitive than culture with improved detection rates (2-23%). However, RT-PCR is expensive, complex and must be performed in specialized laboratories.

PRINCIPLE

CoviGnost AG (left side of the test panel) is a qualitative chromatographic immunoassay for the detection of SARS-CoV-2 antigens in human nasopharyngeal swab specimens. There is a test membrane inside of the test covered with SARS-CoV-2 antibody-coated particles. The specimen reacts with SARS-CoV-2 antibody-coated particles in the test, and then migrates upward on the membrane by capillary action and reacts with the SARS-CoV-2 antibody in test line region. If the specimen contains SARS-CoV-2 antigens, a colored line will appear in the test line region (T) as a result of this. If the specimen does not contain antigens to SARS-CoV-2, no colored line will appear in the test line region, indicating a negative result. To serve as a procedural control, a colored line will always appear in the control line region (C), indicating that the proper volume of specimen has been added and membrane wicking has occurred.
InfluGnost A+B (right side of the test panel) is a qualitative chromatographic immunoassay for the detection of Influenza A and Influenza B antigens in human nasopharyngeal swab specimens. Test membrane contains particles coated with antibodies to Influenza A and antibodies to Influenza B, and two separate detection zones (test lines A and B) coated with specific antibodies to Influenza A, i.e, to Influenza B. During testing, the extracted specimen reacts with the antibody to Influenza A and/or Influenza B that are coated onto particles. The mixture then migrates up the membrane to react with the antibody to Influenza A and/or Influenza B on the membrane and generate one or two colored lines in the test regions. The coloration of one or both test lines (A and/or B) indicates a positive result. To serve as a procedural control, a colored line will always appear in the control region (C) if the test has performed properly.

REAGENTS

The test contains SARS-CoV-2 antibodies, Influenza A and Influenza B virus antibodies as the capture reagents and detection reagents.

STORAGE AND STABILITY

Store as packaged in the sealed pouch at room temperature or refrigerated (2-30°C). The test is stable through the expiration date printed on the sealed pouch. The test must remain in the sealed pouch until use. DO NOT FREEZE. Do not use beyond the expiration date.

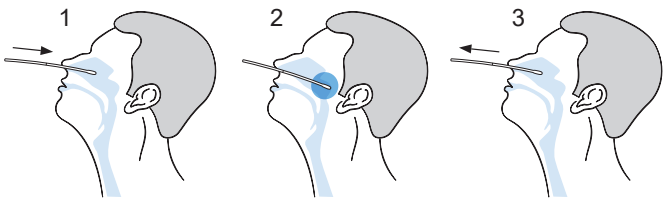
PRECAUTIONS

1. This package insert must be read completely before performing the test. Failure to follow directions in the package insert may yield inaccurate test results.
2. For professional *in vitro* diagnostic use only. Do not use after the expiration date.
3. Do not eat, drink or smoke in the area where the specimens or kits are handled.
4. Do not use the test if the pouch is damaged.
5. Observe established precautions against microbiological hazards.
6. Wear protective clothing such as laboratory coats, disposable gloves and eye protection when specimens are assayed.
7. Wash hands thoroughly after handling.
8. Ensure that an appropriate amount of samples are used for testing. Too large or too small sample size may lead to deviation of results.
9. The used test panel should be discarded according to local regulations.
10. Humidity and temperature can adversely affect results.

SPECIMEN COLLECTION AND PREPARATION

Sampling the specimen

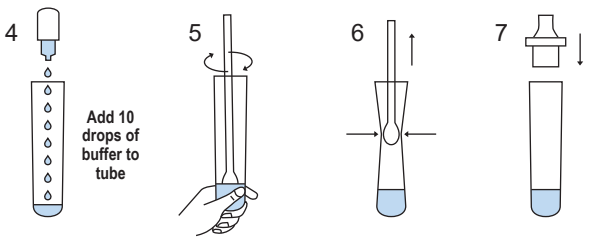
1. Insert a sterile swab into the nostril of the patient, reaching the surface of the posterior nasopharynx.
2. Swab over the surface of the posterior nasopharynx.
3. Withdraw the sterile swab from the nasal cavity.



NOTE: Specimens should be tested as soon as possible after collection. If swabs are not being processed immediately, it is highly recommended the swab sample is placed into a dry, sterile, and tightly sealed plastic tube for storage. The swab specimen in the dry and sterile condition is stable for up to 8 hours at room temperature and 24 hours at 2-8°C.

Preparing the specimen

4. Add 350 µL (10 drops) of extraction buffer to the extraction tube.
5. Place the swab specimen in the extraction tube. Rotate the swab for approximately 10 seconds while pressing the head against the inside of the tube to release the antigen in the swab.
6. Press the swab onto the central part of the tube in order to extract as much fluid from the swab as possible while removing the swab from the tube.
7. Screw the tube cap tightly.



NOTE: The specimen is stable for 2 hours after extraction at room temperature or 24 hours at 2-8°C.

MATERIALS FOR CONDUCTING THE TEST

Materials provided:
- Test panel
- Instructions for use
- Extraction buffer.
- Sampling tubes. They may contain buffer
- Sterile swabs

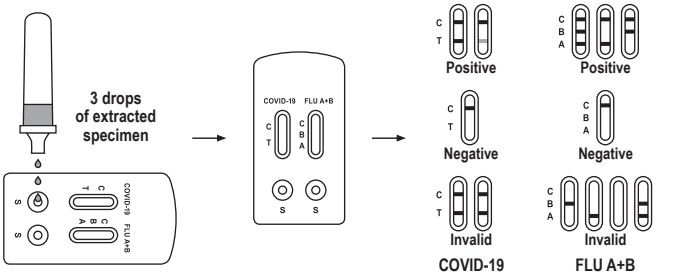
Materials required but not provided:
- Timer

DIRECTIONS FOR USE

Carefully read the provided instructions for use before conducting the test.

Allow the test, extracted specimen and/or controls to equilibrate to room temperature (15-30°C) prior to testing.

1. Remove the test panel from the sealed foil pouch and use it within one hour. Best results will be obtained if the test is performed immediately after opening the foil pouch.
2. Invert the specimen extraction tube and add 3 drops of extracted specimen (approx. 75µl) to each of the specimen wells (S) respectively and then start the timer.
3. Wait for the colored line(s) to appear. Read the result at 15 minutes. Do not interpret the result after 20 minutes.



INTERPRETATION OF RESULTS

(please refer to the illustration above)

POSITIVE COVID-19:* Two distinct colored lines appear in the left window. One colored line should be in the control region (C) and another colored line should be in the test region (T). A positive result in the test region indicates detection of SARS-CoV-2 antigens in the sample.

POSITIVE Influenza A:* Two distinct colored lines appear in the right window. One colored line should be in the control region (C) and another colored line should be in the Influenza A region (A). A positive result in the Influenza A region indicates that Influenza A antigen was detected in the sample.

POSITIVE Influenza B:* Two distinct colored lines appear in the right window. One colored line should be in the control region (C) and another colored line should be in the Influenza B region (B). A positive result in the Influenza B region indicates that Influenza B antigen was detected in the sample.

POSITIVE Influenza A and Influenza B:* Three distinct colored lines appear in the right window. One colored line should be in the control region (C) and two colored line should be in the Influenza A region (A) and Influenza B region (B). A positive result in the Influenza A region and Influenza B region indicates that Influenza A antigen and Influenza B antigen were detected in the sample.

***NOTE:** The intensity of the color in the test line region (T) will vary based on the amount of SARS-CoV-2 antigen, Influenza A and/or B antigen present in the sample; any shade of color in the test region should be considered positive.

NEGATIVE: One colored line appears in the control region (C). No apparent colored line appears in the test line region.

INVALID: The control line fails to appear. Insufficient specimen volume or incorrect procedural techniques are the most likely reasons for control line failure. Review the procedure and repeat the test with a new test panel. If the problem persists, discontinue using the test kit immediately and contact your local distributor.

QUALITY CONTROL

Internal quality control

Internal procedural controls are included in the test. A colored line appearing in the control region (C) is an internal positive procedural control. It confirms sufficient specimen volume and correct procedural technique. A clear background is an internal negative procedural control. If the test is working properly, the background in the result area should be white to light pink and not interfere with the ability to read the test result

External quality control

Controls are not included in this kit. However, in compliance with Good Laboratory Practice (GLP) positive/ negative controls are recommended.

LIMITATIONS

1. The test Procedure and the Interpretation of the test Result must be followed closely when testing for the presence of SARS-CoV-2/Influenza A/Influenza B antigens in the human nasopharyngeal specimens from suspected individuals. For optimal test performance, proper sample collection is critical. Failure to follow the procedure may give inaccurate results.
2. The test is intended for in vitro diagnostic use only. This test should be used for the detection of SARS-CoV-2/ Influenza A/Influenza B antigens in human nasopharyngeal specimens as an aid in the diagnosis of patients with suspected SARS-CoV-2, Influenza A or Influenza B infection in conjunction with clinical presentation and the results of other laboratory tests. Neither the quantitative value nor the rate of increase in the concentration of SARS-CoV-2/Influenza A/Influenza B antigens can be determined by this qualitative test.
3. The test will only indicate the presence of SARS-CoV-2/Influenza A/Influenza B antigens in the specimen and should not be used as the sole criteria for the diagnosis of SARS-CoV-2/Influenza A/Influenza B infections.
4. As with all the other diagnostic tests the results obtained with the test should be considered with other clinical findings from other laboratory tests and evaluations.
5. If the test result is negative or non-reactive and clinical symptoms persist, it is recommended to re-sample the patient a few days later or test using the PCR method to rule out infection in these individuals.
6. The test will show negative results if the concentration of the SARS-CoV-2, Influenza A or Influenza B virus antigens in the sample is lower than the minimum detection limit of the test..
7. Negative results do not rule out SARS-CoV-2 infection, particularly in those who have been in contact with the virus. Follow-up testing using the PCR method should be considered to rule out infection in these individuals.
8. A negative result for Influenza A or Influenza B obtained from this kit should be confirmed by RT-PCR/culture.
9. Excess blood or mucin on the swab specimen may interfere with test performance and may yield a false positive result.
10. The accuracy of the test depends on the quality of the swab sample. False negatives may result from improper sample collection or storage.
11. Positive results of COVID-19 may be due to infection with non-SARS-CoV-2 coronavirus strains. A positive result for influenza A and/or B does not preclude an underlying co-infection with another pathogen, therefore the possibility of an underlying bacterial infection should be considered.

EXPECTED VALUES:

The test has been compared with leading commercial RT-PCR tests. The correlation between these two systems is no less than 91%.

PERFORMANCE CHARACTERISTICS

Sensitivity, specificity and accuracy

RT-PCR is used as the reference method. Specimens were considered positive if RT-PCR indicated a positive result. Specimens were considered negative if RT-PCR indicated a negative result.

COVID-19 test:

CoviGnost AG+InfluGnost A+B test panel		RT-PCR		Total
		Positive	Negative	
COVID-19	Positive	80	1	81
	Negative	3	120	123
Total		83	121	204
Relative sensitivity		96.40% (95% CI*: 89.8%~99.2%)		
Relative specificity		99.2% (95% CI*: 95.5%~>99.9%)		
Accuracy		98.0% (95% CI*: 95.1%~99.5%)		

Influenza A+B test:

CoviGnost AG+ InfluGnost A+B test panel		**type A**			**type B**		
		RT-PCR		Total	RT-PCR		Total
		Positive	Negative		Positive	Negative	
Influenza A+B	Positive	38	2	40	39	2	41
	Negative	2	215	217	3	213	216
Total		40	63	217	257	42	215
Relative sensitivity		95.0% (95% CI*: 82.63%~99.5%)			92.9% (95% CI*: 80.3%~99.2%)		
Relative specificity		99.1% (95% CI*: 96.5%~99.9%)			99.1% (95% CI*: 96.5%~99.9%)		
Accuracy		98.4% (95% CI*: 95.9%~99.5%)			98.1% (95% CI*: 95.4%~99.3%)		

* Confidence intervals

Specificity

CoviGnost AG+InfluGnost A+B test panel was tested with the following viral strains. No discernible line at either of the test-line regions was observed at these concentrations listed:

COVID-19 test:

Virus	*Test level*
Adenovirus type 3	3.16 x 10^4 TCID50/mL
Adenovirus type 7	1.58 x 10^5 TCID50/mL
Human coronavirus OC43	2.45 x 10^6 LD50/mL
Human rhinovirus 2	2.81 x 10^4 TCID50/mL
Human rhinovirus 14	1.58 x 10^5 TCID50/mL
Human rhinovirus 16	8.89 x 10^6 TCID50/mL
Measles	1.58 x 10^4 TCID50/mL
Mumps	1.58 x 10^4 TCID50/mL
Parainfluenza virus 2	1.58 x 10^7 TCID50/mL
Parainfluenza virus 3	1.58 x 10^5 TCID50/mL
Influenza A H1N1	3.16 x 10^5 TCID50/mL
Influenza A H3N2	1 x 10^5 TCID50/mL
Influenza B	3.16 x 10^6 TCID50/mL
Respiratory syncytial virus	8.89 x 10^4 TCID50/mL

Influenza A and B:

Virus	*Test level*
Adenovirus type 3	3.16 x 10^4 TCID50/mL
Adenovirus type 7	1.58 x 10^5 TCID50/mL
Human coronavirus OC43	2.45 x 10^6 LD50/mL
Human rhinovirus 2	2.81 x 10^4 TCID50/mL
Human rhinovirus 14	1.58 x 10^5 TCID50/mL
Human rhinovirus 16	8.89 x 10^6 TCID50/mL
Measles	1.58 x 10^4 TCID50/mL
Mumps	1.58 x 10^4 TCID50/mL
Parainfluenza virus 2	1.58 x 10^7 TCID50/mL
Parainfluenza virus 3	1.58 x 10^5 TCID50/mL
Respiratory syncytial virus	8.89 x 10^4 TCID50/mL

TCID50 = Tissue Culture Infectious Dose is the dilution of virus that under the conditions of the assay can be expected to infect 50% of the culture vessels inoculated.

LD50 = Lethal Dose is the dilution of virus that under the conditions of the assay can be expected to kill 50% of the suckling mice inoculated.

Precision

Intra-assay and Inter-assay

Within-run and Between-run precision has been determined by using SARS-CoV-2 and Influenza A and B standard controls with three different lots of the test panel. Seven SARS-CoV-2 and influenza control samples were tested: negative; low and high concentration of SARS-CoV-2 antigens; low and high concentration of Influenza A antigens; low and high concentration of Influenza B antigens. Each control has been tested 10 times for three consecutive days. The specimens were correctly identified >99% of the time.

Cross-reactivity

The following organisms were tested at 1.0x10^8 org/ml and all found to be negative when tested with the test panel:

Arcanobacterium
Candida albicans
Corynebacterium
Pseudomonas aeruginosa
Staphylococcus aureus subsp. *aureus*
Staphylococcus epidermidis

BIBLIOGRAPHY

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3. WHO recommendations on the use of rapid testing for influenza diagnosis. *World Health Organisation*, July 2005.
4. Westgard JO, Barry PL, Hunt MR, Groth T. A multiple-rule Shewhart for quality control in clinical chemistry. *Clinical Chemistry 1981;* 27: 493-501.

COVIN020, COVIN05, COVIN01, V11, 03.12.2020. PO/MB/MŠ/VF

	Do not reuse	Σ	Number of tests in package		Keep dry	°C	Storage temperature range
i	Consult instructions for use		Keep away from sunlight		Use by	CE	European conformity
IVD	*In vitro* diagnostic medical device	LOT	Batch code	REF	Catalogue number		Manufacturer

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