INSTRUCTION FOR USE
A rapid test for detection of coronavirus 2019-nCoV (SARS-CoV-2)

REF: COVID19SEROSpeed-IgM-IgG BSD_0501

CE IVD

INTENDED USE

COVID19SEROSpeed-IgM-IgG Test is an immunochromatographic assay designed for the qualitative detection and differentiation of specific IgM and IgG antibodies to coronavirus 2019-nCoV or SARS-CoV-2 in human fingertip blood samples. It is intended to be used for the detection of SARS-CoV-2 virus infection. This protocol can be carried out in 15 minutes (certain results can be read in 3 minutes), it is simple in its implementation. The results obtained should not be the sole determinant for clinical decision. This test must be performed by an authorized healthcare professional.

CLINICAL INFORMATION

Coronaviruses are enveloped RNA viruses that are distributed broadly among humans, other mammals, and birds that cause respiratory, enteric, hepatic, and neurologic diseases.[1, 2] Six coronavirus species are known to cause human disease.[1] Four viruses — 229E, OC43, NL63, and HKU1 — are prevalent and typically cause common cold symptoms in immunocompetent individuals.[1] The two other strains — severe acute respiratory syndrome coronavirus (SARS-COV) and Middle East respiratory syndrome coronavirus (MERS-COV) — are zoonotic in origin and have been linked to sometimes fatal illness.[3] Coronaviruses are zoonotic, meaning they are transmitted between animals and people. Common signs of infection include respiratory symptoms, fever, cough, shortness of breath and breathing difficulties. In more severe cases, infection can cause pneumonia, severe acute respiratory syndrome, kidney failure and even death.[4]

A novel coronavirus (2019-nCoV, renamed as SARS-CoV-2 by WHO) was identified in early January 2020 as the infectious agent causing an outbreak of viral pneumonia in Wuhan, China, where the first cases had their symptom onset in December 2019.[5] It has since become an international health concern and declared a pandemic by WHO. The health emergency was declared to implement the resources necessary to control the infection (barrier measures, screening, treatment).[6]

Early diagnosis is particularly important in this context, not only for the diagnosis and possible virological monitoring of hospitalized patients but also to ensure the health security of caregivers, first responders, and the general population. In this context, a large-scale serological screening test (IgG, IgM) is necessary, in particular during the end of confinement of the general population as well as for the nursing staff taking care of patients suffering from COVID-19.[7]

PRINCIPLE OF THE TEST

COVID19SEROSpeed-IgM-IgG is a qualitative membrane-based assay for the detection of IgM and IgG to SARS-CoV-2 in whole blood specimen. This test consists of two components, an IgG component and an IgM component. In the IgG component, anti-human IgG is coated in IgG test line region. During testing, the specimen reacts with particles coated with SARS-CoV-2 antigen in the test cassette. The mixture then migrates upward on the membrane chromatographically by capillary action and reacts with the anti-human IgG in IgG test line region, if the specimen contains IgG antibodies to SARS-CoV-2. A coloured line will appear in IgG test line region as a result of this. Similarly, anti-human IgM is coated in IgM test line region and if specimen contains IgM antibodies to SARS-CoV-2, the conjugate-specimen complex reacts with anti-human IgM. A coloured line appears in IgM test line region as a result. If the specimen does not contain SARS-CoV-2 antibodies, no coloured line will appear in either of the test line regions, indicating a negative result. To serve as a procedural control, a coloured line will always appear in the control line region, indicating that the proper volume of specimen has been added and membrane wicking has occurred.

REAGENTS AND MATERIALS SUPPLIED

- Alcohol swab, sterile lancet, capillary blood transfer tube (25 pieces of each).
- COVID19SEROSpeed-IgM-IgG Rapid IgG/IgM Test cassette (25 pieces packed in individually sealed aluminium pouches containing a desiccant sachet).
- One bottle of chase buffer.
- One copy of instruction for use (product insert).

MATERIALS REQUIRED BUT NOT SUPPLIED

- Sample collection and preparation device and equipment.
- Personal protection equipment (gloves, mask, goggles).
- Clock or timer

STORAGE AND STABILITY

Store at 4-30 ºC, do not freeze. Keep the test device sealed until used. Keep away from direct sunlight, moisture and heat. Do not use the kit after the best-before date on the packaging. Do not mix the contents of kits from different lots/batch numbers.

WARNINGS AND PRECAUTIONS

- For professional only. Not for Home Testing.
- This product insert must be strictly followed in order to produce accurate test results.
- Keep the test device sealed until use. Once the device pouch has been opened, the test device must be used immediately.

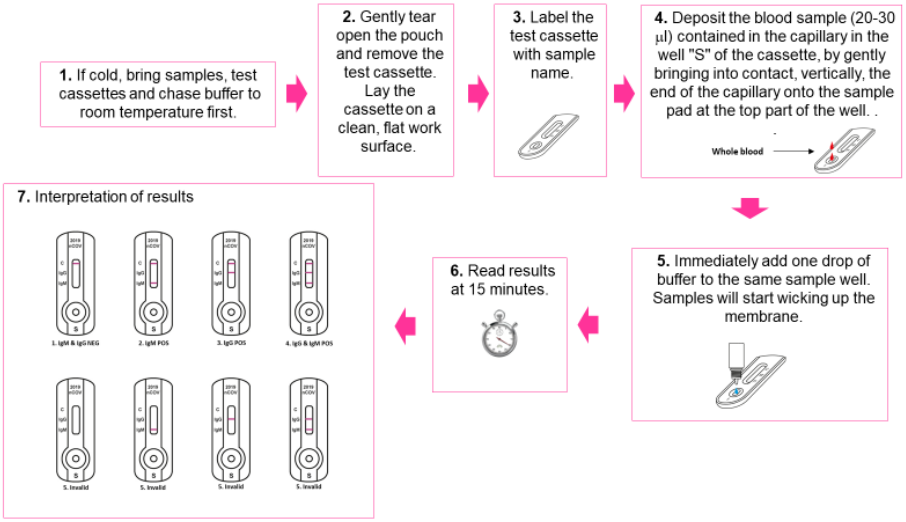
- All test devices, reagents and specimens must be at room temperature (15-30°C) before running the assay. High temperatures (above 30 degrees C) or an elevated humidity may affect the results of the test.
- Do not use device if the sealed pouch is visibly damaged.
- Do not use the kit contents beyond the expiration date.
- Handle all specimens as being potentially infectious. Dispose of all materials that come in contact with the specimen as infectious waste following the standard procedure.
- Wear protective clothing such as lab coat, disposable gloves and eye protection gear when specimens are being tested.
- Wipe any spills of blood promptly with 1% sodium hypochlorite solution or other disinfectant.
- Do not reuse test device.

SAMPLE COLLECTION AND ASSAY PROCEDURE

Read the entire Instruction for Use, check the completeness of the kit to be used and the expiration date, bring the kit and the samples to room temperature before carrying out the test, if they are kept cold. Open the individual pouch and place the cassette on a flat, horizontal surface. The sample well “S” must be located at the bottom of the cassette, towards the user. The test lines for diagnosis are identified to the right of the reaction lines by the letters T1 (to the right of the reaction line) or IgM (to the left of the reaction line), and T2 (to the right of the reaction line) or IgG (to the left of the reaction line). The control line is identified by the letter C at the top right of the reaction lines. Well "S" at the bottom of the cassette is where the sample is to be placed.
Handle all specimens as being potentially infectious. Dispose of all materials that come in contact with the specimen as infectious waste.

To take a sample of whole blood from the fingertip:

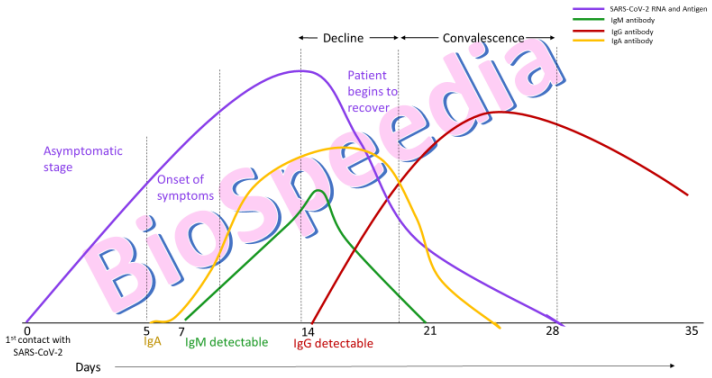
- Wash the patient’s hand with soap and warm water or clean with an alcohol swab. Allow to dry.
- Massage the hand without touching the puncture site by rubbing down the hand towards the fingertip of the middle or ring finger.
- Puncture the skin with the sterile lancet. Wipe away the first sign of blood.
- Gently rub the hand from wrist to palm to finger to form a rounded drop of blood over the puncture site.
- Collect the drop of blood using the capillary tube, allowing the blood to rise in the tube to approximately half of the capillary.
- Deposit the blood sample (20-30 µl) contained in the capillary in the well "S" of the cassette, by gently bringing into contact, vertically, the end of the capillary onto the sample pad at the top part of the well (the needed volume of sample will be issued). Avoid air bubbles.
- Add one drop of buffer to the same sample well (testing should be performed immediately after the specimens have been collected. Do not leave the specimens at room temperature for prolonged periods).



INTERPRETATION OF RESULTS

Read the results at 15 minutes. Do not read the results after 30 minutes. Not following this procedure can lead to inaccurate results.

1. Negative:
Only control line (C) is visible. No IgG or IgM antibodies were detected. The result does not exclude COVID-19 infection. Early negative IgG test results must be rechecked after 21 days from the start of symptoms.
2. Positive for IgM:
Coloured bands appear at the control line (C) and test line (T1 or IgM). The test is positive for IgM antibodies. Patient maybe in early / acute stage of infection (see the limitations section). In case of isolated IgM reactivity without suggestive clinical context, a false positive reactivity cannot be excluded and a new test must be carried out one to two weeks later; the persistence of isolated IgM without clinical signs and without the appearance of IgG likely means the subject is not infected with SARS-CoV-2.
3. Positive for IgM and IgG:
Coloured bands appear at the control line (C) and both test lines (T1 or IgM, and T2 or IgG). The test is positive for IgM and IgG antibodies. Patient is in active stage of infection.
4. Positive for IgG:
Coloured bands appear at the control line (C) and test line (T2). The test is positive for IgG antibodies. Patient maybe in late or recurrent stage of infection.



For information: Theoretical kinetics of appearance of antibodies during infection

STABILITY AND CONDITIONS OF USE

The unopened kit is stable until the expiration date indicated on the product, under the storage conditions defined above. (See STORAGE AND STABILITY, page 2).
Once the kit has been opened, always keep the remaining contents in the original packaging at a temperature of between 4 and 30 degrees C until the expiration date.
Always keep the test cassettes in their closed pouch until use.

QUALITY CONTROL

A control line to check proper procedure is included in the test. A colored line appearing in the control line region (C) represents the internal procedural control. This control allows the user to confirm proper wicking along the membrane, thus indicating correct procedure was used.
Standard controls are not provided with this test; however, it is recommended to perform positive and negative controls as good laboratory practice in order to confirm test procedure and to verify correct test performance.

INTERFERENCES

No interference has been observed in the positive and negative samples of SARS-CoV-2 for the following substances:

Ascorbic acid 20 mg/mL	Bilirubin 1000 mg/dL	Methanol 10%
Hemoglobin 1000 mg/dL	Uric acid 20 mg/mL	Creatine 200 mg/dL
Gentisic acid 20 mg/dL	Acetaminophen 20mg/dL	Albumin 2000 mg/dL
Oxalic acid 60mg/dL	Aspirin 20 mg/dL	Caffeine 20 mg/dL

CROSS-REACTIONS

No cross-reactions have been observed in the negative samples of SARS-CoV-2 and who for:

Positive for Hepatitis A	Positive for Cancer	Positive for HBcAb
Positive for Hepatitis C	Positive for HBsAg	Positive for hCG (urine)
Positive for HIV	Positive for HBsAb	Positive for heterophilic antigens
High rheumatoid factors	Positive for HBcAg	

LIMITATIONS OF THE TEST

1. This product is designed for use with human fingertip whole blood only.
2. This test detects the presence of antibodies to SARS-CoV-2 in the specimen and should not be used as the sole criterion for the diagnosis of a SARS-CoV-2 viral infection.
3. The test is a qualitative assay and is not for quantitative determination of antibody concentration levels. The intensity of the band does not have linear correlation with the antibody titer of the specimen.
4. The results obtained should only be interpreted in conjunction with other diagnostic results and clinical information available to the physician.
5. If the test result is negative but symptoms persist, and a SARS-CoV-2 infection suspicion still exists, it is recommended to retest later or proceed with follow-up testing using other clinical methods, for example RT-PCR method.
6. A negative result at any time does not exclude the possibility of an early infection of SARS-CoV-2 virus. A negative result can occur if the quantity of SARS-CoV-2 virus antibodies present in the specimen is below the detection limits of the assay or the antibodies that are detected are not present during the stage of disease in which a sample is collected.

WARRANTY AND LIMITED LIABILITY

The performance characteristics stated were obtained by using the assay procedure in this insert. Failure to follow the assay procedure may derive inaccurate results. In such event, the manufacturer disclaims all warranties expressed, implied or statutory, including the implied warranty of merchantability and the fitness for use.
BioSpeedia will not be liable for any damage caused by misuse, improper handling and storage, non-compliance with warnings and procedures, damage caused by events occurring after the product is released, failure to ensure the product is in proper condition before use, or any warranty given by independent distributor.
Once the kit is opened, always keep the rest of its components in the primary packaging at a temperature between 4 and 30 ° C until the expiration date. Always keep the "test" cassettes in their closed pouch until use.

PERFORMANCE CHARACTERISTICS

The indicated performance characteristics were obtained by strictly using the described procedure.
COVID19SEROSpeed-IgM-IgG Test was compared with a reference RT-PCR and the comparison results are summarized in tables below:

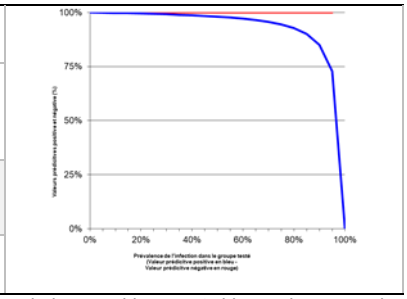
Methods	Results (IgM)*	RT-PCR		Total
		Pos	Neg	
COVID19Speed-IgM-IgG	Pos	42	0	42
	Neg	2	102	104
Total		**44**	**102**	**146**

** Samples collected from symptomatic hospitalized patients between 11 and 23 days after the first symptoms. Relative sensitivity: 95.5 % (42/44) - Relative specificity: 100 % (102/102) - Overall agreement: 98.6 % (144/146).*

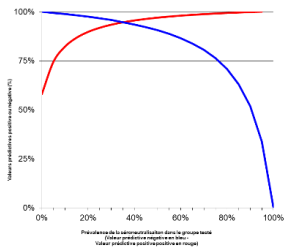
Methods	Results (IgG)*	RT-PCR		Total
		Pos	Neg	
COVID19Speed-IgM-IgG	Pos	54	2	56
	Neg	0	100	100
Total		**54**	**102**	**156**

**Samples collected between 19 and 30 days after the first symptoms Relative sensitivity: 100 % (54/54) - Relative specificity: 98.1 % (100/102) - Overall agreement: 98.7 % (154/156)*

Study in progress. University Hospital of Saint Etienne (preliminary results)

Methods	Results (IgM+IgG)	RT-PCR		Total	
		Pos	Neg		
COVID19SEROSpeed-IgM-IgG	Pos	50	0	50	
	Neg	1*	40***	41	
Total		**51****	40**	**91**	

** blood samples taken at 13 days from the 1st positive PCR. ** 51 symptomatic hospitalized subjects and 1 symptomatic ambulatory subject. *** Subjects whose samples were taken before January 1, 2020 (20 subjects have autoimmune diseases, 2 have positive HIV serology, 1 has positive hepatitis B serology). Relative sensitivity: 98% (50/51) - Relative specificity: 100% (40/40) - Negative predictive value: 98 % - Positive predictive value: 100 % - Overall agreement: 98.9% (90/91).*

Methods	Results (IgM+ or IgG+, or IgM+ and IgG+)	SERONEUTRALIZATION		Total	
		Pos	Neg		
COVID19SEROSpeed-IgM-IgG	Pos	54	1	55	
	Neg	6*	28	34	
Total		**60**	**29**	**89**	

** 1 patient hospitalized in intensive care and 5 pauci symptomatic subjects (blood samples taken before day 11). Sensitivity: 90% (54/60) - Specificity: 97% (28/29) - Negative predictive value: 83% - Positive predictive value: 98% - Overall agreement: 92% (82/89).* Other evaluation studies are in progress.

REFERENCES

1. Weiss SR, Leibowitz JL. Coronavirus pathogenesis. Advances in Virus Research (2011), 81:85-164.
2. Su S, Wong G, Shi W, et al. Epidemiology, genetic recombination, and pathogenesis of coronaviruses. Trends in Microbiology (2016), 24:490-502.
3. Cui J, Li F, Shi ZL. Origin and evolution of pathogenic coronaviruses. Nature Reviews Microbiology (2019), 17:181-192.
4. World Health Organization (WHO). Coronavirus. https://www.who.int/health-topics/coronavirus
5. World Health Organization "WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020" https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020.
6. World Health Organization (WHO). WHO Statement Regarding Cluster of Pneumonia Cases in Wuhan, China. Beijing: WHO; 9 Jan 2020. [Accessed 26 Jan 2020]. https://www.who.int/china/news/detail/09-01-2020-who-statement-regarding-cluster-of-pneumonia-cases-in-wuhan-china.
7. Xingwang Jia et al. 2020. Clinical significance of IgM and IgG test for diagnosis of highly suspected COVID-19 infection. medRxiv doi: https://doi.org/10.1101/2020.02.28.20029025.

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SYMBOLS

	See instruction for use		Expiration date
DIL	Diluant	LOT	Batch number
IVD	In vitro diagnostic only		Manufacturer
	Keep between 4-30°C		Do not reuse
Σ	Tests per kit	RÉF	Catalog reference