# BIOSYNEX COVID-19 BSS (IgG/IgM)

Ref : SW40005A

CE

A rapid test for the qualitative detection of antibodies (IgG and IgM) to SARS-CoV-2 in whole blood, serum, or plasma.
For professional *in vitro* diagnostic use only.

## 1 I INTENDED USE

The BIOSYNEX COVID-19 BSS (IgG/IgM) is a rapid chromatographic immunoassay for the qualitative detection of IgG and IgM antibodies to SARS-CoV-2 in human whole blood, serum, or plasma as an aid in the diagnosis of SARS-CoV-2 infections.

## 2 I SUMMARY

The novel coronaviruses belong to the β genus. COVID-19 is an acute respiratory infectious disease. People are generally susceptible. Currently, the patients infected by the novel coronavirus are the main source of infection; asymptomatic infected people can also be an infectious source. Based on the current epidemiological investigation, the incubation period is 1 to 14 days, mostly 3 to 7 days. The main manifestations include fever, fatigue and dry cough. Nasal congestion, runny nose, sore throat, myalgia and diarrhea are found in a few cases.

## 3 I PRINCIPLE

The BIOSYNEX COVID-19 BSS (IgG/IgM) is a qualitative membrane-based immunoassay for the detection of SARS-CoV-2 antibodies in whole blood, serum or plasma. 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 SARS-CoV-2 antigen-coated particles 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 colored line will appear in IgG test line region. In the IgM component, anti-human IgM is coated in IgM test line region. IgM antibodies to SARS-CoV-2, if present in the specimen, reacts with the anti-human IgM and the SARS-CoV-2 antigen-coated particles in the test cassette, forming a colored line in IgM test line region.
If the specimen does not contain antibodies to SARS-CoV-2, no colored line will appear in either the IgG or IgM test line regions, indicating a negative result.
An internal procedural control is included in the assay, in the form of a colored line appearing in the Control "C" area, indicating that the proper volume of specimen has been added and membrane wicking has occurred.

## 4 I REAGENTS

BIOSYNEX COVID-19 BSS (IgG/IgM) contains specific antigen conjugated gold colloid particles and anti-human IgM, anti-human IgG coated on the membrane. The targeted protein is the spike protein Receptor Binding Domain (RBD).

## 5 I PRECAUTIONS

- For professional *in vitro* diagnostic use only. Do not use after expiration date.
- Do not eat, drink or smoke in the area where the specimens or kits are handled.
- Handle all specimens as if they contain infectious agents. Observe established precautions against microbiological hazards throughout the procedure and follow the standard procedures for proper disposal of specimens.
- Wear protective clothing such as laboratory coats, disposable gloves and eye protection when specimens are assayed.
- The used tests, specimens and potentially contaminated material should be discarded according to the local regulations.
- Humidity and temperature can adversely affect results.

## 6 I STORAGE AND STABILITY

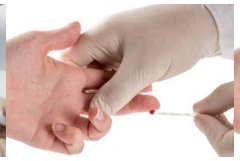
The kit can be stored at room temperature or refrigerated (2-30°C). The test cassette is stable through the expiration date printed on the sealed pouch. The test cassette must remain in the sealed pouch until use. DO NOT FREEZE. Do not use beyond the expiration date.
Use the test cassette within one hour of opening the pouch. The shelf life of the buffer after opening is 1.5 months at room temperature.

## 7 I SPECIMEN COLLECTION AND PREPARATION

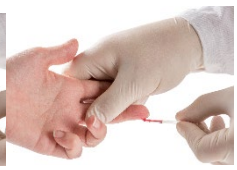
BIOSYNEX COVID-19 BSS (IgG/ IgM) can be performed using whole blood (venipuncture lithium heparin or EDTA or finger stick), serum, or lithium heparin or EDTA plasma.
Testing should be performed immediately after specimen collection. Do not leave the specimens at room temperature for prolonged periods.

To collect fingerstick Whole Blood specimens:
Wash the patient's hand with soap and warm water or clean with an alcohol wipe. Ideally choose the middle or ring finger. Allow to dry.

Prick the finger with the sterile lancet provided. Massage the finger to form a large drop of blood.



Without pressing on the bulb, place the pipette in direct contact with the blood drop. The pipette fills automatically by capillary action.



Repeat the previous step until the volume of blood reaches the line (10 µL).

Serum and plasma collection (Li-heparin and EDTA tubes):
Separate serum or plasma from blood as soon as possible to avoid hemolysis. Use only clear, non-hemolyzed specimens.

Whole Blood conservation (Li-heparin and EDTA tubes):
Whole blood collected by venipuncture should be stored at 2-8°C if the test is to be run within 2 days of collection. Do not freeze whole blood specimens. Whole blood collected by finger stick should be tested immediately.

Serum and Plasma conservation:
Serum and plasma specimens may be stored at 2-8°C for up to 3 days. For long-term storage (up to 3 months), specimens should be kept below -20°C.
Samples should not be frozen and thawed more than three times.

## 8 I MATERIALS

Materials Provided

- Test cassettes
- Buffer
- Package insert
- Microsafe capillary pipettes 10µL
- Sterile lancets

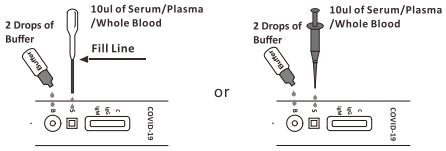
Materials required but not provided

- Specimen collection containers
- Micropipette
- Centrifuge (for plasma only)
- Timer

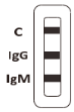
## 9 I PROCEDURE

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

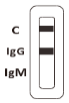
1. Bring the pouch to room temperature before opening. Remove the test cassette from the sealed pouch and use it within one hour.
2. Place the test cassette on a clean and level surface.
3. For Serum or Plasma, or Whole Blood Specimens:
   - *To use a dropper or capillary:* Hold the dropper or capillary vertically, draw the specimen up to the Fill Line (approximately 10µl), and transfer the specimen to the specimen well (S) of the test cassette, then add 2 drops of buffer (approximately 80µl) to the buffer well (B) and start the timer. Avoid trapping air bubbles in the specimen well.
   - *To use a micropipette:* Pipette and dispense 10µl of specimen to the specimen well (S) of the test cassette, then add 2 drops of buffer (approximately 80µl) to the buffer well (B) and start the timer.
4. The test result should be read at 10 minutes. Do not interpret the result after 20 minutes. A positive result may appear within the first few minutes.




## 10 I INTERPRETATION OF RESULTS



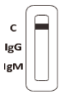

**IgG and IgM POSITIVE:*** Three lines appear. One colored line appears in the control line region (C), and two colored lines should appear in IgG test line region and IgM test line region. The color intensities of the lines do not have to match. The result is positive for SARS-CoV-2 virus specific-IgG and specific-IgM antibodies.




**IgG POSITIVE:*** Two lines appear. One colored line appears in the control line region (C), and a colored line appears in IgG test line region. The result is positive for SARS-CoV-2 virus specific-IgG antibodies.


**IgM POSITIVE:*** Two lines appear. One colored line should be in the control line region (C), and a colored line appears in IgM test line region. The result is positive for SARS-CoV-2 virus specific-IgM antibodies.

**NOTE: The intensity of the color in the IgG and/or IgM test line region(s) will vary depending on the concentration of SARS-COV-2 antibodies in the specimen. Therefore, any shade of color in the IgG and/or IgM test line region(s) should be considered positive.*




**NEGATIVE:** One colored line should be in the control line region (C). No line appears in IgG and IgM test line region(s).

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

## 11 I QUALITY CONTROL

A procedural control is included in the test. A colored line appearing in the control region (C) is the internal procedural control. It confirms sufficient specimen volume and correct procedural technique.
Control standards are not supplied with this kit. However, it is recommended that positive and negative controls be tested as a good laboratory practice to confirm the test procedure and to verify proper test performance.

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## 12 I LIMITATIONS

1. An IgG or IgM positive result alone does not provide a diagnosis of active SARS-CoV-2 infection. Further testing for SARS-CoV-2 RNA should be performed to determine the patient's infectious status.
2. A false negative result may occur in some patients with early symptoms. Repeat the test on subsequent days to demonstrate seroconversion. At the onset of infection, SARS-CoV-2 IgM antibody concentrations may be below detectable levels.
3. The BIOSYNEX COVID-19 BSS (IgG/IgM) is for in vitro diagnostic use only. The test should be used for the detection of SARS-CoV-2 antibodies in whole blood, serum or plasma specimens only. Neither the quantitative value nor the rate of increase in SARS-CoV-2 antibody concentration can be determined by this qualitative test.
4. The BIOSYNEX COVID-19 BSS (IgG/IgM) will only indicate the presence of SARS-CoV-2 antibodies in the specimen and should not be used as the sole criteria for the diagnosis of SARS-CoV-2.
5. The continued presence or absence of antibodies cannot be used to determine the success or failure of therapy.
6. Results from immunosuppressed patients should be interpreted with caution.
7. As with all diagnostic tests, all results must be interpreted together with other clinical information available to the physician.
8. If the test result is negative and clinical symptoms persist, additional testing using other clinical methods is recommended. A negative result does not at any time preclude the possibility of SARS-CoV-2 infection.

## 13 I EXPECTED VALUES

The early stage of SARS-CoV-2 infection is characterized by the presence of detectable IgM antibodies approximately 11 days after the onset of symptoms. Later stage SARS-CoV-2 infection is characterized by the elevation of SARS-CoV-2-specific IgG. In the majority of the cases, this is accompanied by elevated levels of IgM.

## 14 I PERFORMANCE CHARACTERISTICS

***Sensitivity and Specificity***

The BIOSYNEX COVID-19 BSS test was compared with clinical diagnosis (Confirmed). The study included 466 specimens for IgM and 456 specimens for IgG.

IgM Results:

| | |
|---|---|
| Sensitivity: 92.6% | Specificity: 99.2 % |
| Accuracy: 98% | |

IgG Results:

| | |
|---|---|
| Sensitivity: 100% | Specificity: 99.5% |
| Accuracy: 100% | |

A clinical study was carried out at Grand Hôpital de l'Est Francilien, in Jossigny, France[5]. The aim of the study was to determine the clinical performance of antibody appearance in PCR positive patients (138 PCR positive samples, including 129 with confirmed symptoms). It was accompanied by a specificity study on 40 samples collected prior to the beginning of the pandemic. The results are summarized in the tables below:

| | *Delay between the onset of clinical symptoms and a serological test* | | | |
|---|---|---|---|---|
| | 0 to 5 days | 6 to 10 days | 11 to 15 days | > 13 days |
| n | 10 | 17 | 31 | 39 |
| IgG & IgM positive | 2 | 10 | 24 | 36 |
| IgG negative, IgM positive | 1 | 4 | 3 | 2 |
| IgG positive, IgM negative | 0 | 0 | 1 | 1 |
| IgG & IgM negative | 7 | 3 | 3 | 0 |
| Overall sensitivity | 30,0% | 82,4% | 90,3% | 100,0% |
| Sensitivity IgM | 30,0% | 82,4% | 87,1% | 97,4% |
| Sensitivity IgG | 20,0% | 58,8% | 80,6% | 94,9% |
| PPV | 100% | 100% | 100% | 100% |
| NPV | 85% | 93% | 93% | 100% |

*The specificity is 100% on 40 sera (collected before December 2019).*

| | *Delay between positive PCR and serological test* | | |
|---|---|---|---|
| | 1 to 5 days | 6 to 10 days | >10 days |
| n | 55 | 63 | 20 |
| IgG & IgM positive | 31 | 51 | 16 |
| IgG negative, IgM positive | 11 | 6 | 0 |
| IgG positive, IgM negative | 0 | 1 | 3 |
| IgG & IgM negative | 13 | 5 | 1 |
| Overall sensitivity | 76,4% | 92,1% | 95,0% |
| Sensitivity IgM | 76,4% | 90,5% | 80,0% |
| Sensitivity IgG | 56,4% | 82,5% | 95,0% |
| PPV | 100% | 100% | 100% |
| NPV | 75,5% | 88,9% | 97,6% |

*PPV: positive predictive value / NPV: negative predictive value*

***Sample matrix study***

For each matrix, 29 negative and 29 spiked positive samples were tested with five test cassettes and read by two independent operators. With an agreement of 99% or higher when testing different sample matrices, it can be concluded that the assay yields equivalent performance when testing in serum, EDTA whole blood, EDTA plasma, lithium heparin whole blood and lithium heparin plasma.

***Cross-reactivity***

A total of 68 samples were tested. No cross-reactivity was observed with specimens positive for anti-influenza A virus, anti-influenza B virus, anti-RSV, anti-Adenovirus, HBsAg, anti-Syphilis, anti-H. Pylori, anti-HIV, anti-HCV and HAMA positive specimens. The results showed no cross-reactivity. Some cross reactivity was observed with samples positive for SARS-CoV antibodies and Rheumatoid Factor. It is possible to cross-react with samples positive for MERS-CoV antibody.

***Interfering Substances***

The following potentially interfering substances were added to SARS-CoV-2 negative and positive specimens.

| | | |
|---|---|---|
| Acetaminophen: 20 mg/dL | Caffeine: 20 mg/dL | Albumin: 2 g/dL |
| Acetylsalicylic Acid: 20 mg/dL | Gentisic Acid: 20 mg/dL | Ethanol: 1% |
| Ascorbic Acid: 2 g/dL | Creatine: 200 mg/dL | Bilirubin: 1g/dL |
| Hemoglobin: 1000 mg/dL | Oxalic Acid: 60mg/dL | Uric acid: 20mg/mL |
| Triglycerides: 500 mg/dL | | |

None of the substances at the concentration tested interfered in the assay.

## 15 I BIBLIOGRAPHY

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4. Lei *et al*. A preliminary study on serological assay for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in 238 admitted hospital patients. medRxiv preprint doi doi.org/10.1101/2020.03.06.20031856
5. Ahmed TSOURIA, Perrine BOURGEOIS, Isabelle RAUZY, Laurine KRZECZOWSKI, Yannick COSTA du Laboratoire de biologie médicale, Evaluation BIOSYNEX COVID-19 BSS (IgG/IgM), Grand Hôpital de l'Est Francilien, data on file.

## SYMBOLS

| | | | | | |
|---|---|---|---|---|---|
| | Attention, see instruction for use | Σ | Tests per kit | REF | Catalog number |
| IVD | For *in vitro* diagnostic use only | | Store between 2-30°C | | Do not reuse |
| | Do not use if package is damaged | LOT | Lot number | | Expiry |
| | Manufacturer | DIL | Buffer | | |

IFU_SW40005A_EN_V04202007R02
Date of last revision: 10/2020

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