NexScreen™
NEXT GENERATION SCREENING SOLUTIONS

RightSign COVID-19 IgG/IgM Rapid Test Cassette

Emergency Use Authorized by US FDA

NexScreen

www.nexscreen.com

Basic Information

1. What is COVID-19?

COVID-19 is caused by the SARS-CoV-2 virus. The virus, which can cause mild to severe respiratory illness has spread globally, including the United States.The current information available to characterize the spectrum of clinical illness associated with COVID-19 suggests that symptoms include cough, shortness of breath or difficulty breathing, fever, chills, muscle pain, headache, sore throat or new loss of taste or smell.

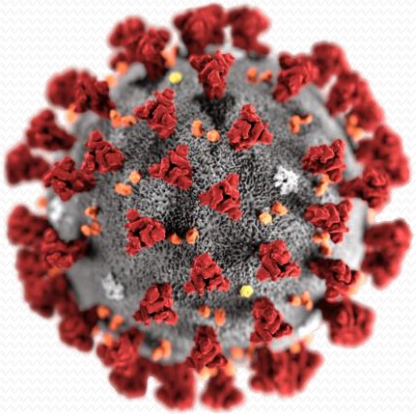

Illustration of a SARS-CoV-2 virion

- Genus: Betacoronavirus
- Shape: Round or Oval
- Diameter: 60-140nm
- Original: Bat-SL-CoVZC45

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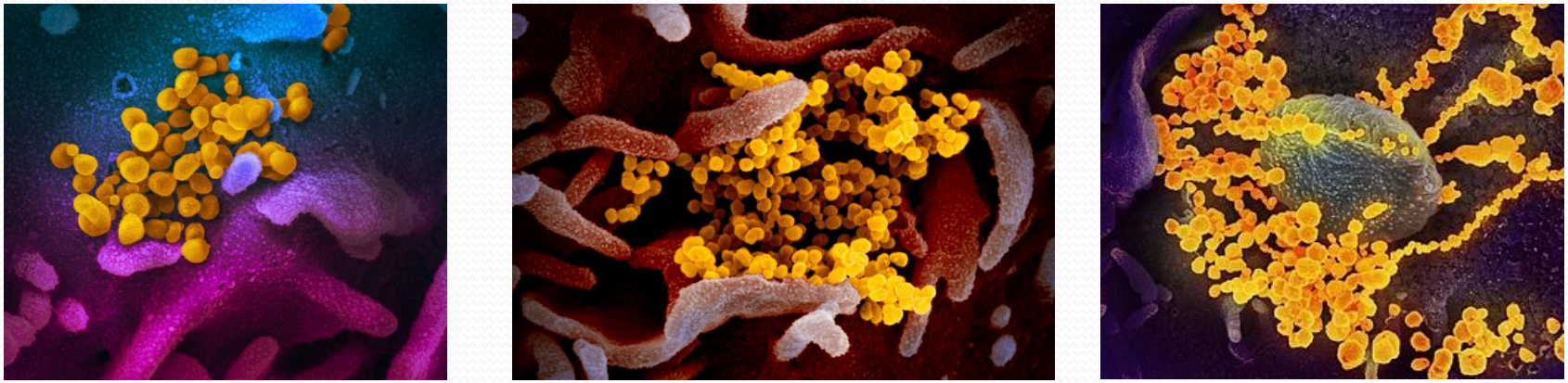
Basic Information

2. How are people tested for COVID-19?

Two kinds of tests are currently available for COVID-19: Diagnostic tests and Antibody tests.

- A diagnostic test tells you if you have a current infection.
- An antibody test tells you if you had a previous infection.



Digitally colorized electron micrographs of SARS-CoV-2

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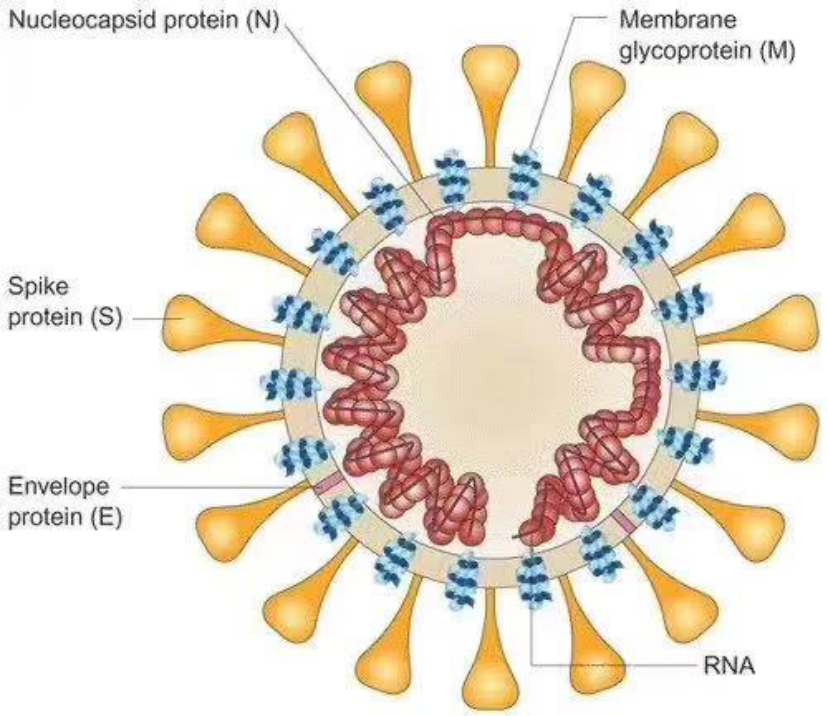
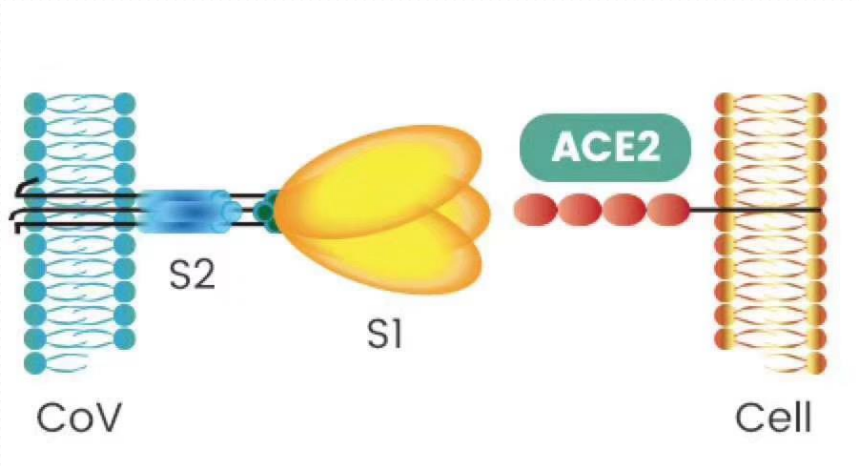
Basic Information

Structural Biology



SARS-CoV-2 has four structural proteins, known as the S (spike), E (envelope), M (membrane), and N (nucleocapsid) proteins



Surface S protein recognizes ACE2 receptor protein in human cells

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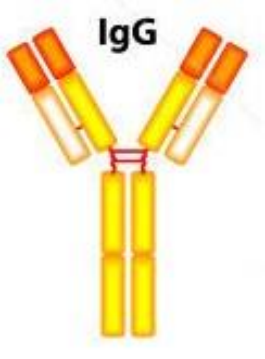
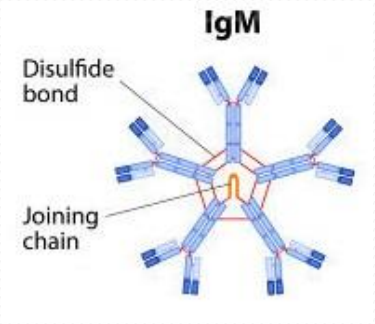
Basic Information

What are IgG & IgM ?

After the virus invades the human body, the human body will produce corresponding specific antibodies for defense. Among them, the specific antibody IgM is first produced and used for early defense, and then IgG antibodies are produced. Serological testing is to detect the presence and content of specific antibodies IgM and IgG in blood samples to indirectly determine whether there are viruses and viral infections in the body.





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Basic Information

Differences Between IgG and IgM

Name	Titer	Antibody production time	Duration	Affinity	Function
IgM	Lower	Produced earlier, Once infected, produce quickly	Short term: usually 2-3 weeks, 2Months sometimes	Lower	Acute infection diagnostic indicators
IgG	Higher	Usually later than IgM	Long term	Higher	Prompt in the middle and late stages of infection or previous infection

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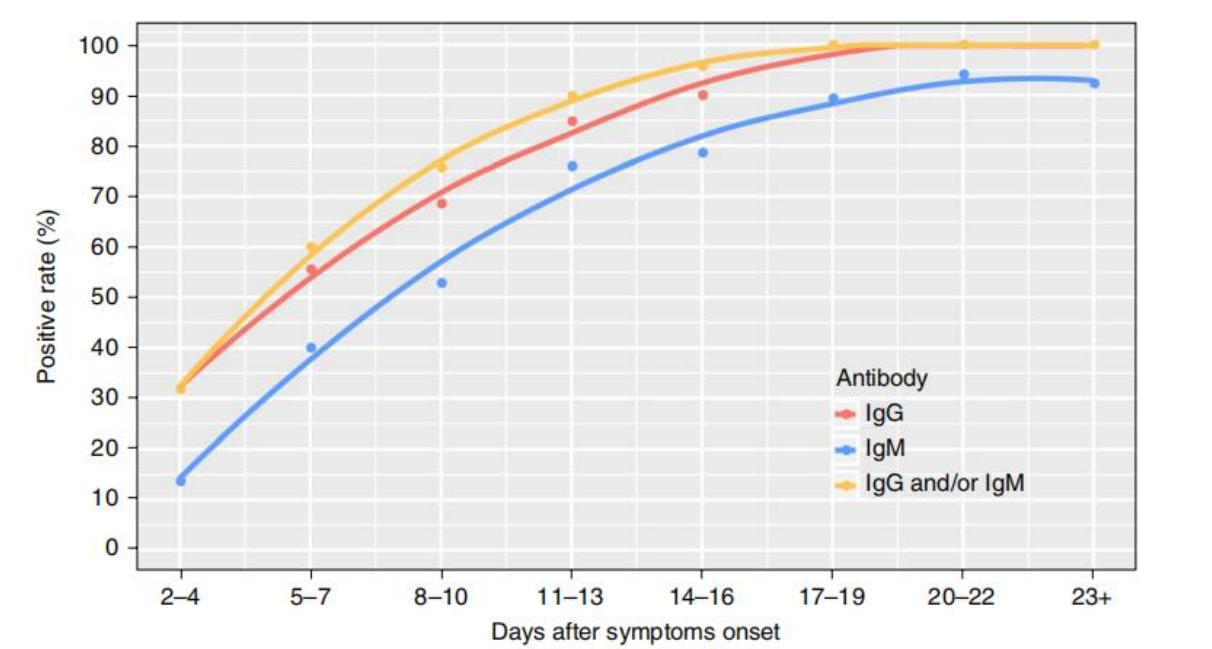
Basic Information

What is the appropriate time to detect IgG and IgM antibodies?

According to relevant research, it is speculated that IgM antibodies usually begin to appear positive 3-5 days after onset [1].The positive rate of antibodies is closely related to the onset time, the longer the onset time, the higher the positive rate.

Antibody responses against SARS-CoV-2[2]



Reference:1.Novel Coronavirus Pneumonia Diagnosis and Treatment Plan-Provisional 7th Edition backup
2.Quan-Xin Long. et al.Antibody responses to SARS-CoV-2 in patients with COVID-19. nature medicine.

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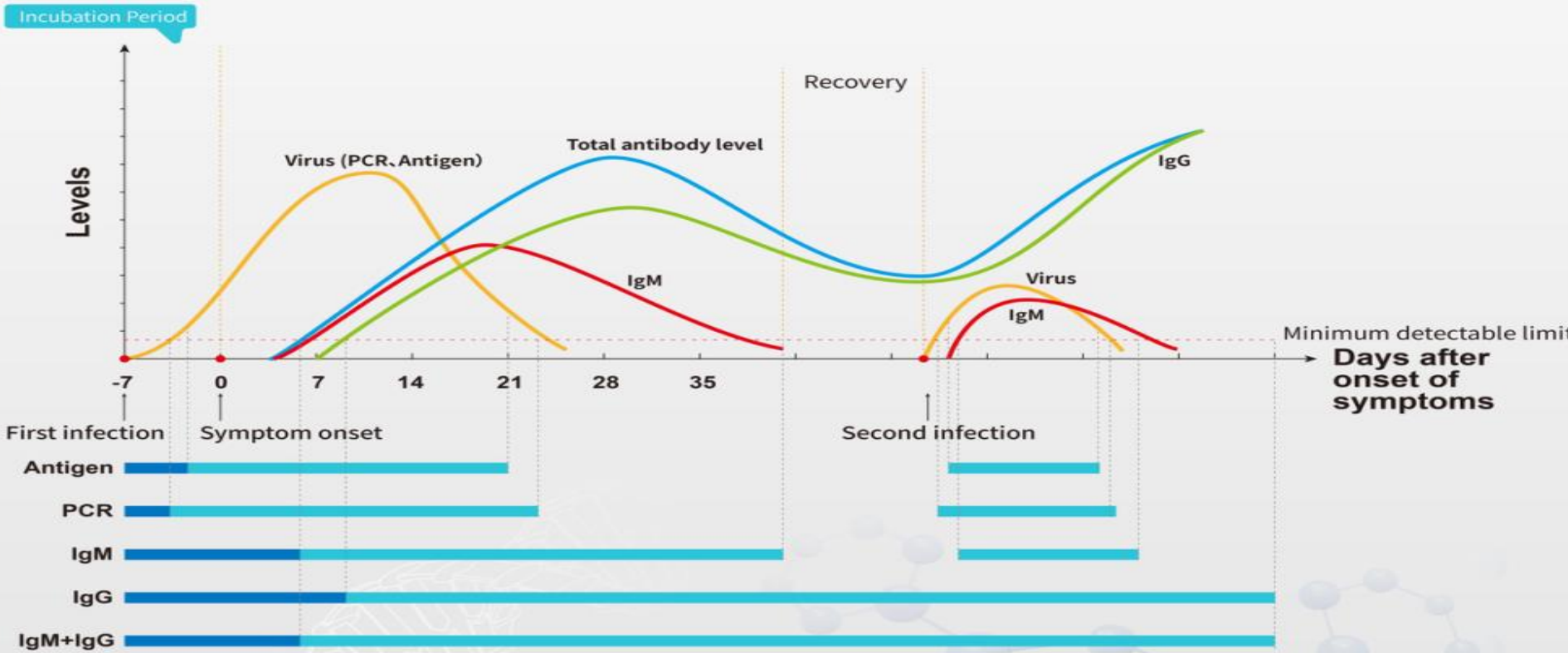
Levels of SARS-CoV-2 virus and antibodies after infection

*For illustrative purpose only



* Incubation Period: 1~14 Days, Mostly 3~7 Days

*Antibody Window Period: 5-10 days after onset of symptoms

*The minimum detectable limit varies with methodology and sensitivity of test

Window Period Testing Period

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EUA Information

1. What is an EUA?

The United States FDA has made these tests available under an emergency access mechanism called an Emergency Use Authorization (EUA). The EUA is supported by the Secretary of Health and Human Service's (HHS) declaration that circumstances exist to justify the emergency use of in vitro diagnostics (IVDs) for the detection and/or diagnosis of the virus that causes COVID-19.

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EUA Information

2. What about RightSign COVID-19 antibody test?

RightSign COVID-19 IgG/IgM Rapid Test Cassette detects human SARS-CoV-2 IgM and IgG that are generated as part of the human adaptive immune response to the COVID-19 virus and is to be performed only using human serum, plasma, or venipuncture whole blood specimens.

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EUA Information

3. What does it mean if the specimen tests positive for antibodies against the virus that causes COVID-19?

A positive test result with the RightSignTM COVID-19 IgG/IgM Rapid Test Cassette indicates that antibodies to SARS-CoV-2 were detected, and the individual has potentially been exposed to SARS-CoV-2.

Antibodies to SARS-CoV-2 are generally detectable in blood several days following infection. Individuals may have detectable virus present for several weeks following seroconversion. A positive result can indicate recent or past infection but does not exclude recently infected patients who are still contagious. **It is unknown how long antibodies to SARS-CoV-2 will remain present in the body after infection and if they confer immunity to infection. Incorrect assumptions of immunity may lead to premature discontinuation of physical distancing requirements and increase the risk of infection for individuals, their households and the public.**

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EUA Information

4. What does it mean if the specimen tests negative for antibodies against virus that causes COVID-19?

A negative test result with this test means that SARS -CoV-2 specific antibodies were not present in the specimen above the limit of detection. **However, patients tested early after infection may not have detectable antibodies despite active infection; in addition, it is not certain that all infected patients will develop a detectable antibody response to SARS-CoV-2 infection. A negative result should not be used to rule out infection. Direct testing of SARS-CoV-2 should be performed if acute infection is suspected.**

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EUA Information

LIMITATIONS

For use under an Emergency Use Authorization Only

1. This test has not been FDA cleared or approved.
2. This test is intended for laboratory professional use , not for home use and screening of donated blood.
3. This test is has been authorized only for the presence of IgM and IgG antibodies against SARS-CoV-2, not for any other viruses or pathogens.
4. This test has been authorized by FDA under an EUA for use by authorized laboratories.

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EUA Information

LIMITATIONS

For use under an Emergency Use Authorization Only

5. This test is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

6. Results from antibody testing should not be used as the sole basis to diagnose or exclude SARS-CoV-2 infection or to inform infection status.

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Fact sheets

FACT SHEET FOR HEALTHCARE PROVIDERS

FACT SHEET FOR HEALTHCARE PROVIDERS

Hangzhou Biotest Biotech Co., Ltd.
RightSign™ COVID-19 IgG/IgM Rapid Test Cassette

June 4, 2020

Coronavirus Disease 2019 (COVID-19)

This Fact Sheet informs you of the significant known and potential risks and benefits of the emergency use of the RightSign™ COVID-19 IgG/IgM Rapid Test Cassette.

RightSign™ COVID-19 IgG/IgM Rapid Test Cassette is authorized for the detection of IgG and IgM antibodies to SARS-CoV-2 in human serum, plasma, or venous whole blood (sodium heparin, potassium EDTA, and sodium citrate).

All individuals whose specimens are tested with one of these tests will receive the Fact Sheet for Recipients: RightSign™ COVID-19 IgG/IgM Rapid Test Cassette.

What are the symptoms of COVID-19?
Many individuals with confirmed COVID-19 have developed fever and/or symptoms of acute respiratory illness (e.g., cough, fever, difficulty breathing). The current information available to characterize the spectrum of clinical illness associated with COVID-19 suggests that symptoms include cough, shortness of breath or dyspnea, fever, chills, myalgias, headache, sore throat or new loss of taste or smell. Based on what is known about the virus that causes COVID-19, signs and symptoms may appear any time from 2 to 14 days after exposure to the virus. Based on preliminary data, the median incubation period is approximately 5 days, but may range 2-14 days.

Public health officials have identified cases of COVID-19 infection throughout the world, including the United States, which poses risks to public health. Please check the CDC webpage for the most up-to-date information.

What do I need to know about COVID-19 antibody testing?
Current information on COVID-19 for healthcare providers is available at CDC's webpage, *Information for Healthcare Professionals* (see links provided in "Where can I go for updates and more information" section).

- RightSign™ COVID-19 IgG/IgM Rapid Test Cassette can be ordered by healthcare providers to test human venous whole blood, plasma, or serum (sodium heparin, potassium EDTA, and sodium citrate) to detect if there has been an adaptive immune response to COVID-19, indicating recent or prior infection.
- RightSign™ COVID-19 IgG/IgM Rapid Test Cassette should not be used to diagnose or exclude acute infection and should not be used as the sole basis for treatment or patient management decisions. Direct testing for SARS-CoV-2 should be performed if acute infection is suspected.
- RightSign™ COVID-19 IgG/IgM Rapid Test Cassette is authorized for use in laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform moderate or high complexity tests.
- Please refer to the RightSign™ COVID-19 IgG/IgM Rapid Test Cassette instructions for use for additional information.

This test detects human SARS-CoV-2 IgM and IgG that are generated as part of the human adaptive immune response to the COVID-19 virus and is to be performed only using human serum, plasma, or venipuncture whole blood specimens.

Specimens should be collected with appropriate infection control precautions. Current guidance for COVID-19 infection control precautions are available at the CDC's website (see links provided in "Where can I go for updates and more information" section).

Use appropriate personal protective equipment when collecting and handling specimens from individuals suspected of having COVID-19 as outlined in the CDC *Interim Laboratory Biosafety Guidelines for Handling and Processing Specimens Associated with Coronavirus Disease 2019 (COVID-19)*. For additional information, refer to CDC *Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens from Persons Under Investigation (PUIs) for Coronavirus Disease 2019 (COVID-19)* (see links provided in "Where can I go for updates and more information" section).

Report Adverse events, including problems with test performance or results, to MedWatch by submitting the online FDA Form 3500 (https://www.accessdata.fda.gov/scripts/medwatch/index.cfm?action=reporting.home) or by calling **1-800-FDA-1088**

FACT SHEET FOR RECIPIENTS

FACT SHEET FOR RECIPIENTS

Hangzhou Biotest Biotech Co., Ltd.,
RightSign™ COVID-19 IgG/IgM Rapid Test Cassette

June 4. 2020

Coronavirus Disease 2019 (COVID-19)

You are being given this Fact Sheet because your sample(s) is being tested or was tested for antibodies to the virus that causes Coronavirus Disease 2019 (COVID-19) using the RightSign™ COVID-19 IgG/IgM Rapid Test Cassette.

This Fact Sheet contains information to help you understand the risks and benefits of using this test to evaluate your adaptive immune response to SARS-CoV-2, the virus that causes COVID-19. After reading this Fact Sheet, if you have questions or would like to discuss the information provided, please talk to your healthcare provider.

- **For the most up to date information on COVID19 please visit the CDC Coronavirus Disease 2019 (COVID-19) webpage:**
- **https://www.cdc.gov/COVID19**

What is COVID-19?
COVID-19 is caused by the SARS-CoV-2 virus.
The virus, which can cause mild to severe respiratory illness has spread globally, including the United States.
The current information available to characterize the spectrum of clinical illness associated with COVID-19 suggests that symptoms include cough, shortness of breath or difficulty breathing, fever, chills, muscle pain, headache, sore throat or new loss of taste or smell.

How are people tested for COVID-19?
Two kinds of tests are currently available for COVID-19: diagnostic tests and antibody tests.

- A diagnostic test tells you if you have a current infection.
- An antibody test tells you if you had a previous infection

What is this test?
This test is an antibody test. It will help assess if you have antibodies to the virus that causes COVID-19. An antibody test may not be able to show if you have a current infection, because it can take 1-3 weeks after infection to make antibodies.

What are the known and potential risks and benefits of the test?
Potential risks include:

- Possible discomfort or other complications that can happen during blood collection.
- Possible incorrect test result (see below for more information).

Potential benefits include:

- The results, along with other information, can help you and your healthcare provider make informed recommendations about your care.

What does it mean if I have a positive test result?
If you have a positive test result, it is possible that you have had recent or prior COVID-19 infection and that you have developed an antibody response to the virus. Your healthcare provider will work with you to determine how best to care for you based on the test results along with other factors of your medical history, your symptoms, possible exposures, and geographic location of places you have recently traveled. There is also the small possibility that this test can give a positive result that is wrong (a false positive result). Even a high-performing antibody test when used in a population without many cases of COVID-19 infection may produce as many or more false results as true results because the likelihood of finding someone who has been infected is very small. Your healthcare provider will work with you to determine the likelihood of false result.

- **Where can I go for updates and more information?** The most up-to-date information on COVID-19 is available at the CDC General webpage: https://www.cdc.gov/COVID19. In addition, please also contact your healthcare provider with any questions/concerns.

Documents are available on www.fda.gov.

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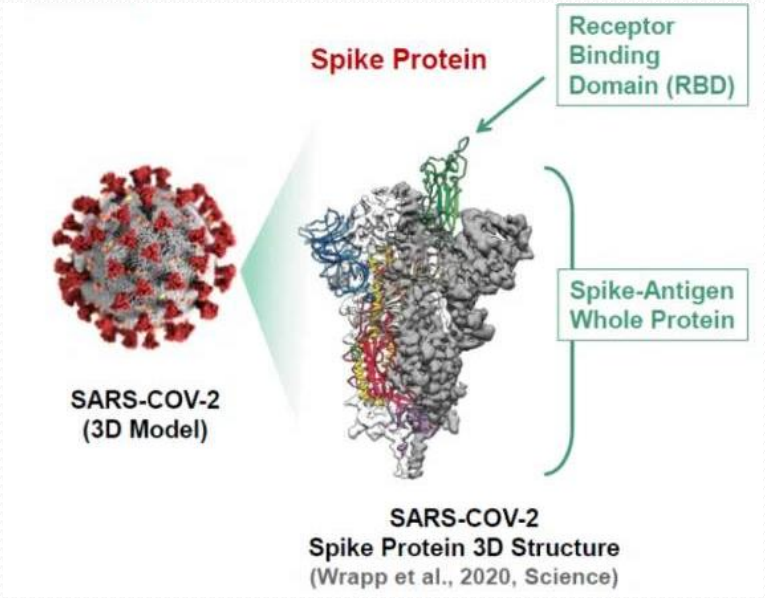
Advantages

1. What's the Advantage of RightSign COVID-19 IgG/IgM Rapid Test ?

SARS-CoV-2 mainly consists of RNA, Nucleocapsid, and Spike protein. RBD is the outstanding part of spike protein. Full name of RBD is Receptor Binding Domain which is the key point to bind ACE2 in human lung. However, Nucleocapsid is inside of the virus and only after the virus is broken, the immune system can detect the Nucleocapsid. The body immune system will develop the IgG sensitive to RBD (Spike protein), and the IgG sensitive to Nucleocapsid antigen. Nucleocapsid antigen is considered to be nonspecific to SARS-CoV-2 and a common antigen seen in other Coronavirus types according to current research. RBD, however, is known to be specific for SARS-CoV-2.



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Advantages

Analysis of using Nucleocapsid and Spike protein

RightSign COVID-19 IgG/IgM Rapid Test Cassette

- Only RBD of Spike protein is used in the test.
- **Advantages:**
  a. The target IgG is only sensitive to RBD and valuable to protect the body against SARS-CoV-2.
  b. High Sensitivity of IgM.
  c. High specificity and no cross-reactivity to the normal Coronavirus strains.
- **Disadvantage**: False negative risk of IgG. When RBD is fully binding ACE2, the immune system is not available to detect it. So, in these cases, the target IgG to RBD will be not developed or later developed.

For the serological COVID-19 rapid test with Nucleocapsid and Spike protein:

- Both RBD of Spike protein and Nucleocapsid antigen are used.
- **Advantage:** High sensitivity of both IgG and IgM;
- **Disadvantages: a. Potential false Positive risk of IgG since Nucleocapsid is known to be common antigen of Coronaviruses. b. Not all the detected IgG is sensitive to RBD and the target IgG to Nucleocapsid antigen is not useful to protect the body against the virus because the Nucleocapsid antigen is inside of the live virus and the IgG is not available to bind the live virus.**

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Advantages

2.What are the PPV and NPV?

- PPV is positive predictive value, The percentage of true positives measured by a particular test method, PPV=True Positive Number/(True Positive Number+ False Positive Number) X100%

- NPV is negative predictive value. The percentage of true negative measured by a particular test method. NPV=True Negative Number/(True Negative Number+ False Negative Number) X100%

√ **PPV and NPV are the main indicators reflecting the accuracy of the test reagent results.**

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Advantage

Comparison Data (PPV and NPV)

Antibody	Performance Measure	Estimate of Performance	
		Company A EUA Product	RightSign EUA Product
IgM	Sensitivity	96.7% (29/30)	100% (30/30)
IgM	Specificity	95.0% (76/80)	100% (80/80)
IgG	Sensitivity	96.7% (29/30)	93.3% (28/30)
IgG	Specificity	95.0% (76/80)	100% (80/80)
Combined	Sensitivity	96.7% (29/30)	100% (30/30)
Combined	Specificity	95.0% (76/80)	100% (80/80)
Combined	PPV at prevalence = 5%	50.40%	100%
Combined	NPV at prevalence = 5%	99.80%	100%

*** Referenced from FDA website** www.fda.gov

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Advantages

Detail analysis about PPV and NPV

Prevalence is 5%, which means there are 50,000 positive cases and 950,000 negative cases in 1 million people.

Company A test:

PPA

- The combined sensitivity is 96.7%, which means there are 48350(50000X 96.7%) positive cases (true positive) are tested positive.
- The combined specificity is 95.0%, which means there are 950,000 negative cases but there are 47500(950000 X (1-95%) =47500) persons false positive.
- Total PPV=48350/ (48350+47500) X100%=50.4%.
- This means that only 50.4% positive results are true positive cases among the positive results

NPA

- The combined specificity is 95%, which means there are 902,500 (950,000X95%) negative cases (true negative) are tested negative.
- The combined sensitivity is 96.7% meaning there are 50,000 positive cases but 1650 (50000X (1-96.7%) =1650) persons are false negative.
- Total NPV= 902500/ (902500+1650) X100%=99.8%.
- This means that 99.8% negative results are true negative cases among the negative results

√ **Both PPA and NPA of RightSign COVID-19 IgG/IgM Rapid Test Cassette are 100%.**

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Product Information

RightSign COVID-19 IgG/IgM Rapid Test Cassette

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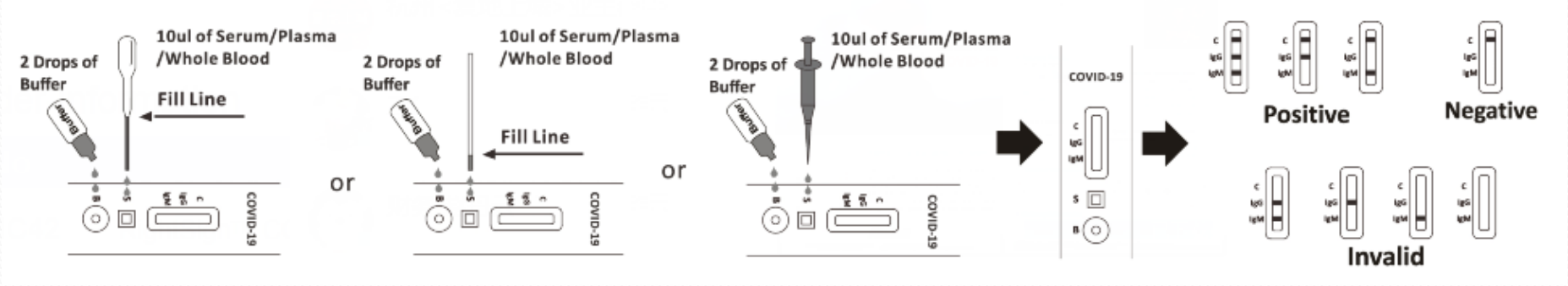
Product Information

- Convenient Procedure



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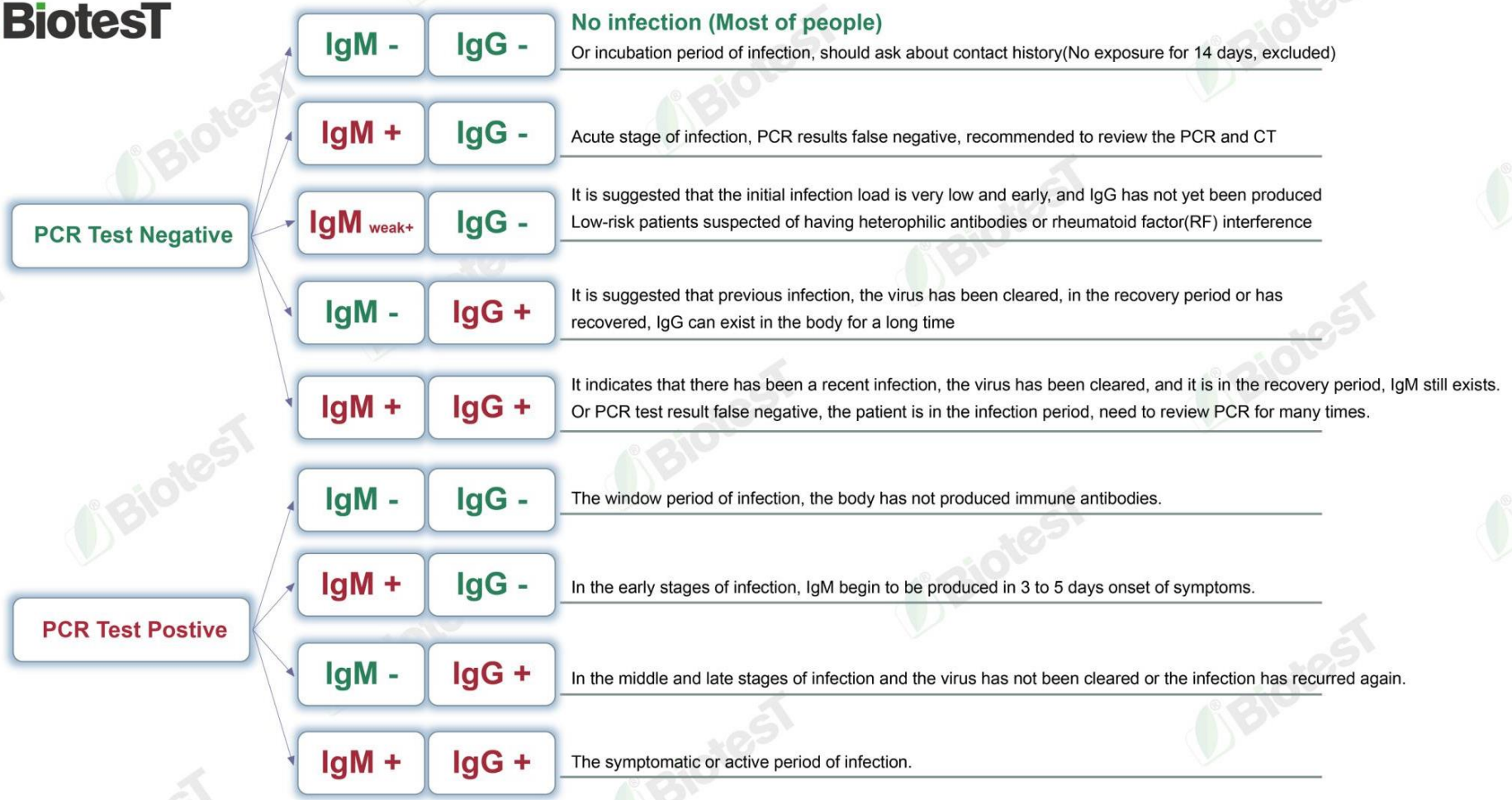
Results Analysis

BiotesT

Interpretation of relevant laboratory results about SARS-Cov-2



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Analysis Of False Negative

1.Improper preservation of specimens: When specimens are stored in the refrigerator for too long, IgG in the serum aggregates into multimers, and the immune activity of antibodies is weakened.

2.Operator error, insufficient specimen volume, or improper storage of the kit: the test product are not equilibrated to room temperature before use, the volume of specimen added is insufficient, the incubation time or temperature is insufficient; the test product are not stored as specified, contaminated or invalid, etc.

3.Chromatography is too fast: the antigen-antibody complex has not yet combined with the antibody on the detection line, and it goes out of the detection line, causing false negatives in colloidal gold immunochromtographic assay (GICA).

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Analysis Of False Positive

1.Hemolyzed or red blood cell specimens, the detection area accumulates to form a lighter non-specific band, which interferes with the visual method to determine the result of colloidal gold test.

2.Bacteria contaminate the specimen, the hydrophobic bacterial fragments are combined with gold-labeled particles or capture antibodies, which affects GICA interpretation.

3.The patient's own reasons: there are autoantibodies, heterophile antibodies, etc. in the body, such as certain underlying diseases or abnormal immune function, or long-term use of certain drugs, can produce abnormal protein antibodies or special substances, such as rheumatoid factor, alpha-fetoprotein , Complement, etc., have a certain adsorption effect, resulting in false positive antibody detection.

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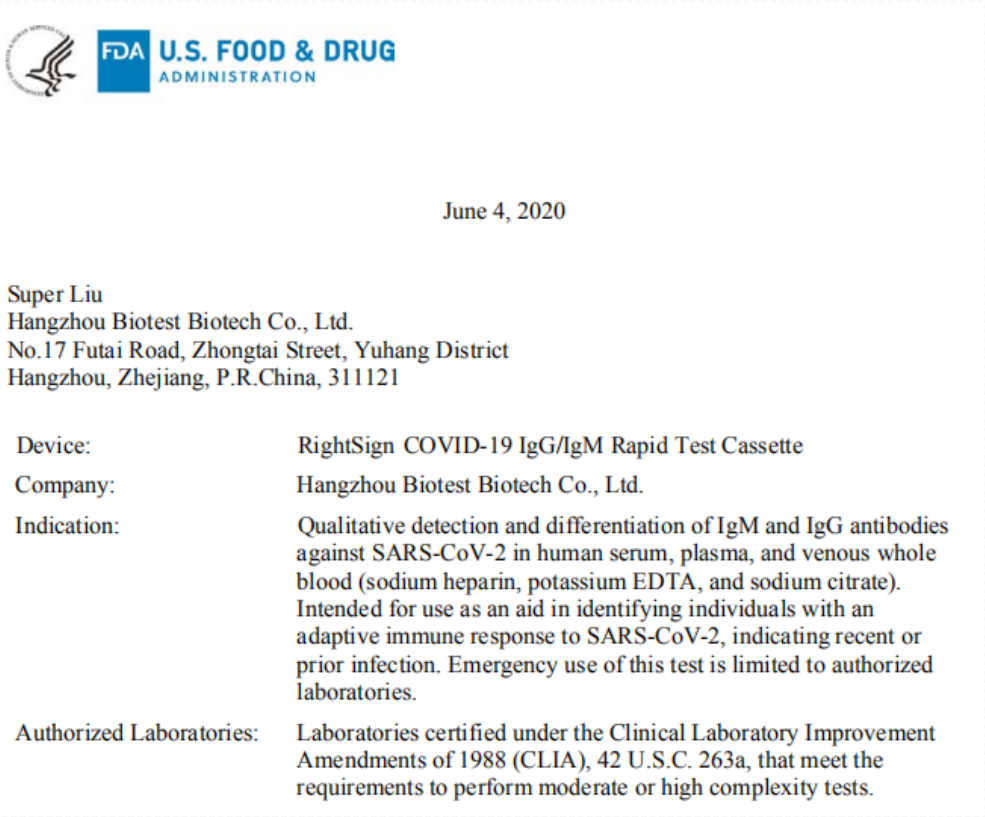
Certificates

☑ FDA Emergency Use Authorized



FDA U.S. FOOD & DRUG ADMINISTRATION

June 4, 2020

Super Liu
Hangzhou Biotest Biotech Co., Ltd.
No.17 Futai Road, Zhongtai Street, Yuhang District
Hangzhou, Zhejiang, P.R.China, 311121

Device:	RightSign COVID-19 IgG/IgM Rapid Test Cassette
Company:	Hangzhou Biotest Biotech Co., Ltd.
Indication:	Qualitative detection and differentiation of IgM and IgG antibodies against SARS-CoV-2 in human serum, plasma, and venous whole blood (sodium heparin, potassium EDTA, and sodium citrate). Intended for use as an aid in identifying individuals with an adaptive immune response to SARS-CoV-2, indicating recent or prior infection. Emergency use of this test is limited to authorized laboratories.
Authorized Laboratories:	Laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. 263a, that meet the requirements to perform moderate or high complexity tests.

BiotesT®

Certificates

☑ ISO13485

TÜV SÜD ◆ CERTIFICATE ◆ 認證證書 ◆ СЕРТИФИКАТ ◆ CERTIFICADO ◆ CERTIFICAT

DAkkS
Deutsche Akkreditierungsstelle
D-ZM-11321-01-00

TÜV SÜD Product Service

Certificate

No. Q5 077434 0014 Rev. 01

Holder of Certificate: **HANGZHOU BIOTEST BIOTECH CO., LTD.**
17#, Futai Road, Zhongtai Street
Yuhang District
311121 Hangzhou
PEOPLE'S REPUBLIC OF CHINA

Certification Mark:

Scope of Certificate: **Design and Development,
Production and Distribution of
In Vitro Diagnostic Kit for the Detection of
Hormone, Drug of Abuse,
Infectious Disease,
Tumour Marker and Cardiac Marker**

The Certification Body of TÜV SÜD Product Service GmbH certifies that the company mentioned above has established and is maintaining a quality management system, which meets the requirements of the listed standard(s). See also notes overleaf.

Report No.: SH1970812

Valid from: 2019-12-18
Valid until: 2020-09-05

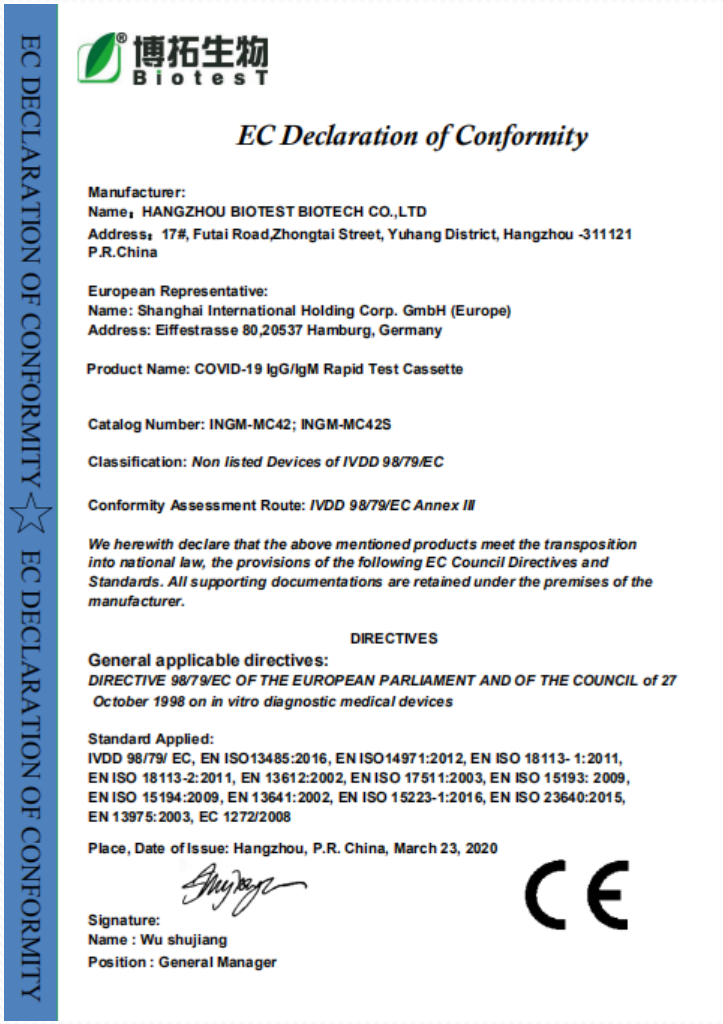
Date, 2019-12-18

Christoph Dicks
Head of Certification/Notified Body

BiotesT®

Certificates

☑ CE Marked



EC DECLARATION OF CONFORMITY ☆ EC DECLARATION OF CONFORMITY

博拓生物 BiotesT

EC Declaration of Conformity

Manufacturer:
Name：HANGZHOU BIOTEST BIOTECH CO.,LTD
Address：17#, Futai Road,Zhongtai Street, Yuhang District, Hangzhou -311121 P.R.China

European Representative:
Name: Shanghai International Holding Corp. GmbH (Europe)
Address: Eiffestrasse 80,20537 Hamburg, Germany

Product Name: COVID-19 IgG/IgM Rapid Test Cassette

Catalog Number: INGM-MC42; INGM-MC42S

Classification: ***Non listed Devices of IVDD 98/79/EC***

Conformity Assessment Route: ***IVDD 98/79/EC Annex III***

We herewith declare that the above mentioned products meet the transposition into national law, the provisions of the following EC Council Directives and Standards. All supporting documentations are retained under the premises of the manufacturer.

DIRECTIVES

General applicable directives:
DIRECTIVE 98/79/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 27 October 1998 on in vitro diagnostic medical devices

Standard Applied:
IVDD 98/79/ EC, EN ISO13485:2016, EN ISO14971:2012, EN ISO 18113- 1:2011, EN ISO 18113-2:2011, EN 13612:2002, EN ISO 17511:2003, EN ISO 15193: 2009, EN ISO 15194:2009, EN 13641:2002, EN ISO 15223-1:2016, EN ISO 23640:2015, EN 13975:2003, EC 1272/2008

Place, Date of Issue: Hangzhou, P.R. China, March 23, 2020

Signature:
Name : Wu shujiang
Position : General Manager

CE

BiotesT