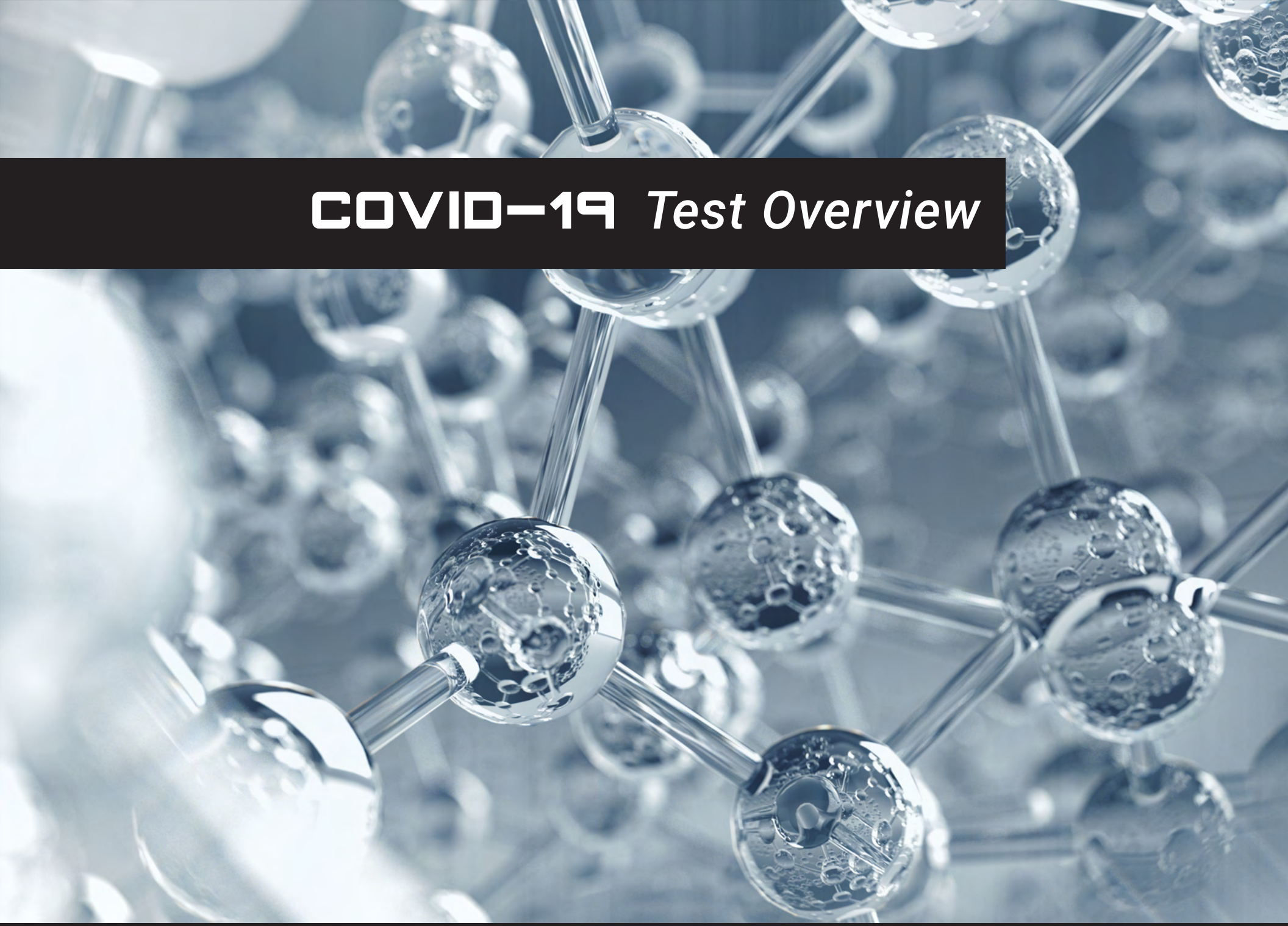
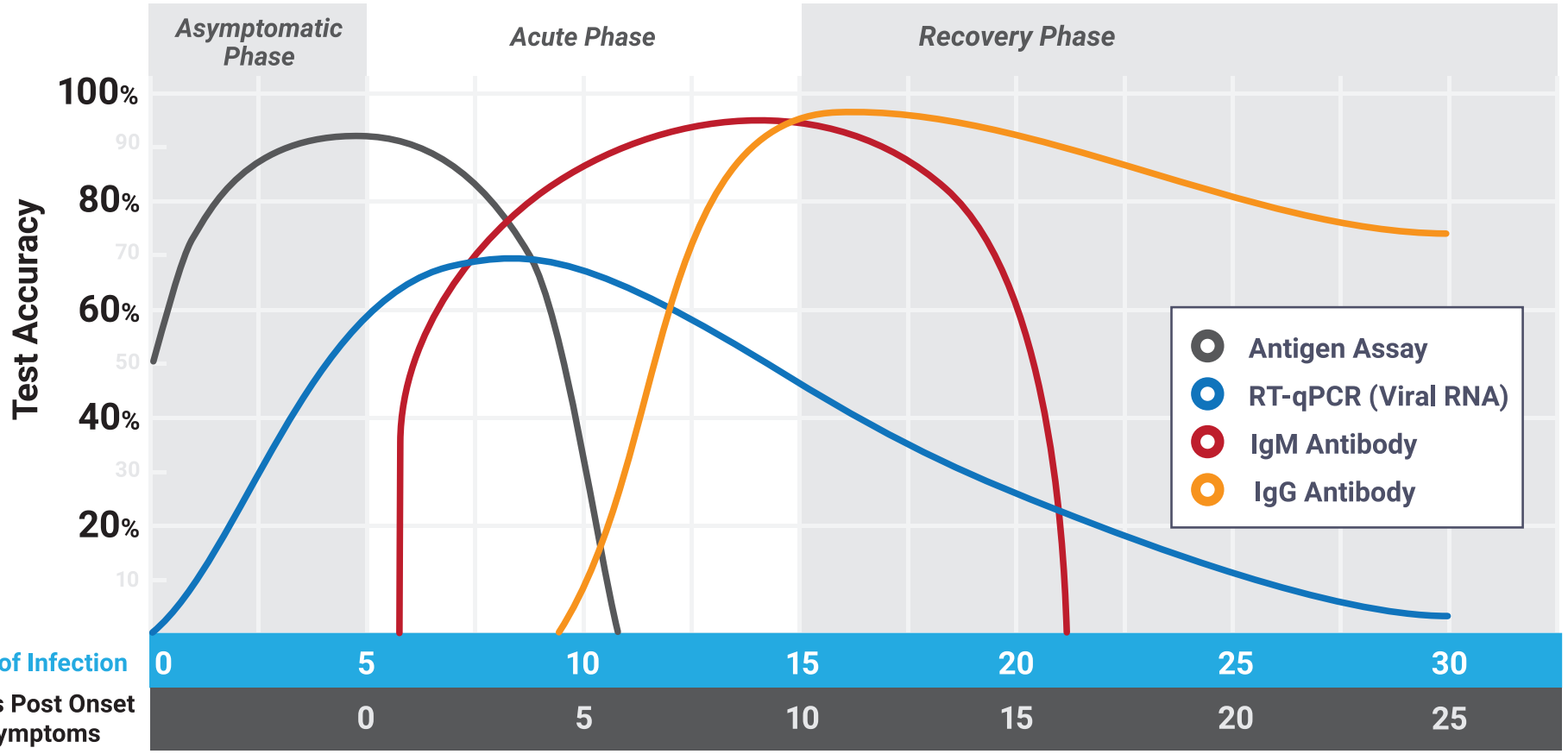


COVID-19 *Test Overview*

COVID-19 DETECTION TEST COMPARISON



This graph is intended to demonstrate the relative accuracies of the tests listed as a function of progression of infection. It is NOT meant to represent precise accuracy values.

Biohit SARS-CoV-2 LFA Antibody Test Kit

Studies	IgM *Sensitivity*	IgM *Specificity*	IgG *Sensitivity*	IgG *Specificity*	Total Antibody Sensitivity *(IgG + IgM)*	Total Antibody Specificity *(IgG + IgM)*
Biohit Study[1]	97.5%	99.5%	97.5%	100%		
Yale Study[2] *(American Patients > 14 days of infection)*	100%	97.6%	100%	100%		
FDA EUA Authorization[3]	96.7%	95%	96.7%	95%	96.7%	95%

In a study of ten LFA Antibody Detection Kits completed at the University of California at San Francisco (UCSF) an assessment and contrast of test results was reported.[4] The Biohit SARS-CoV-2 LFA Antibody Test Kit results reported in the Yale Study above, demonstrated higher sensitivity values for IgG and IgM for patients with infection times greater than 14 days compared with the very best test evaluated in the UCSF study. Also, the IgG and IgM specificities of the Biohit kit was comparable to the best performing assays evaluated by the UCSF group.

The human immune response to a COVID-19 infection encompasses the host synthesis of anti-SARS-CoV-2 IgM antibodies that are detectable after about 5 to 7 days of infection which, in turn, is followed by an IgG antibody response after 10 plus days of infection. The selectivity and specificity of a SARS-CoV-2 IgM/IgG Antibody Test is most accurate eleven plus days after infection onset. Thus, detection of the immune response to a COVID-19 infection by an Antibody Assay may be inaccurate during early infection from days 0 to 7. During this same time period, RNA detectability by RT-qPCR is at best about 67%. This "window period" is best approached by using an orthogonal approach. Effective orthogonal algorithms are generally based on testing a patient sample with two tests, each with unique design characteristics (e.g., antigens or formats). This results in increasing detection or assessment accuracy. Such an approach would be exemplified by utilizing a Biohit SARS-CoV-2 IgM/IgG Antibody test and a RT-qPCR molecular study or a Biohit SARS-CoV-2 Antigen Assay. ***References***

1. Bio Hit Study
https://biotestingsupplies.com/wp-content/uploads/2020/05/BioHit-Clinical-Examination-Results-Sheet.pdf

2. Yale Study

**Minteer C. et al. Multi-site Validation of a SARS-CoV-2 IgG/IgM Rapid Antibody Detection Kit (pre-publication), 2020.*
https://www.medrxiv.org/content/10.1101/2020.05.25.20112227v1.full.pdf

3. FDA EUA Documentation
https://www.fda.gov/media/139280/download

4. UCSF Study
Whitman, J.D. et al. Test performance evaluation of SARSCoV-2 serological assays. medRxiv, 2020.
https://www.medrxiv.org/content/10.1101/2020.04.25.20074856v2.full.pdf

SARS-CoV-2 IgM/IgG LFA Antibody Test Kit

This form of a Laminar Flow Immunoassay (LFA) is a point of care (POC) rapid test that produces qualitative antibody results in <15 minutes. A cassette contains paper strips impregnated with recombinant COVID-19 viral proteins and also in 2 discrete areas, anti-human IgM and anti-human IgG antibodies. There is a small trough in the cassette for placement of 1 drop of finger stick blood and a small volume of buffer. Once the blood solution is placed, it diffuses from the trough through the paper. If the blood solution contains anti-COVID-19 antibodies to specific viral antigens, then this is detected. Specifically, either anti-COVID-19 IgM or IgG will bind with the recombinant protein in the strip. Subsequently, the anti-human IgG antibody will bind and display a dark band at the IgG area while the anti-human IgM antibody in the strip will bind and display a dark band at the IgM area of the strip. In addition, a constant (internal control) band will also be depicted which verifies that the results are valid.

COVID-19 Antigen Assay

This is a quantitative microplate dependent assay in which detection of SARS-CoV-2 nucleocapsid protein (N protein) is detected in human serum or plasma. The microtiter plates are pre-coated with Anti-SARS-CoV-2 (N protein) antibodies. Then the serum sample is added and if it contains SARS-CoV-2 N protein, it will bind to the coated plate. Then this is combined with an added labeled N protein antibody to form an antibody-antigen-labeled antibody sandwich complex. Then after the addition of a few additional reagents and subsequent washing, microplate wells containing complexes of serum N protein and labeled N protein antibody will produce a frequency specific color that is detected and quantified to yield the N protein content in the serum sample analyzed. In a typical microtiter plate, 96 samples can be run simultaneously. This assay requires a complex CLIA authorization.

COVID-19 Antigen Rapid Assay

This is a qualitative rapid POC assay in which a finger stick drop of blood is assayed for the detectable presence of a COVID-19 protein, such as the nucleocapsid N protein. The methodology will parallel that described above for the SARS-CoV-2 IgM/IgG LFA Antibody Test Kit except, the cassette strips will be impregnated with anti- N protein antibody only that form an antibody-antigen (N protein) complex, if the test serum contains this COVID-19 component. If the complex forms, then the presence of a dark band will signify the presence of serum containing COVID-19 nucleocapsid N protein. This test will also contain a built in validity test.

The human immune response to a COVID-19 infection encompasses the host synthesis of anti-SARS-CoV-2 IgM antibodies that are detectable after about 5 to 7 days of infection which, in turn, is followed by an IgG antibody response after 10 plus days of infection. The selectivity and specificity of a SARS-CoV-2 IgM/IgG Antibody Test is most accurate eleven plus days after infection onset. Thus, detection of the immune response to a COVID-19 infection by an Antibody Assay may be inaccurate during early infection from days 0 to 7. This "window period" is best approached by using an orthogonal approach. Effective orthogonal algorithms are generally based on testing a patient sample with two tests, each with unique design characteristics (e.g., antigens or formats). This results in increasing detection or assessment accuracy. Such an approach would be exemplified by utilizing a SARS-CoV-2 IgM/IgG Antibody test and a COVID-19 Antigen Rapid Assay.

Combined SARS-CoV-2 IgM/IgG Antibody test and a COVID-19 Antigen Rapid Assay

Such a combination kit can be a rapid LFA POC assay. By utilizing such an assay, the COVID-19 detection and immune response can be more accurately assessed than the results of either test alone. This would particularly be advantageous during the early infectious period (days 0 to 7) described above. Performing both tests simultaneously on the same cassette saves both time and cost and maximizes detection accuracy.

June 18, 2020

Brian Yang
Chief Executive Officer
Biohit Healthcare (Hefei) Co. Ltd.
Suite 0617, 6th Floor, Building 1 Guoyingyuan
Xicheng District
Beijing, 100035 China

Device:	Biohit SARS-CoV-2 IgM/IgG Antibody Test Kit
Company:	Biohit Healthcare (Hefei) Co. Ltd.
Indication:	Qualitative detection and differentiation of IgM and IgG antibodies to SARS-CoV-2 in human serum, plasma (heparin, dipotassium EDTA, or sodium citrate) and venipuncture whole blood (heparin, dipotassium EDTA, or 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 requirements to perform moderate or high complexity tests.

Dear Mr. Yang:

This letter is in response to your[1] request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for emergency use of your product,[2] pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3).

On February 4, 2020, pursuant to Section 564(b)(1)(C) of the Act, the Secretary of the Department of Health and Human Services (HHS) determined that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and that involves the virus that causes COVID-19. Pursuant to Section 564 of the Act, and on the basis of such determination, the Secretary of

[1] For ease of reference, this letter will use the term "you" and related terms to refer to Biohit Healthcare (Hefei) Co. Ltd.
[2] For ease of reference, this letter will use the term "your product" to refer to the Biohit SARS-CoV-2 IgM/IgG Antibody Test Kit for the indication identified above.

HHS then declared that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of the virus that causes COVID-19 subject to the terms of any authorization issued under Section 564(a) of the Act.[3]

Having concluded that the criteria for issuance of this authorization under Section 564(c) of the Act are met, I am authorizing the emergency use of your product, described in the Scope of Authorization of this letter (Section II), subject to the terms of this authorization.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of your product meets the criteria for issuance of an authorization under Section 564(c) of the Act, because I have concluded that:

1. The SARS-CoV-2 can cause a serious or life-threatening disease or condition, including severe respiratory illness, to humans infected by this virus;

2. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that your product may be effective in diagnosing recent or prior infection with SARS-CoV-2 by identifying individuals with an adaptive immune response to the virus that causes COVID-19, and that the known and potential benefits of your product when used for such use, outweigh the known and potential risks of your product; and

3. There is no adequate, approved, and available alternative to the emergency use of your product.[4]

II. Scope of Authorization

I have concluded, pursuant to Section 564(d)(1) of the Act, that the scope of this authorization is limited to the indication above.

Authorized Product Details

Your product is a qualitative test intended for the detection and differentiation of IgM and IgG antibodies against SARS-CoV-2 in human serum, plasma (heparin, dipotassium EDTA or sodium citrate), and venipuncture whole blood specimens (heparin, dipotassium EDTA, or sodium citrate). The product is intended for use as an aid in identifying individuals with an adaptive immune response to SARS-CoV-2, indicating recent or prior infection. At this time, it is unknown for how long antibodies persist following infection and if the presence of antibodies confers protective immunity.

To use your product, the device cassette, specimen, and buffer solution are allowed to equilibrate to room temperature. Specimen (10 µL) is transferred to the sample well. After the sample well is free of liquid, 2 drops (80 µL) of Sample Diluent are then added to the sample well. Wait for

[3] U.S. Department of Health and Human Services, *Determination of a Public Health Emergency and Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3*. 85 FR 7316 (February 7, 2020).

[4] No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

15 to 20 minutes and read the test results. Results are not to be read after 20 minutes. An IgM Positive Result occurs when a colored band appears at both the M Test Line (M) and Control Line (C) and indicates that IgM against SARS-CoV-2 is present. An IgG Positive Result occurs when a colored band appears at both the G Test Line (G) and Control Line (C) and indicates that IgG against SARS-CoV-2 is present. A positive result for IgM and IgG occurs when colored bands occur at both M and G as well as at C. A Negative Result occurs when a colored band appears at C only and indicates that IgM and IgG antibodies against SARS-CoV-2 were not detected. An Invalid Result occurs when no colored band occurs at C and the test should be repeated.

Your product requires the following internal control, that is processed along with the sample on the device cassette. The internal control listed below must generate expected results in order for a test to be considered valid, as outlined in the Instructions for Use:

- Internal Control – The C line should appear on each strip for every test and checks that flow of reagents is satisfactory.

Your product also recommends use of external positive and negative controls, or other authorized controls, to be purchased separately:

- Positive Control: Anti-SARS-CoV-2 antibodies (IgG and IgM) in heat inactivated serum.
- Negative Control: Heat inactivated serum.

Your product also requires the use of additional authorized materials and authorized ancillary reagents that are not included with your product and are described in the Instruction for Use.

The above described product is authorized to be accompanied with labeling entitled "Biohit SARS-CoV-2 IgM/IgG Antibody Test Kit Instruction For Use" (available at https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations), and the following product-specific information pertaining to the emergency use, which is required to be made available to healthcare providers and recipients:

- Fact Sheet for Healthcare Providers: Biohit SARS-CoV-2 IgM/IgG Antibody Test Kit
- Fact Sheet for Recipients: Biohit SARS-CoV-2 IgM/IgG Antibody Test Kit

The above described product, when accompanied by the Instruction for Use (identified above) and the two Fact Sheets (collectively referenced as "authorized labeling") is authorized to be distributed to and used by authorized laboratories under this EUA, despite the fact that it does not meet certain requirements otherwise required by applicable federal law.

I have concluded, pursuant to Section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of your product, when used consistent with the Scope of Authorization of this letter (Section II), outweigh the known and potential risks of your product.

I have concluded, pursuant to Section 564(d)(3) of the Act, based on the totality of scientific

evidence available to FDA, that it is reasonable to believe that your product may be effective in diagnosing recent or prior infection with SARS-CoV-2 by identifying individuals with an adaptive immune response to the virus that causes COVID-19, when used consistent with the Scope of Authorization of this letter (Section II), pursuant to Section 564(c)(2)(A) of the Act.

FDA has reviewed the scientific information available to FDA, including the information supporting the conclusions described in Section I above, and concludes that your product (as described in the Scope of Authorization of this letter (Section II) meets the criteria set forth in Section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of your product under this EUA must be consistent with, and may not exceed, the terms of this letter, including the Scope of Authorization (Section II) and the Conditions of Authorization (Section IV). Subject to the terms of this EUA and under the circumstances set forth in the Secretary of HHS's determination under Section 564(b)(1)(C) described above and the Secretary of HHS's corresponding declaration under Section 564(b)(1), your product is authorized for the indication above.

III. Waiver of Certain Requirements

I am waiving the following requirements for your product during the duration of this EUA:

- Current good manufacturing practice requirements, including the quality system requirements under 21 CFR Part 820 with respect to the design, manufacture, packaging, labeling, storage, and distribution of your product, but excluding Subpart H (Acceptance Activities, 21 CFR 820.80 and 21 CFR 820.86), Subpart I (Nonconforming Product, 21 CFR 820.90), and Subpart O (Statistical Techniques, 21 CFR 820.250).

IV. Conditions of Authorization

Pursuant to Section 564(e) of the Act, I am establishing the following conditions on this authorization:

Biohit Healthcare (Hefei) Co. Ltd. (You) and Authorized Distributor(s)[5]

A. Your product must comply with the following labeling requirements under FDA regulations: the intended use statement (21 CFR 809.10(a)(2), (b)(2)); adequate directions for use (21 U.S.C. 352(f)), (21 CFR 809.10(b)(5), (7), and (8)); appropriate limitations on the use of the device including information required under 21 CFR 809.10(a)(4); and any available information regarding performance of the device, including requirements under 21 CFR 809.10(b)(12).

B. You and authorized distributor(s) will make your product available with the authorized labeling to authorized laboratories. You may request changes to the authorized labeling. Such requests will be made in consultation with, and require concurrence of,

[5] "Authorized Distributor(s)" are identified by you, Biohit Healthcare (Hefei) Co. Ltd., in your EUA submission as an entity allowed to distribute your device.

DMD/OHT7-OIR/OPEQ/CDRH.

C. You and authorized distributor(s) will make available on your website(s) the Fact Sheet for Healthcare Providers and the Fact Sheet for Recipients.

D. You and authorized distributor(s) will inform authorized laboratories and relevant public health authorities of this EUA, including the terms and conditions herein, and any updates made to your product and authorized labeling.

E. Through a process of inventory control, you and authorized distributor(s) will maintain records of the authorized laboratories to which they distribute the test and number of tests they distribute.

F. You and authorized distributor(s) will collect information on the performance of your product. You will report to FDA any suspected occurrence of false positive and false negative results and significant deviations from the established performance characteristics of the product of which you become aware.

G. You and authorized distributor(s) are authorized to make available additional information relating to the emergency use of your product that is consistent with, and does not exceed, the terms of this letter of authorization.

H. You and authorized distributor(s) will make available the internal control material or other authorized control materials at the same time as your product.

I. You and authorized distributor(s) will make available the SARS-CoV-2 IgM and IgG Positive Control(s) and Negative Control by July 3, 2020 (refer to condition Y).

Biohit Healthcare (Hefei) Co. Ltd. (You)

J. You will notify FDA of any authorized distributor(s) of your product, including the name, address, and phone number of any authorized distributor(s).

K. You will provide authorized distributor(s) with a copy of this EUA and communicate to authorized distributor(s) any subsequent amendments that might be made to this EUA and its authorized accompanying materials (e.g., Fact Sheets).

L. You may request to make available additional authorized labeling specific to an authorized distributor. Such additional labeling may use another name for the product, but otherwise must be consistent with the authorized labeling, and not exceed the terms of authorization of this letter. Such requests will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

M. You will comply with the following requirements under FDA regulations: Subpart H (Acceptance Activities, 21 CFR 820.80 and 21 CFR 820.86), Subpart I (Nonconforming Product, CFR 820.90), and Subpart O (Statistical Techniques, 21 CFR 820.250).

N. You may request changes to the Scope of Authorization (Section II in this letter) of your product. Such requests will be made in consultation with DMD/OHT7-OIR/OPEQ/CDRH, and require concurrence of, Office of Counterterrorism and Emerging Threats (OCET)/Office of the Chief Scientist (OCS)/Office of the Commissioner (OC) and DMD/OHT7-OIR/OPEQ/CDRH.

O. You may request the addition of other ancillary methods for use with your product. Such requests will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

P. You may request the addition of other specimen types for use with your product. Such requests will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

Q. You may request the addition and/or substitution of control materials for use with your product. Such requests will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

R. You may request substitution for or changes to the authorized materials used in the detection process of human antibodies against SARS-CoV-2. Such requests will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

S. You will evaluate the performance and assess traceability[6] of your product with any FDA-recommended reference material(s) or established panel(s) of characterized clinical specimens. After submission to FDA and DMD/OHT7-OIR/OPEQ/CDRH's review of and concurrence with the data, you will update your labeling to reflect the additional testing. Such labeling updates will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

T. You will track adverse events, including any occurrence of false results and report to FDA under 21 CFR Part 803.

U. You must have lot release procedures and the lot release procedures, including the study design and statistical power, must assure that the tests released for distribution have the clinical and analytical performance claimed in the authorized labeling.

V. If requested by FDA, you must submit lot release procedures to FDA within 48 hours of such request, including sampling protocols, testing protocols, and acceptance criteria, that you use to release lots of your product for distribution in the US.

W. If requested by FDA, you will periodically submit new lots for testing at NCI, or by another government agency designated by FDA, to confirm continued performance characteristics across lots. In addition, FDA may request records regarding lot release

[6] Traceability refers to tracing analytical sensitivity/reactivity back to an FDA-recommended reference material.

data for tests to be distributed or already distributed. If such lot release data are requested by FDA, you must provide it within 48 hours of the request.

X. You will complete the agreed upon real-time stability study for your product. After submission to FDA and DMD/OHT7-OIR/OPEQ/CDRH's review of and concurrence with the data, you will update your product labeling to reflect the additional testing. Such labeling updates will be made in consultation with, and require concurrence of, DMD/OHT7- OIR/OPEQ/CDRH.

Y. You recommend use of external positive and negative controls, to be run as outlined in the Instruction for Use. You will develop SARS-CoV-2 IgM and IgG Positive Control(s) and a Negative Control and submit data demonstrating reactivity levels sufficient to serve as proper control for the performance of your product. After submission to FDA and DMD/OHT7-OIR/OPEQ/CDRH's review of and concurrence, you will update your labeling to include the external controls by July 3, 2020.

Authorized Laboratories

Z. Authorized laboratories using your product will include with test result reports, all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.

AA. Authorized laboratories will use your product as outlined in the authorized labeling. Deviations from the authorized procedures, including the authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and authorized materials required to use your product are not permitted.

BB. Authorized laboratories that receive your product will notify the relevant public health authorities of their intent to run your product prior to initiating testing.

CC. Authorized laboratories using your product will have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.

DD. Authorized laboratories will collect information on the performance of your product and report to DMD/OHT7-OIR/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov) and you (public@chinabiohit.com or 86-551-65652770) any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of your product of which they become aware.

EE. All laboratory personnel using your product must be appropriately trained in immunochromatographic techniques and use appropriate laboratory and personal protective equipment when handling this kit, and use your product in accordance with the authorized labeling. All laboratory personnel using the assay must also be trained in and be familiar with the interpretation of results of the product.

Biohit Healthcare (Hefei) Co. Ltd. (You), Authorized Distributors and Authorized Laboratories

FF. You, authorized distributors, and authorized laboratories using your product will ensure that any records associated with this EUA are maintained until otherwise notified by FDA. Such records will be made available to FDA for inspection upon request.

Conditions Related to Advertising and Promotion

GG. All descriptive printed matter, including advertising and promotional materials, relating to the use of your product, shall be consistent with the authorized labeling, as well as the terms set forth in this EUA and the applicable requirements set forth in the Act and FDA regulations.

HH. No descriptive printed matter, including advertising or promotional materials, relating to the use of your product, may represent or suggest that this test is safe or effective for the detection of SARS-CoV-2.

II. All descriptive printed matter, including advertising and promotional materials, relating to the use of your product, shall clearly and conspicuously state that:

- This test has not been FDA cleared or approved;
- This test has been authorized by FDA under an EUA for use by authorized laboratories;
- This test has been authorized only for the presence of IgM and IgG antibodies against SARS-CoV-2, not for any other viruses or pathogens; and
- This test is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnosticsfor 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.

The emergency use of your product as described in this letter of authorization must comply with the conditions and all other terms of this authorization.

V. Duration of Authorization

This EUA will be effective until the declaration that circumstances exist justifying the authorization of the emergency use of in vitro diagnosticss for detection and/or diagnosis of COVID-19 is terminated under Section 564(b)(2) of the Act or the EUA is revoked under Section 564(g) of the Act.

Sincerely,

Denise M. Hinton -S3

Digitally signed by Denise M. Hinton -S3
Date: 2020.06.18 20:56:13 -04'00'

RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

Enclosures