Jiangsu Well Biotech Co., Ltd.
Orawell IgM/IgG Rapid Test

For in-vitro diagnostic use only.
For prescription use only.
For Emergency Use Authorization only.

Intended Use

The Orawell IgM/IgG Rapid Test is a lateral flow immunoassay intended for qualitative detection and differentiation of IgM and IgG antibodies to SARS-CoV-2 in human serum and acid citrate dextrose (ACD) plasma. The Orawell IgM/IgG Rapid Test 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. The Orawell IgM/IgG Rapid Test should not be used to diagnose acute SARS-CoV-2 infection. Testing is limited to 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 testing.

Results are for the detection and differentiation of SARS CoV-2 antibodies. IgM and IgG antibodies to SARS-CoV-2 are generally detectable in blood several days after initial infection, although the duration of time antibodies are present post-infection is not well characterized. Individuals may have detectable virus present for several weeks following seroconversion.

Laboratories within the United States and its territories are required to report all results to the appropriate public health authorities.

The sensitivity of Orawell IgM/IgG Rapid Test early after infection is unknown. Negative results do not preclude acute SARS-CoV-2 infection. If acute infection is suspected, direct testing for SARS-CoV-2 is necessary.

False positive results for Orawell IgM/IgG Rapid Test may occur due to cross-reactivity from pre-existing antibodies or other possible causes. Due to the risk of false positive results, confirmation of positive results should be considered using second, different IgM and IgG assay.

The Orawell IgM/IgG Rapid Test is only for use under the Food and Drug Administration's Emergency Use Authorization.

Orawell IgM/IgG Rapid Test Principle

The test kit is based on immunoassay technology. The test devices contain: 1) Conjugate pad: recombinant SARS-CoV-2 antigen (Receptor binding domain (RBD) of 2019nCoV Spike Protein) labeled with colloidal gold and quality control antibody gold marker. 2) NC membrane: coated with two detection lines (IgG line and IgM line) and one quality control line (C line). The IgM line coated with mouse anti-human IgM monoclonal antibody detects the COVID-19 IgM antibody. The IgG line coated with mouse anti-human IgG monoclonal antibody detects the COVID-19 IgG antibody. The C line is coated with quality control antibody.

When sample is added to the sample well of the test device, it will move forward along the test device. If the sample contains IgM antibodies, antibodies will bind to the virus antigen labeled with colloidal gold, then form a sandwich complex with the coated anti-human IgM monoclonal antibody at IgM line, the IgM line will appear purplish red, indicating that the sample is positive for the COVID-19 IgM antibody.

If the sample contains IgG antibodies, antibodies will bind to the virus antigen labeled with colloidal gold, then form a sandwich complex with the coated anti-human IgG monoclonal antibody at IgG line, the IgG line will appear purplish red, indicating that the sample is positive for the COVID-19 IgG antibody.

If neither the IgG line nor the IgM line appears, the result is negative. The test device also contains a quality control line; whether the test is positive or negative for IgG and/or IgM, the quality control line C should appear as purplish red. The test result is invalid if the there is no quality control line C. The sample should be retested.

Composition

Each test kit contains the test device, buffer, pipette, and package insert.

Materials required but not provided: timer and external quality controls (Orawell IgM/IgG Controls, Cat# CC-001), available upon request.

Kit Storage and Handling

- Store the test kit in a cool, dry place between 2-30℃ for up to 16 months. Keep away from light. Exposure to temperature and / or humidity outside the specified conditions may result in inaccurate results.
- Do not freeze.
- Use the test kits at temperatures between 18-25℃.
- Use the test kits between 10-90% humidity.
- Do not use test kits beyond the expiry date (printed on the foil pouch and box label).

All expiry dates are printed in Year-Month format. 2021-06 indicates June, 2021.

Test Procedure

Specimen collection:

1. Serum: Collect the blood specimen obtained by venipuncture into a tube without anticoagulant and allow sample to clot for about 30 minutes. Separate serum from the supernatant by centrifugation.

2. Plasma: Collect the blood specimen obtained by venipuncture into a tube/container containing anticoagulant (ACD), and separate plasma from the supernatant by centrifugation.

Specimen storage and handling:

If specimens are not tested immediately, store at 2-8°C for up to 5 days. Serum and plasma, specimens may be frozen at -70°C for longer storage. Avoid multiple freeze thaws for frozen specimens.

Test steps:

1. Take out the test kit and leave it at room temperature for a minimum of 30 minutes.
2. Place the test device on a dust-free clean surface.
3. Apply 10μL serum or ACD plasma onto the sample well of a test device.
   Note: The pipette provided with the kit has a small capillary at the bottom. When the capillary is filled, a 10μL sample is collected.
4. Apply 2 drops (about 60-80 μL) of buffer onto the sample well of a Test Device.
5. Read the result after 10 minutes. Do not read after 15 minutes.

Note: *Avoid contact with eyes and skin. Flush abundantly with water if reagents are spilled.*

Handle all specimens as potentially infectious. The used device and pipette dropper should be discarded according federal, state and local regulation.

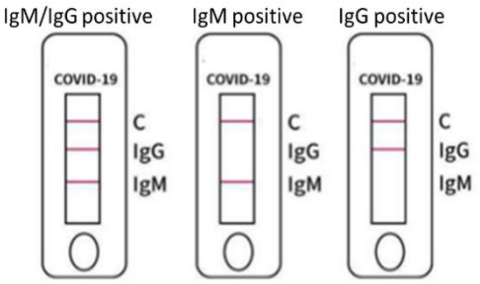
Warnings and Precautions

1. Test cassettes are single use only. Do not reuse.
2. For use under Emergency Use Authorization only. For IN VITRO Diagnostic use only.
3. This test has not been FDA cleared or approved; the test has been authorized by FDA under an Emergency Use Authorization (EUA) for use by 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.
4. This test has been authorized only for the presence of IgM and IgG antibodies against SARS-CoV2, not for any other viruses or pathogens.
5. This test is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostic tests for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 360bbb3(b)(1), unless the authorization is terminated or revoked sooner.
6. The test result cannot be used for diagnosis of COVID-19. Assay results should be utilized in conjunction with other clinical and laboratory methods to assist the clinician in making individual patient decisions.
7. Do not use highly hemolytic samples.
8. The test kit can only be used with serum or ACD plasma.
9. Read the result at 10 minutes. Do not interpret the result after 15 minutes.
10. Follow the package insert when testing.

Interpretation of the test results

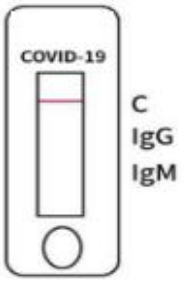
1. Positive result:

1. The anti-SARS-CoV-2 IgM antibody is detected if the control line (C) and the IgM detection line (M) are both colored, and the IgG detection (G) line is not colored.
2. The anti-SARS-CoV-2 IgG antibody is detected if the control line (C) and the IgG detection (G) line are both colored, and the IgM detection line (M)is not colored.
3. The anti-SARS-CoV-2 IgG and IgM antibodies are both detected if the control line (C), the IgM (M) and IgG (G) detection lines are all colored.



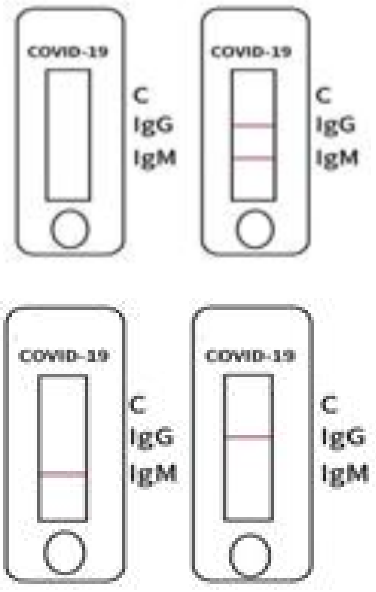
2. Negative result:

The test result is negative if only the quality control line C is colored, and IgG and IgM detection lines are not colored.



3. Invalid result:

If the quality control line C is not colored, no matter whether the detection line IgM/IgG is colored or not, the result is invalid. The sample should be tested again with a new cassette.



Quality Control

Internal control: The Orawell IgM/IgG Rapid Test includes a built-in control band at the control region (C) to indicate that proper flow of reagents has occurred. This control band should always appear

regardless of the presence of anti-SARS-CoV-2 antibodies. If the control bands do not appear, the test is invalid, and the test device should be discarded.

External control: It is recommended that negative and positive controls be used to test each new lot of product to ensure proper kit performance. The Jiangsu Well Biotech Controls, Orawell IgM/IgG Controls, available upon request under catalogue number CC-001, may be used as external quality control material. The Jiangsu Well Biotech Controls include 1 negative and 2 positive controls. The test procedure provided above and in the control package insert should be followed. Each laboratory should establish and run its own QC program. When external controls do not produce the expected results, repeat with a new unopened bottle of controls.

Quality control testing at regular intervals is good laboratory practice and laboratories should comply with all federal, state, and local laws, guidelines and regulations. Always check with the appropriate licensing or accrediting bodies to ensure that the quality program employed meets the established standards.

Limitations

For use under an Emergency Use Authorization Only

1. This test is only to be used in CLIA certified laboratories that meet requirements to perform moderate or high complexity tests and not in point-of-care or at-home testing settings.
2. The test is for qualitative detection of anti-SARS-CoV-2 IgM and IgG antibody in human serum or ACD plasma and does not indicate the quantity of the antibodies. The intensity of the test line does not correlate to SARS-CoV-2 antibody titer in the specimen.
3. Performance has only been established with the specimen types listed in the Intended Use. Other specimen types have not been evaluated and should not be used with this assay. This test should not be used to test fingerstick whole blood.
4. The test results should be interpreted between 10 and 15 minutes after addition of buffer. The test results should not be interpreted after 15 minutes.
5. The test is for in vitro diagnostic use only.
6. Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions. The sensitivity of the Orawell IgM/IgG Rapid Test after infection is unknown. False positive results for IgM and IgG antibodies may occur due to cross-reactivity from pre-existing antibodies or other possible causes.
7. A negative result can occur if the quantity of antibodies for the SARS-CoV-2 virus present in the specimen is below the detection limit of the assay, or if the virus has undergone minor amino acid mutation(s) in the epitope recognized by the antibody used in the test.
8. SARS-CoV-2 IgM and IgG antibodies may be below detectable levels in patients who have been exhibiting symptoms for less than 8 days.
9. Testing with a molecular diagnostic should be performed to evaluate symptomatic patients for acute SARS-CoV-2 infection, particularly in those who have been in contact with the virus.
10. Results from antibody testing should not be used to diagnose or exclude acute SARS-CoV-2 infection or to inform infection status.
11. A positive result may not indicate previous SARS-CoV-2 infection. Consider other information, including clinical history and local disease prevalence, in assessing the need for a second but different serology test to confirm an immune response. Positive results may be due to past or present infection with non-SARS-CoV-2 coronavirus strains, such as coronavirus HKU1, NL63, OC43, or 229E.
12. It is not known at this time if the presence of antibodies to SARS-CoV-2 confers immunity to reinfection.
13. Not for the screening of donated blood.
14. The presence of rheumatoid factor in samples may interfere with the IgM results of the test. If interference is suspected, samples should be retested with another, alternative antibody test.
15. The performance of this device has not been established in individuals that have received a COVID-19 vaccine. The clinical significance of a positive or negative antibody result following COVID-19 vaccination has not been established, and the result from this assay should not be interpreted as an indication or degree of protection from infection after vaccination.
16. The performance of this test was established based on the evaluation of a limited number of clinical specimens. Clinical performance has not been established with all circulating variants but is anticipated to be reflective of the prevalent variants in circulation at the time and location of the clinical evaluation. Performance at the time of testing may vary depending on the variants circulating, including newly emerging strains of SARS-CoV-2 and their prevalence, which change over time.

Conditions of Authorization for Laboratories

The Orawell IgM/IgG Rapid Test Letter of Authorization, along with the authorized Fact Sheet for Healthcare Providers, the authorized Fact Sheet for Recipients, and authorized labeling are available on the FDA website:

https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas

Authorized laboratories using the Orawell IgM/IgG Rapid Test Letter of Authorization ("your product" in the conditions below), must adhere to the Conditions of Authorization indicated in the Letter of Authorization as listed below:

1. 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.
2. Authorized laboratories will use your product as outlined in the Instructions for Use. 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.
3. Authorized laboratories that receive your product will notify the relevant public health authorities of their intent to run your product prior to initiating testing.
4. 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.
5. 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 Jiangsu Well Biotech Co. Ltd. (xiulan.zhang@wellbioscience.com) 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.
6. All laboratory personnel using your product must be appropriately trained in immunoassay techniques and use appropriate laboratory and personal protective equipment when handling this kit and use this 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.
7. Jiangsu Well Biotech Co., Ltd. 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.

*The letter of authorization refers to, "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" as "authorized laboratories."

Performance Characteristics

A) Cross-Reactivity

The Orawell IgM/IgG Rapid Test was evaluated with a total of 20 other viruses, bacteria or autoantibodies (215 samples total). The results show that the Orawell IgM/IgG Rapid Test has no cross-reactivity with samples containing antibodies to other viruses or microorganisms.

Table 1: Cross Reactivity Test Results

		Result	
No	**Virus Antibody positive**	**IgM**	**IgG**
1	anti-Influenza A IgG	5/5-/-	5/5-/-
2	anti- Influenza A IgM	5/5-/-	5/5-/-
3	anti- Influenza B IgG	5/5-/-	5/5-/-
4	anti- Influenza B IgM	5/5-/-	5/5-/-
5	anti-respiratory syncytial virus IgM	5/5-/-	5/5-/-
6	anti-respiratory syncytial virus IgG	5/5-/-	5/5-/-
7	anti-Haemophilus influenza IgM	5/5-/-	5/5-/-
8	anti-Haemophilus influenza IgG	5/5-/-	5/5-/-
9	anti-Hepatitis C Virus IgG	5/5-/-	5/5-/-
10	anti-Hepatitis C Virus IgM	5/5-/-	5/5-/-
11	anti-Hepatitis B Virus IgG	5/5-/-	5/5-/-
12	anti-Hepatitis B Virus IgM	5/5-/-	5/5-/-
13	anti-*Chlamydia pneumonia* IgM	5/5-/-	5/5-/-
14	anti-*Chlamydia pneumonia* IgG	5/5-/-	5/5-/-
15	anti-*Legionella pneumophila* IgM	5/5-/-	5/5-/-
16	anti-Legionella pneumophila IgG	5/5-/-	5/5-/-
17	anti-*Mycoplasma pneumonia* IgM	5/5-/-	5/5-/-
18	anti-*Mycoplasma pneumonia* IgM	5/5-/-	5/5-/-
19	anti-TP IgG	5/5-/-	5/5-/-
20	RF 118	-	-
21	RF 222	-	+
22	RF 800	-	-
23	RF4 68.7	-	-
24	RF 21,1	-	-
25	Rf 262	-	-
26	RF 23.6	-	-
27	RF 98.7	-	-
28	RF 182	-	-
29	RF 338	-	-
30	RF 180	-	-
31	RF 559	-	-
32	RF173	-	-
33	RF 93.7	-	-
34	RF389	-	-
35	RF37.2	-	-
36	RF 1040	-	+
37	RF 1810	-	+
38	RF77	-	-
39	RF51.7	-	-
40	N1-N100	100-/-	100-/-

B) Clinical Agreement Study

1) Jiangsu Well Biotech Clinical Agreement Study

Results obtained using the Orawell IgM/IgG Rapid Test Device were compared to results obtained from patients confirmed positive or negative for SARS-CoV-2 by a PCR assay. Serum specimens from 60 negative subjects and 70 positive patients were evaluated. The results show that overall sensitivity (PPA) is 97.14%, and the overall specificity is 100%.

Table 2. Clinical performance analysis

		Reference method (RT-PCR)		
		Positive	Negative	Total
Test device	Positive	68	0	68
	Negative	2	60	62
	Total	70	60	130

i. Sensitivity (PPA) = 97.14% (68/70) (95% CI: 90.17%~99.21%)

ii. Specificity (NPA) = 100% (60/60) (95% CI: 93.98%~100.00%)

Table 3. Clinical performance analysis per IgM and IgG separately

IgM Test Result				
		Reference method (RT-PCR)		
		Positive	Negative	Total
Test device	Positive	67	0	67
	Negative	3	60	63
	Total	70	60	130
IgG Test Result				
		Reference method (RT-PCR)		
		Positive	Negative	Total
Test device	Positive	68	0	68
	Negative	2	60	62
	Total	70	60	130

i. IgM Sensitivity (PPA) = 95.71% (67/70) (95% CI : 88.14%~98.53%)

ii. IgG Sensitivity (PPA) = 97.14% (68/70) (95% CI: 90.17%~99.21%)

Table 4. Clinical performance analysis per days of symptom onset for IgM and IgG separately

IgM		
Days after symptom onset	**PPA**	**95% CI**
≤7	0 %	N/A
8~14	96.4 %	87.88% - 99.02%
≥15	100 %	77.19% - 100.00%
IgG		
Days after symptom onset	**PPA**	**95% CI**
≤7	0 %	N/A
8~14	98.2 %	90.56% - 99.68%
≥15	100 %	77.19% - 100.00%
IgM/IgG		
Days after symptom onset	**PPA**	**95% CI**
≤7	0 %	N/A
8~14	98.2 %	90.56% - 99.68%
≥15	100 %	77.19% - 100.00%

2) Independent Clinical Agreement Validation Study

The Orawell IgM/IgG Rapid Test was tested on June 23, 2020 and on September 4, 2020 at the Frederick National Laboratory for Cancer Research (FNLCR) sponsored by the National Cancer Institute (NCI). The test was validated against 2 panels of previously frozen samples consisting of a total of 58 independent SARS-CoV-2 antibody-positive serum samples and 97 independent antibody-negative serum and anticoagulant citrate dextrose (ACD) plasma samples. Each of the antibody-positive samples were confirmed with a nucleic acid amplification test (NAAT) and both IgM and IgG antibodies were confirmed to be present in all samples. The presence of antibodies in the samples was confirmed by several orthogonal methods prior to testing with the Orawell IgM/IgG Rapid Test. The presence of IgM and IgG antibodies specifically was confirmed by one or more comparator methods. Antibody-positive samples were selected at different antibody titers.

All antibody-negative samples were collected prior to 2020 and include i) eighty-seven (87) samples selected without regard to clinical status, "Negatives" and ii) ten (10) samples selected from banked plasma from HIV+ patients, "HIV+". Testing was performed using 1 lot of the Orawell IgM/IgG Rapid Test. Confidence intervals for sensitivity and specificity were calculated per a score method described in CLSI EP12-A2 (2008).

For the evaluation of cross-reactivity with HIV+, it was determined whether an increased false positive rate among antibody-negative samples with HIV was statistically higher than the false positive rate among antibody-negative samples without HIV (for this, a confidence interval for the difference in false positive rates was calculated per a score method described by Altman). The results and data analysis are shown the tables below.

Table 5. Summary results

	Comparator Method			**Collected pre-2020**		
	Antibody Positive			Antibody Negative		
Test Device	IgM+, IgG+	IgM, IgG-	IgM-, IgG+	Neg.	HIV+	Total
IgM+, IgG+	54					54
IgM+, IgG-				3	1	4
IgM-, IgG+	4			1		5
IgM-, IgG-				83	9	92
Total	58			87	10	155

Table 6. Summary statistics

Measure	**Estimate**	**Confidence Interval**
IgM Sensitivity	93.1% (54/58)	(83.6%; 97.3%)
IgM Specificity	95.9% (93/97)	(89.9%; 98.4%)
IgG Sensitivity	100% (58/58)	(93.8%; 100%)
IgG Specificity	99.0% (96/97)	(94.4%; 99.8%)
Combined Sensitivity	100% (58/58)	(93.8%; 100%)
Combined Specificity	94.8% (92/97)	(88.5%; 97.8%)
Combined PPV for prevalence = 5.0%	50.5%	(30.0%; 70.3%)
Combined NPV for prevalence = 5.0%	100%	(99.6%; 100%)
Cross-reactivity with HIV+	10.0% (1/10), may be present	

Important Limitations:

1. Sensitivity and specificity estimates in this report may not be indicative of the real world performance of the device.
2. These results are based on serum and plasma samples only and may not be indicative of performance with other sample types, such as whole blood, including finger stick blood.

3. The number of samples in the panel is a minimally viable sample size that still provides reasonable estimates and confidence intervals for test performance, and the samples used may not be representative of the antibody profile observed in patient populations.

C) Class Specificity

Orawell IgM/IgG Rapid Test showed 100% agreement with expected result before and after dithiothrietol treatment (DTT) to establish antibody class specificity.

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Symbols:

Symbol	Meaning
	Consult instruction for use
	In-Vitro Diagnostic Medical Device
	Manufacturer
	Batch code
	Caution, consult accompanying documents
	Keep away from sunlight
	Keep away from moisture
	Do not reuse
	Temperature Limitation
	Use by date
	Sufficient for Use
	European Authorized Representative
	Meet the requirements of EC Directive 98/79/EC

Revision date: March 01, 2022