

MEGNA HEALTH RAPID COVID-19 IgM/IgG COMBO TEST KIT

FOR THE QUALITATIVE ASSESSMENT OF IgG AND IgM ANTIBODIES TO COVID-19 VIRUS IN HUMAN SERUM AND ACID CITRATE DEXTROSE (ACD) PLASMA

For Emergency Use Authorization Only

For Prescription Use only.

For In Vitro Diagnostic Use Only

INTENDED USE

The Rapid COVID-19 IgM/IgG Combo Test Kit is a lateral flow immunoassay intended for qualitative detection and differentiation of Immunoglobulin M (IgM) and Immunoglobulin G (IgG) antibodies to SARS-CoV-2 in human serum and acid citrate dextrose (ACD) plasma. The Rapid COVID-19 IgM/IgG Combo Test Kit 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 Rapid COVID-19 IgM/IgG Combo Test Kit 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 tests.

Results are for the detection 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 positive results to the appropriate public health authorities.

The sensitivity of the Rapid COVID-19 IgM/IgG Combo Test Kit after early 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 Rapid COVID-19 IgM/IgG Combo Test Kit 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 IgG or IgM assay.

The Rapid COVID-19 IgM/IgG Combo Test Kit is only for use under the Food and Drug Administration's Emergency Use Authorization.

SUMMARY

Corona Virus Disease 2019 (COVID-19) is an acute infectious disease caused by COVID-19 Virus. The incubation period of the disease ranges from 1-14 days, during which time infected individuals may infect other people. Asymptomatic infections may also be the source of infection. Respiratory droplets and contact are the main routes of transmission. The initial symptoms of the patients include fever, fatigue and coughing, which gradually develops into dyspnea and other serious manifestations. Some of the severe cases may have acute respiratory distress syndrome or septic shock, or even death. At present, there is no specific treatment for the disease.

There are several days of incubation period after infection with COVID-19 Virus. IgM antibodies can be detected soon after the incubation period and remain for a short time. IgG antibodies appear after a few days of incubation period and remain in circulation in the blood for a number of weeks. IgG positive in blood samples can be an indicator of recent or previous infection.

PRINCIPLE

Rapid COVID-19 IgM/IgG Combo Test Kit utilizes the principle of immuno-chromatography. Mouse anti-human IgM and human IgG antibodies are immobilized on the nitrocellulose membrane respectively, as two individual test lines (IgM line and IgG line) in the test window of the test device. The IgM line in the test window is closer to the sample well followed by IgG line. As the test sample flows through the membrane

within the test device, the colored COVID-19 virus recombinant antigen-colloidal gold conjugate forms complexes with specific antibodies (IgM and/or IgG) to COVID-19 virus, if present in the sample. The antigen targets a segment of the SARS-CoV-2 nucleocapsid (N) protein. This complex moves further on the membrane to the test region where it is captured by the anti-human IgM and/or human IgG antibodies coated on the membrane leading to formation of a colored band, which indicates positive test results. Absence of this colored band in the test window indicates a negative test result. A built-in control line will always appear in the test window when the test is performed properly, regardless of the presence or absence of anti-2019 novel coronavirus antibodies in the specimen.

MATERIALS PROVIDED

1. Rapid COVID-19 IgM/IgG Combo Test Kit
2. Sample buffer
3. 2 µL capillary pipet
4. Instructions for Use

MATERIALS REQUIRED BUT NOT SUPPLIED

Clock or timer, specimen collection container, centrifuge, biohazard waste container. disposable gloves, disinfectant.

STORAGE

1. Store the test device at 4 to 30°C in the original sealed pouch. Do Not Freeze.
2. The expiration date indicated on the pouch was established under these storage conditions.
3. The test device should remain in its original sealed pouch until ready for use. After opening, the test device should be used immediately. Do not reuse the device.

WARNINGS AND PRECAUTIONS

1. For use under an Emergency Use Authorization Only. For *in vitro* diagnostic use only.
2. This test has not been FDA cleared or approved; this test has been authorized by FDA under an EUA for use by laboratories certified under CLIA, that meet requirements to perform moderate or high complexity tests.
3. 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.
4. 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. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.
5. Do not use the product beyond the expiration date.
6. Do not use the product if the pouch is damaged or the seal is broken.
7. Handle all specimens as potentially infectious.
8. Follow standard Lab procedure and biosafety guidelines for handling and disposal of potentially infectious material. When the assay procedure is completed, dispose specimens after autoclaving at 121° C for at least 20 min or treating with 0.5% Sodium Hypochlorite for 1-2 hours.
9. Tests are for single use only.

SPECIMEN COLLECTION AND PREPARATION

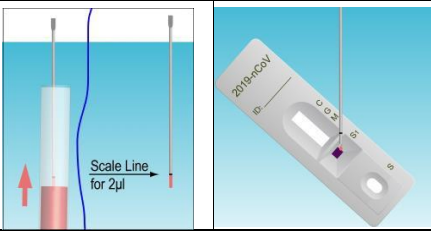
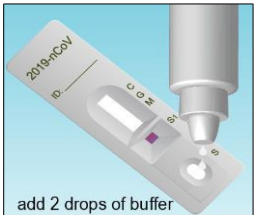
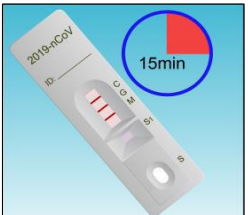
1. The serum or ACD plasma specimen should be collected under standard laboratory conditions.
2. Heat inactivation of specimens, which may cause hemolysis and protein denaturation, should be avoided.
3. The test works best on fresh samples. If testing cannot be performed immediately, serum and ACD plasma may be stored at 2-8°C up to 3 days in case of delay in testing. For long-term storage, serum and ACD plasma specimens can be frozen at -20°C for 3 months or -70°C for longer period. Avoid repeated freezing/thawing cycles.

QUALITY CONTROL

1. A procedure quality control is included in the test. It will appear as a red line in the control mark area if the test has been performed correctly and the reagents are reactive.
2. External control standards are not included with the kit. However, external control standards are commercially available by contacting the manufacturer directly.
 - a. The controls are comprised of inactivated negative serum and inactivated positive IgG and IgM serum. The controls are inactivated to minimize risks not only to COVID-19, but also to HIV, HBV and HCV.




- b. Controls are available through Megna Health under catalog number: RAK-CON-001
3. Good Laboratory Practice, recommends that external positive and negative controls be tested per new lot of test kits to validate the reliability of the test kits.


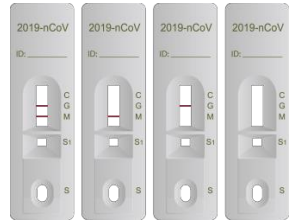
PROCEDURE

| | |
|---|---|
| 1 | Bring the kit components to room temperature before testing. |
| 2 | Open the pouch and remove the Card. Once opened, the test card must be used immediately. |
| 3 | Label the test card with patient identity. |
| 4 | |
|  | Withdraw the serum or ACD plasma specimen with the capillary pipet provided, gently squeeze out the extra specimen to leave 2 µL in the pipet as marked with the scale line. Apply 2 µL of blood specimen to the "S1" area as marked. |
| 5 | 6 |
|  |  |
| add 2 drops of sample buffer (approximately 80-100 µL) to well marked as "S". | Read the result at 15 minutes. Note: Results after 20 minutes may not be accurate. |

INTERPRETATION OF RESULTS

POSITIVE

| | | |
|--|--|--|
|  |  |  |
| Both IgG/IgM Positive | IgM Positive IgG Negative | IgM Negative IgG Positive |
| Control line and both test lines appear. It indicates the presence of both IgM and IgG antibodies to SARS-CoV-2. | Both control line and the second test line (the lower test line which is closer to the sample well) appear. It indicates the presence of IgM antibodies to SARS-CoV-2. | Both control line and the second test line (the higher test line) appear. It indicates the presence of IgG antibodies to SARS-CoV-2. |

| | |
|---|--|
| NEGATIVE | |
|  | Only control line appears. |
| INVALID | |
|  | The test result is invalid if a colored band does not form in the control region. The sample must be re-tested, using a new test device. |

CONDITIONS OF AUTHORIZATION FOR LABORATORIES

The Rapid COVID-19 IgM/IgG Combo Test Kit 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/vitro-diagnostics-euas>

Authorized laboratories using the Rapid COVID-19 IgM/IgG Combo Test Kit ("your product" in the conditions below), must adhere to the Conditions of Authorization indicated in the Letter of Authorization as listed below:

- 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.
- Authorized laboratories using your product 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.
- Authorized laboratories that receive your product will notify the relevant public health authorities of their intent to run your product prior to initiating testing.
- 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.
- 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 Megna Health Inc. (email: info@megnahealth.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.
- 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 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.
- Megna Health Inc., 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:

1. Clinical Performance:

A. Megna Health Inc. Clinical Agreement Study

Serum samples from a total of 126 positive patients, confirmed using an acceptable comparator RT-PCR method, and 285 negative patients were tested. The results showed overall positive percent agreement (PPA)/sensitivity of 90.48% and overall negative percent agreement (NPA)/specificity of 98.95%.

Total Clinical Performance Analysis for IgM

| | | Reference method | | |
|---------------------------|----------|------------------|----------|-------|
| | | Positive | Negative | Total |
| Test device IgM result | Positive | 93 | 1 | 94 |
| | Negative | 33 | 284 | 317 |
| | Total | 126 | 285 | 411 |

- 1) Sensitivity (Positive percent agreement): 73.81% (95% CI: 65.51% - 80.70%)
- 2) Specificity (Negative percent agreement): 99.7% (95% CI: 98.04% - 99.94%)

Total Clinical Performance Analysis for IgG

| | | Reference method | | |
|---------------------------|----------|------------------|----------|-------|
| | | Positive | Negative | Total |
| Test device IgM result | Positive | 93 | 2 | 95 |
| | Negative | 33 | 283 | 316 |
| | Total | 126 | 285 | 411 |

- 1) Sensitivity (Positive percent agreement): 73.81% (95% CI: 65.51% - 80.70%)
- 2) Specificity (Negative percent agreement): 99.3% (95% CI: 97.48% - 99.81%)

When estimating the sensitivity of IgM and IgG over time from symptom onset for all positive samples, the percent of IgM positive patients and IgG positive patients reached a peak of 90.9% when the test was performed >15 days after symptom onset. The overall PPA for IgM/IgG reached a peak of 100% when the test was performed >15 days after symptom onset.

Sensitivity Estimates for IgM Over Time

| Days after symptom onset (days) | IgM Positive |
|---------------------------------|--|
| ≤7 | 66.7% (46/69) (95% CI: 54.93%~76.65%) |
| 8~14 | 77.1% (27/35) (95% CI: 60.98%~87.94%) |
| ≥15 | 90.9% (20/22) (95% CI: 72.19%~97.47%) |

Sensitivity Estimates for IgG Over Time

| Days after symptom onset (days) | IgG Positive |
|---------------------------------|--|
| ≤7 | 62.3% (43/69) (95% CI: 50.52%~72.82%) |
| 8~14 | 85.7% (30/35) (95% CI: 70.63%~93.74%) |
| ≥15 | 90.9% (20/22) (95% CI: 72.19%~97.47%) |

Sensitivity Estimates for IgM/IgG Combined Over Time

| Days after symptom onset (days) | IgM/IgG Positive |
|---------------------------------|--|
| ≤7 | 84.1 (58/69) (95% CI: 73.67%~90.86%) |
| 8~14 | 97.1% (34/35) (95% CI: 85.47%~99.50%) |
| ≥15 | 100% (22/22) (95% CI: 5.14%~100.00%) |

B. Independent Clinical Agreement Validation Study

The Rapid COVID-19 IgM/IgG Combo Test Kit was tested on June 24, 2020 at the Frederick National Laboratory for Cancer Research (FNLRC) sponsored by the National Cancer Institute (NCI). The test was validated against a panel of previously frozen samples consisting of 30 SARS-CoV-2 antibody-positive serum samples and 80 antibody-negative serum and ACD plasma samples. Each of the 30 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 30 samples. The presence of antibodies in the samples was confirmed by several orthogonal methods prior to testing with the Rapid COVID-19 IgM/IgG Combo Test Kit. 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) seventy (70) samples selected without regard to clinical status. "Negatives" and ii) ten (10) samples selected from banked serum from HIV+ patients, "HIV+". Testing was performed by one operator using 1 lot of Rapid COVID-19 IgM/IgG Combo Test Kit. 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 in Tables 13 and 14 below.

Summary Results

| | Comparator Method | | | Collected pre-2020 | | Total |
|--|-------------------|------------|------------|--------------------|------|-------|
| | Antibody Positive | | | Antibody Negative | | |
| Megna Health Rapid COVID-19 IgM/IgG Combo Test Kit | IgM+, IgG+ | IgM+, IgG- | IgM-, IgG+ | Negative | HIV+ | |
| IgM+, IgG+ | 25 | | | | | 25 |
| IgM+, IgG- | | | | 2 | 0 | 2 |
| IgM-, IgG+ | 5 | | | 2 | | 7 |
| IgM-, IgG- | | | | 66 | 10 | 76 |
| Total | 30 | | | 70 | 10 | 110 |

Summary Statistics

| Measure | Estimate | Confidence Interval |
|------------------------------------|---------------------------|---------------------|
| IgM Sensitivity | 83.3% (25/30) | (66.4%; 92.7%) |
| IgM Specificity | 97.5% (78/80) | (91.3%; 99.3%) |
| IgG Sensitivity | 100% (30/30) | (88.7%; 100%) |
| IgG Specificity | 97.5% (78/80) | (91.3%; 99.3%) |
| Combined Sensitivity | 100% (30/30) | (88.7%; 100%) |
| Combined Specificity | 95.0% (76/80) | (87.8%; 98%) |
| Combined PPV for prevalence = 5.0% | 51.3% | (27.7%; 72.9%) |
| Combined NPV for prevalence = 5.0% | 100% | (99.3%; 100%) |
| Cross-reactivity with HIV+ | 0.0% (0/10), not detected | |

2. Cross-Reactivity

A. Other Infectious Diseases

Rapid COVID-19 IgM/IgG Combo Test Kit has tested samples that were infected by the following diseases: Influenza A Virus, Influenza B Virus, Adenovirus, Rotavirus and Mycoplasma Pneumoniae. All the samples showed no effect on the specificity of the assay.

B. Endogenous Substances

Rapid COVID-19 IgM/IgG Combo Test Kit has tested samples with high Rheumatoid Factor (RF), Bilirubin, Triglyceride and Hemoglobin. The results showed that these compounds had no effect on the specificity of the assay up to the listed concentration.
 Rheumatoid Factor 80 IU/mL
 Bilirubin 342 µmol/L

Triglyceride 37 mmol/L
Hemoglobin 10 mg/mL

C. Common Drugs

Rapid COVID-19 IgM/IgG Combo Test Kit has tested samples with common drugs. The results showed that these drugs had no effect on the specificity of the assay: Histamine Hydrochloride, Interferon- α , Zanamivir, Ribavirin, Oseltamivir, Peramivir, Lopinavir, Ritonavir, Arbidol, Levofloxacin, Azithromycin, Ceftriaxone, Meropenem, Tobramycin.

3. Antibody Class Specificity

Rapid COVID-19 IgM/IgG Combo Test Kit showed 100% agreement with expected result before and after dithiothriol treatment (DTT) to establish antibody class specificity.

LIMITATIONS

For use under an Emergency Use Authorization Only

1. This test is only to be used in CLIA certified laboratories and not in point-of-care or at-home testing settings.
2. The test is limited to the qualitative detection of anti-COVID-19 antibody levels in human serum and ACD plasma samples and does not indicate the quantity of the antibodies. The intensity of the test line does not necessarily 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.
4. Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions. IgM antibodies may not be detected in the first few days of infection; the sensitivity of the Rapid COVID-19 IgM/IgG Combo Test Kit early 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.
5. 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.
6. SARS-CoV-2 IgG antibodies may be below detectable levels in patients who have been exhibiting symptoms for less than 15 days.
7. Testing with a molecular diagnostic should be performed to evaluate for acute SARS-CoV-2 infection in symptomatic individuals.
8. Results from antibody testing should not be used to diagnose or exclude SARS-CoV-2 infection or to inform infection status.
9. Positive results may not indicate previous SARS-CoV-2 infection. Consider other information, including clinical history and local disease prevalence, in assessing the need for an alternative serology test to confirm an adaptive 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.
10. The test is limited to the qualitative detection of antibodies specific for the SARS-CoV-2 virus. The intensity of the test line does not necessarily correlate to SARS-CoV-2 antibody titer in the specimen.
11. Not for screening of donated blood.
12. The test is for in vitro diagnostic use only.
13. It is not known at this time if the presence of antibodies to SARS-CoV-2 confers immunity to reinfection.
14. The test may have lower sensitivity for IgG detection in symptomatic individuals prior to 8 days since symptom onset.



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