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 PLASMA (ACD) AND FINGERSTICK WHOLE BLOOD

For use under 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, acid citrate dextrose (ACD) plasma and fingerstick whole blood. 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. The Rapid COVID-19 IgM/IgG Combo Test Kit should not be used to diagnose or exclude acute SARS-CoV-2 infection. At this time, it is unknown for how long antibodies persist following infection and if the presence of antibodies confers protective immunity.

Testing of serum and plasma 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.

Testing of fingerstick whole blood specimens is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet the requirements to perform high, moderate or waived complexity tests. Testing of fingerstick whole blood specimens is authorized for use at the Point of Care (POC), i.e., in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation.

Results are for the detection of IgM and IgG 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 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

COVID-19 is an acute infectious disease caused by the SARS-CoV-2 virus. The incubation period of the disease ranges from 1-14 days, during which time infected individuals may infect other people. Acute SARS-CoV-2 infection may also present without symptoms. Respiratory droplets and contact are the main routes of transmission. The initial symptoms of the patients include fever, fatigue and coughing, which can develop into dyspnea and other serious manifestations. Some of the severe cases may have acute respiratory distress syndrome or septic shock, or even death.

There are several days of incubation period after infection with SARS-CoV-2 virus. IgM antibodies may be detected soon after the incubation period and remain for a short time. IgG antibodies may appear after a few days of incubation period and remain in circulation in the blood for a number of weeks. An IgG positive result 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

- Rapid COVID-19 IgM/IgG Combo Test Kit
- Individual sample buffer
- 2 µL capillary pipet (serum and plasma only)
- 5 µL capillary pipet (fingerstick only)
- Sterile Safety Lancet
- Package Insert

MATERIALS REQUIRED BUT NOT SUPPLIED

- Clock or timer, specimen collection container, biohazard waste container, disposable gloves, disinfectant.
- **External controls are not included with the kit but are commercially available through Megna Health under catalog number: RAK-CON-001.**

STORAGE

1. Store the test device at 4 to 30ºC 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

- For use under an Emergency Use Authorization Only. For ***in vitro*** diagnostic use only.

- This test has not been FDA cleared or approved but has been authorized for emergency use by FDA under an EUA for use by authorized laboratories.
- Testing of fingerstick whole blood specimens is authorized for use at the Point of Care (POC), i.e., in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance or Certificate of Accreditation.
- This test has been authorized only for detecting the presence of IgM and IgG antibodies to SARS-CoV-2, not for any other viruses or pathogens.
- The emergency use of 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 Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization is revoked sooner.
- Do not use the product beyond the expiration date.
- Do not use the product if the pouch is damaged or the seal is broken.
- Handle all specimens as potentially infectious.
- Follow standard Lab procedure and biosafety guidelines for handling and disposal of potentially infectious material. When the assay procedure is completed, dispose specimens based on relevant state and federal requirement for biological samples.
- Tests are for single use only.

SPECIMEN COLLECTION PREPARATION

The serum, ACD plasma or fingerstick whole blood specimen should be collected under standard laboratory conditions.

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

The fingerstick specimens should be collected using approved lancets and tested immediately.

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 reliability of the test kits. Users should refer to the instruction for use for the external controls. External controls should be run like human specimens using the instructions described herein. It is recommended that positive and negative controls are tested each time a new lot is used, when a new operator performs the test, or when the test is run in a new room/laboratory, etc. as a good laboratory practice to confirm the test procedure and to verify proper test performance.
4. If controls do not provide the expected results, repeat the test with a new Rapid COVID-19 Test Card and controls.; If the results are still not correct, contact Megna Health at support@megnahealth.com.

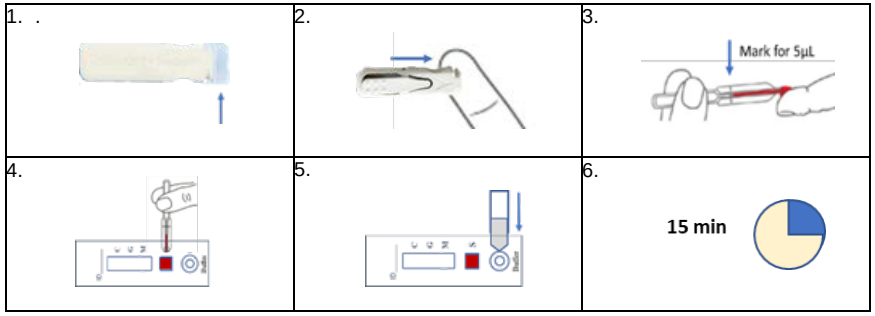
PROCEDURE

Preparation

- Bring the kit components to room temperature before testing.
- Tear open the pouch to take out the Rapid COVID-19 Test cCard. Place the Rapid COVID-19 Test Card on a table or other flat surface. Once opened, the test card must be used immediately.
- Label the test card with patient identity.

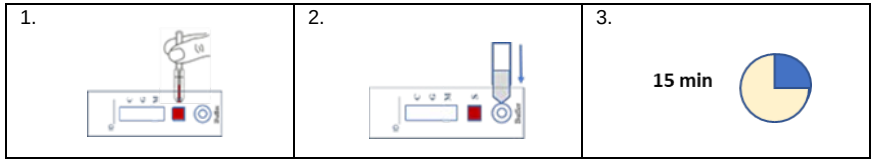
For Fingerstick Whole Blood

1. Clean the fingertip from which the blood sample will be taken using clean water or alcohol wipe.
2. Twist cap of the lancet 360 degrees to remove the cap. Apply the lancet to fingertip of the middle or ring finger, then press the trigger.
3. Collect blood sample using the 5 µL capillary straw provided. Hold the 5 µL capillary straw horizontally and touch tip of the straw to the blood drop on fingertip. Capillary action will automatically draw the sample to the fill mark, then stop. ***Caution:*** *Filling is automatic. Never squeeze before or while sampling.*
4. Add one drop (5 µL) of blood sample to the "S" area of the Rapid COVID-19 Test Card. To expel the sample, align the tip of the capillary straw with the sample well**.** Squeeze the bulb of the 5 µL capillary straw.
5. Add sample buffer. Tear open the sample buffer ampule, add 2 drops to the "Buffer" well on the test card.
6. Wait for 15 minutes.
7. Read the result. Determine if test is negative or positive by comparing to possible results shown below. Note: Results recorded after 20 minutes may not be accurate.



For Serum or Plasma Specimens

1. Withdraw the serum or ACD plasma specimen from the tube with the 2 µL 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 "S" area of the Rapid COVID-19 Test Card as marked.
2. Add sample buffer. . Add 2 drops of sample buffer (approximately 80-100 µL) to well marked as "Buffer" on the test card.
3. Read the results at 15 minutes. Note: Results after 20 minutes may not be accurate.

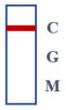


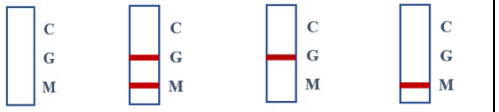
For External Positive and Negative Controls

1. Thaw the material at room temperature until they are completely thawed prior to use.
2. Add one drop or 5 µL of control sample to "S" well on the test card. Test positive or negative controls separately.
3. Tear open the buffer ampule, add 2 drops to the "Buffer" well on the test card.
4. Read the results at 15 minutes.

Run the controls in the same manner as serum or plasma samples outlined above.

INTERPRETATION OF RESULTS

POSITIVE			NEGATIVE
			
Both IgG/IgM Positive	**IgM Positive IgG Negative**	**IgM Negative IgG Positive**	**Both IgG/IgM Negative**

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:

1. Authorized laboratories* using your product must 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 must 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.
3. Authorized laboratories that receive your product must notify the relevant public health authorities of their intent to run your product prior to initiating testing.
4. Authorized laboratories using your product must have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
5. Authorized laboratories must 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.
6. 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.
7. Megna Health Inc., authorized distributors, and authorized laboratories using your product must 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 "authorized laboratories" as the following:
Testing of serum and plasma 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.

*Testing of fingerstick whole blood specimens is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet the requirements to perform high, moderate or waived complexity tests. Testing of fingerstick whole blood specimens is authorized for use at the Point of Care (POC), i.e., in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation.

PERFORMANCE CHARACTERISTICS:

1. CLINICAL PERFORMANCE:

A. Megna Health 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. Samples were collected in China between January 2020 and February, 2020. 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 & IgG

Days of Symptoms Onset	PCR Positives	IgM			IgG		
		Positives	PPA	95% CI	Positives	PPA	95% CI
< 7 days	69	46	66.67%	54.93 - 76.65	43	62.32%	50.52 - 72.82
8 - 14 days	35	27	77.14%	60.98 - 87.94	30	85.71%	70.63 - 93.74
> 15 days	22	20	90.91%	72.19 - 97.47	20	90.91%	72.19 - 97.47
All	*126*	*93*	*73.81%*	*65.51 - 80.70*	*93*	*73.81%*	*65.51 - 80.70*
		Negatives	NPA	95% CI	Negatives	NPA	95% CI
All	*285*	*284*	*99.6%*	*98.04 - 99.94*	*283*	*99.3%*	*97.48 - 99.81*

1) IgM sensitivity (Positive percent agreement): 73.81% (95% CI: 65.51% - 80.70%)
2) IgM specificity (Negative percent agreement): 99.7% (95% CI: 98.04% - 99.94%)
3) IgG sensitivity (Positive percent agreement): 73.81% (95% CI: 65.51 – 80.70%)
4) IgG specificity ((Negative percent agreement): 99.3% (95% CI: 97.48 – 99.81%)

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 (FNLCR) 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 below.

	Comparator Method			Collected pre-2020		
	Antibody Positive			Antibody Negative		
Megna Health Rapid COVID-19 IgM/IgG Combo Test Kit	IgM+, IgG+	IgM+, IgG-	IgM-, IgG+	Negative	HIV+	Total
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	

C. Clinical Agreement at Point of Care (with fingerstick whole blood)

The Rapid COVID-19 IgM/IgG Combo Test Kit was tested with 130 fresh whole blood samples (45 positives and 85 negatives) collected using fingerstick devices at one Point of Care clinic. Subjects were confirmed to be either positive or negative for SARS-CoV-2 infection using a FDA authorized RT-PCR test and then confirmed samples were tested using the Megna Health Rapid COVID-19 IgM/IgG Combo Test kit. The sensitivity/PPA and specificity/(NPA) are summarized in the following tables.

Summary of Clinical Performance with Fingerstick Whole Blood at POC

Days of Symptoms Onset	PCR Positives	IgM			IgG		
		Positives	PPA	95% CI	Positives	PPA	95% CI
< 7 days	0	0	n/a	n/a	0	n/a	n/a
8 - 14 days	9	8	88.9%	56.5 - 98.0%	7	77.8%	45.3 - 93.7%
> 15 days	36	26	72.2%	57.6 – 86.9%	36	100.0%	92.2 - 100.0%
All	*45*	*34*	*75.6%*	*63.0 - 88.1%*	*43*	*95.6%*	*85.2 - 98.8%*
		Negatives	NPA	95% CI	Negatives	NPA	95% CI
All	*85*	*85*	*100.0%*	*97.0 - 100.0%*	*85*	*100.0%*	*97.0 - 100.0%*

Overall IgM: Sensitivity (positive agreement): 75.6% (95% CI: 63.0 – 88.1%)
Specificity (negative agreement): 100.0% (P5% CI: 97.0 – 100.0%)
Overall IgG: Sensitivity (positive agreement): 95.6% (95% CI: 85.2 – 98.8%)
Specificity (negative agreement): 100.0% (97.0 – 100.0%)

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. CLASS SPECIFICITY

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

LIMITATIONS:

- For use under an Emergency Use Authorization Only
- Not for use in at-home testing settings.
- This test is only to be used in CLIA certified laboratories and point-of-care testing settings.
- The test is limited to the qualitative detection of anti- SARS-CoV-2 antibody levels in serum, ACD plasma and finger stick whole blood 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.
- 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.
- 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.
- 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.
- SARS-CoV-2 IgG antibodies may be below detectable levels in patients who have been exhibiting symptoms for less than 15 days.
- SARS-CoV-2 serology tests should not be used to diagnose acute COVID-19. An assay that directly detects the virus should be used to evaluate symptomatic individuals for acute COVID-19, particularly those who have been in contact with the virus.
- 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

- 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.
- This test should not be used for screening donated blood.
- It is not known at this time if the presence of antibodies to SARS-CoV-2 confers immunity to reinfection.
- The test may have lower sensitivity for IgG detection in symptomatic individuals prior to 15 days since symptom onset.
- The performance of this test 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 test should not be interpreted as an indication or degree of protection from infection after vaccination.
- The performance of this test was established based on the evaluation of a limited number of clinical specimens. Samples for the clinical agreement study were collected in China between January 2020 and February 2020. Samples collected in the point-of care study were collected in the Unites States between January 2021 and March 2021. The clinical performance has not been established in 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.

Megna Health Inc.
436 Creamery Way, Suite 200
Exton, PA 19341.
Tech Support: (855) 253-3634
Email: support@megnahealth.com

EC REP MDSS Gmbh Schiffgraben 41, 30175
Hanover, Germany

IVD

4°C 30°C

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