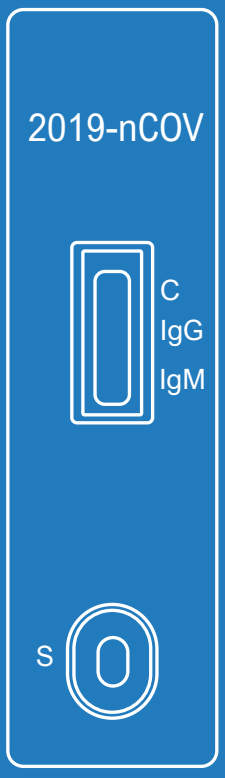
MEDFLOW
CLINICAL

2019-nCoV IgG/IgM Rapid Test Kits



Simple | Rapid | Effective

Abount US

MedFlow Clinical Ltd is a medical logistics company dealing primarily with medical consumables. We know that effective outcomes rely on receiving the right equipment, at the right time, and in the right location. As a small team, we are able to offer tailored solutions to the dynamic challenges of healthcare in the 21st century. Our highly personalised and efficient system means your needs are taken care of without compromise.

Our Mission to improve the available treatments for patients

To support healthcare professionals in the research, diagnoses and treatment of medical conditions by delivering quality products and outstanding service to meet the expectations of our customers and patients around the world.

Our Measures define how we perform as a business

- COMMERCIAL & VALUE EXCELLENCE
- CUSTOMER RESPONSIVENESS
- SERVICE EXCELLENCE

Our Values demonstrate what we do every day

- BE ACCOUNTABLE
- CLEARLY COMMUNICATE
- DEMOSTRATE FLEXIBILITY
- INNOVATE
- INTEGRITY FIRST

Our Team is passionate about exceeding your expectations

CHRIS SMITH
DIRECTOR

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DIRECTOR

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DIRECTOR

Rapid Testing of COVID-19

Background

In early January 2020, a novel coronavirus (2019-nCoV) was identified as being the infectious agent causing an outbreak of viral pneumonia in Wuhan, Hubei, China, where the first cases had their symptom onset in December 2019.[1] This coronavirus has been named COVID-19 (coronavirus disease 2019). From it's origin in Wuhan, cases of the disease has been confirmed in over 200 countries and territories around the world. To date (13th May 2020) there have been over 4.1 million confirmed cases and over 287,000 deaths reported[2].

Coronaviruses are enveloped RNA viruses that are distributed amongst humans, other mammals, and birds and cause respiratory, enteric, hepatic, and neurologic diseases.[3] Six coronavirus species are known to cause human disease.[4] Four viruses *229E, OC43, NL63, and HKU1* are prevalent and typically cause common cold symptoms in immunocompetent individuals.[4] The two other strains *Severe Acute Respiratory Syndrome coronavirus (SARS-COV) and Middle East Respiratory Syndrome coronavirus (MERS-COV)* are zoonotic in origin and have been linked to sometimes fatal illness.[5] Coronaviruses are zoonotic, meaning that they are transmitted between animals and people. Common signs of an infection include: respiratory symptoms, fever, cough, shortness of breath and breathing difficulties. In more severe cases, infection can cause: pneumonia, severe acute respiratory syndrome, kidney failure and even death.[6] Symptoms of COVID-19 typically take 2-14 days to appear and they present as: fever, dry cough, sore throat, headache and muscular pain. Most cases are mild and patients recover quickly. However, a smaller number of cases are severe and require medial care.

Standard recommendations to prevent infection spread include: regular hand washing, covering mouth and nose when coughing and sneezing, thoroughly cooking meat and eggs. Avoid close contact with anyone showing symptoms of respiratory illness such as coughing and sneezing.[6]

Current diagnosis of COVID-19 involves: measuring body temperature, CT scans and Real-Time PCR (RT-PCR), which sequences the viral genome, allowing identification of SARS-CoV-2. However, RT-PCR test kits have some limitations: they take at least 2 hours to obtain a result, they require certified laboratories and personnel and they are known to give several false positives[7]. Hence, there is a need for rapid diagnostics, which are easy to use and can give fast results from the lowest volume of sample possible.

1. World Health Organization (WHO) statement regarding cluster of pneumonia cases in Wuhan, China. Beijing: WHO; 9 Jan 2020. [Accessed 26 Jan 2020].

2. World Health Organization (WHO) Coronavirus disease (COVID-2019) situation report – 114 [Accessed 14 May 2020].

3. Weiss SR, Leibowitz JL Coronavirus pathogenesis Adv Virus Res 2011;81:85-164.

4. Su S, Wong G, Shi W, et al. Epidemiology, genetic recombination, and pathogenesis of coronaviruses. Trends Microbiol 2016;24:490-502.

5. Cui J, Li F, Shi ZL. Origin and evolution of pathogenic coronaviruses. Nat Rev Microbiol 2019;17:181-192.

6. World Health Organization (WHO). Coronavirus.

7. Gallagher J. Are Coronavirus Tests Flawed? BBC News (www.bbc.com/news/health-51491763). 13 Feb 2020 [Accessed 12 May 2020].

Understanding IgM and IgG

IgG and IgM are types of immunoglobulins, what are commonly called antibodies. When a person becomes infected with a pathogen such as COVID-19, immunoglobulins are produced as a response. The immunoglobulins bind to specific binding sites (antigens) on the surface of the pathogen, this flags the pathogen as foreign matter. This in turn triggers a secondary immune response which attacks and clears the pathogen.

IgM (immunoglobulin M) is the largest immunoglobulin in humans and it is the first antibody to be produced when a person becomes infected. IgM has multiple antigen binding sites and it is commonly thought of as a 'general' antibody since it is able to bind to many different pathogens. For COVID-19 the levels of IgM in the blood are at a detectable level between 3-7 days after the onset of infection.

IgG (immunoglobulin G) is a much smaller immunoglobulin and it is produced in response to a specific antigen on the pathogen. The levels of IgG rise later than IgM and it indicates previous exposure to COVID-19. IgG also has a function in long term immunity, but exactly how long IgG remains after the infection is cleared appears to be highly variable, IgG has a half-life of 7-30 days[8], although it may be detected after many half-lives.

In combination, IgM and IgG can be used to detect both early and late stage COVID-19 and also long term immunity after recovery. It is important to understand that the IgG is specific to 2019-nCoV, but using this specific IgG and the general IgM a simple lateral flow immunoassay diagnostic test for the COVID-19 can be produced.

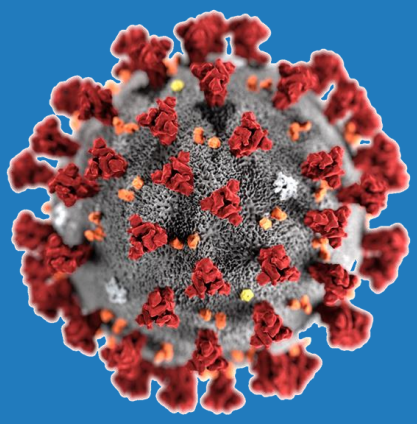
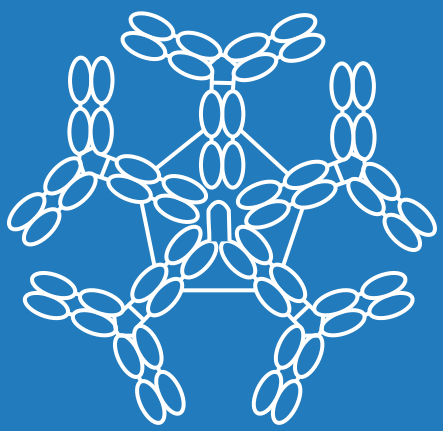
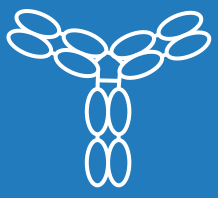


Illustration of Coronavirus
the surface antigens are red



Immunoglobulin M (IgM) Illustration



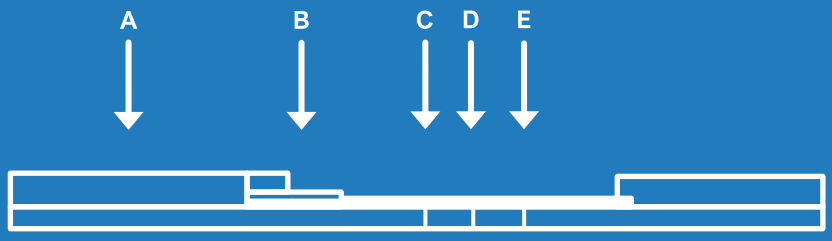
Immunoglobulin G (IgG) Illustration

8. Mankarious S, Lee M, Fischer S, Pyun KH, Ochs et al. (1988). The half-lives of IgG subclasses and specific antibodies in patients with primary immunodeficiency who are receiving intravenously administered immunoglobulin. J Lab Clin Med 112(5); 634-640

The Rapid Test

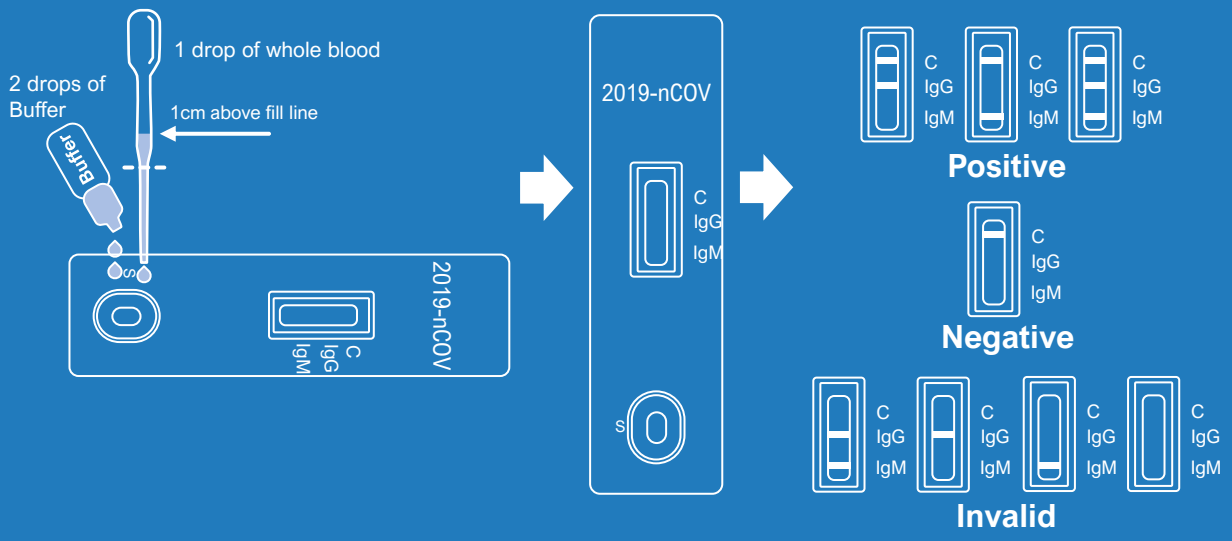
The 2019-nCoV IgG/IgM Rapid Test Cassette (Whole Blood/Serum/Plasma) is a qualitative membrane-based immunoassay for the detection of IgG and IgM antibodies to 2019-nCoV in whole blood, serum or plasma specimen. This test consists of two components, an IgG component and an IgM component. In the IgG component, anti-human IgG is coated in IgG test line region. During testing, the specimen reacts with 2019-nCoV antigen-coated particles in the test cassette. The mixture then migrates upward on the membrane chromatographically by capillary action and reacts with the anti-human IgG in IgG test line region. If the specimen contains IgG antibodies to 2019-nCoV, a coloured line will appear in IgG test line region as a result. Similarly, anti-human IgM is coated in IgM test line region and if specimen contains IgM antibodies to 2019-nCoV; the conjugate-specimen complex reacts with anti-human IgM and a coloured line appears in IgM test line region as a result.

Therefore, if the specimen contains 2019-nCoV IgG antibodies, a coloured line will appear in IgG test line region. If the specimen contains 2019-nCoV IgM antibodies, a coloured line will appear in IgM test line region. If the specimen does not contain 2019-nCoV antibodies, no coloured line will appear in either of the test line regions, indicating a negative result. To serve as a procedural control, a coloured line will always appear in the control line region, indicating that the proper volume of specimen has been added and membrane wicking has occurred.



As shown in illustration above, the specimen (A) migrates via capillary action along the membrane to react with the gold conjugate (B). 2019-nCoV IgG or/and IgM present in the specimen binds to the conjugate, forming a coloured Novel coronavirus antibody-antigen complex. The mouse anti-human IgG and mouse anti-human IgM immobilized in the test zone of the membrane captures the test region (C) and test region (D). The formation of a visible coloured line in the test region indicates a positive result (C) or (D). The absence of a coloured line in the test zones suggests a negative result. In the control zone of the membrane, immobilized reagents capture coloured conjugate regardless of test specimen composition. The resulting visible coloured band (E) confirms control line.

How To Use & Understand The 2019-nCoV IgG/IgM Rapid Test Cassette



To perform a finger prick test, a sample of whole blood is placed at the inlet, before the addition of a buffer solution. Any IgG/IgM present in the sample will bind to the gold-COVID-19 antigen conjugate and flow to the two test lines, which will capture any IgG/IgM in the sample. The control line will then capture the other gold-antibody conjugate, confirming the test is valid. In approximately 10 minutes, test lines will appear for both IgG and IgM for a positive result, and a control line for quality control. Only one test line (IgG or IgM) is required for a positive diagnosis. This test has the advantages of being portable, rapid and low cost.

Accuracy of The 2019-nCoV IgG/IgM Rapid Test Cassette

While the test is highly accurate, it should also be understood that no test infallible. As stated previously the 'gold-standard' PCR test is also know to give false positive results. To establish the accuracy of the 2019-nCoV IgG/IgM Rapid Test Cassette there are two important sets of results to consider; Relative Sensitivity and Relative Specificity.

Relative Sensitivity is the sensitivity of a medical screening test as determined by comparison with the same type of test; for example, sensitivity of a new serologic test relative to sensitivity of an established serologic test, in this case the 2019 n-CoV IgG/IgM Rapid Test and RT-PCR Test.

IgM (Present Infection) | IgG (Antibody Detection) | **Accuracy**

Relative Specificity is the specificity of a medical screening test as determined by comparison with the same type of test (for example, specificity of a new serologic test relative to specificity of an established serologic test. In this case the 2019 n-CoV IgG/IgM Rapid Test and RT-PCR Test.

IgM (Present Infection) | IgG (Antibody Detection) | **Accuracy**

Frequently Asked Questions

Where is the 2019-nCoV IgG/IgM Rapid Test Manufactured?

All test kits supplied by MedFlow Clinical Ltd are manufactured by a specialist manufacturer (IDT Diagnostics t/a ICT International) based in South Africa. The reason for us choosing to supply this test kit is that the manufacturer have been producing test kits of this type for more than 25 years.

Is the 2019-nCoV IgG/IgM Rapid Test CE marked?

Yes, the 2019-nCoV IgG/IgM Rapid Test is CE marked for professional use and is therefore a registered IDV device.

What does the 2019-nCoV IgG/IgM Rapid Test detect?

The test detects IgG and IgM immunoglobulins (antibodies) to the COVID-19 virus in human whole blood, serum or plasma.

Is the test specific for COVID19?

Yes, the IgG that the test detects is specific to COVID-19, a positive result would indicate COVID-19 infection. The IgM is more general, its detection combined with IgG and/or symptoms of COVID-19 would also indicate infections. This rapid test can be used for primary and secondary diagnosis of COVID-19.

What sample can be used with the test?

The test may be used with whole blood, plasma or serum. Whole blood obtained by finger prick is easiest. The type of sample used does not affect the sensitivity or accuracy of the test.

Can babies, young children, pregnant women or breast feeding women be tested?

Yes, there are no issues with testing babies and young children. There is no harm to pregnant or breast feeding women or their baby when performing a test.

Is there anyone who should not be tested using the 2019-nCoV IgG/IgM Rapid Test?

No, testing is a vital strategy for helping to control and understand the virus and may result in improved measures to prevent its spread. However, as a blood sample is required anyone with a blood related health condition such as haemophilia or haemochromatosis should discuss this with a healthcare professional before receiving this test.

What is the self-life of the 2019-nCoV IgG/IgM Rapid Test?

The shelf-life is 24 months from date of manufacture. Do not use after the expiry date.

How should the 2019-nCoV IgG/IgM Rapid Tests be stored?

We recommend that the tests are stored between 2-30°C, this does not mean you should refrigerate them as the tests should be performed at room temperature (15-30°C). Do not freeze.

When can the 2019-nCoV IgG/IgM Rapid Test detect an infection?

In general terms detectable levels of IgM are present in blood from day 7 of a new infection and reach a peak level by day 14 after infection. Detectable levels of IgG are normally present after day 14 of an infection. However, there is limited knowledge as to the exact nature of the immune response to COVID-19.

How does this test compare with RT-PRC test?

The 2019-nCoV IgG/IgM Rapid Test has been compared with RT-PCR. Specimens from patients with confirmed COVID-19 status (by RT-PCR) were compared against the same specimens tested using the 2019-nCoV IgG/IgM Rapid Test. The accuracy of the rapid test is 93% for IgM detection and 99% for IgG detection.

Can you get a false positive result?

It is possible to get a false positive result if you have had a past or present infection with a non-COVID-19 coronavirus strain. For this reason, PCR is recommended in conjunction with clinical symptoms to confirm a patients current status.

Can you get a false negative result?

It is possible to get a false negative result, this is because the level of anti bodies present in each whole blood sample varies from person to person. If the amount of COVID-19 antibodies present in the sample is very low, then it may not be detectable for up to 14 days from the onset of infection. For this reason, PCR would be recommended in conjunction with clinical symptoms for anyone shown a negative result.

How do you know if the test was conducted properly?

The appearance of a coloured line in the control line region (C) indicates that the testing procedure was performed correctly and the proper amount of specimen was absorbed by the test media.

What should you do if a positive result is indicated?

Follow all government advise. If your IgM line is positive seek urgent medical attention and self quarantine immediately – your status should be confirmed by RT-PCR. If your IgG line is positive it indicates you have had the infection, if you have symptoms you should self-isolate.

What if the test is positive but the patient doesn't display any symptoms?

Either the patient is infected and may begin to display symptoms in the next few days, or the patient is infected but are asymptomatic. In both cases they should be treated as positive for the virus and should follow current guidelines.

What should I do if a negative result is indicated?

A negative result indicates that the test was not able to detect the presence of antibodies to COVID-19 – it does not rule out the presence of infection. If you have symptoms then you should follow-up with a RT-PCR Test for more accurate confirmation of you status.

Conclusion

The 2019-nCoV IgG/IgM Rapid Test is suitable for both clinical diagnosis and screening of COVID-19. Provided the testis performed correctly it has a high sensitivity, specificity and accuracy against the 2 biomarkers of COVD-19 (IgM and IgG). In addition, a variety of samples may be used in low sample volumes (single droplets of either whole blood, plasma or serum). This test is a valuable tool in the diagnosis of COVID-19 and may serve as a first line screening test before clinical assessment by RT-PCR.

RESULTS FROM A RAPID ANTIBODY TEST SHOULD NOT BE USED AS THE SOLE BASIS FOR A DEFINATIVE POSITIVE OR NEGATIVE DIAGNOSIS. ALWAYS SEEK MEDICAL ADVICE IF YOU EXPERIENCE SYMPTOMS OF COVID-19

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