



The Diagnostic Specialist

DiaSorin S.p.A.

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This document presents information regarding the use of the LIAISON[®] SARS-CoV-2 S1/S2 IgG and LIAISON[®] SARS-CoV-2 IgM tests, in the context of the current COVID-19 pandemic.

For detailed technical information on this test, please refer to the Instruction for Use document available via DiaSorin's [Dialog documentation database](#).

All the information on this document is based on data from scientific publications available as of July 10th 2020. DiaSorin reserves the right to amend any information contained in this document, should new data become available which presents new relevant information.

FOR OUTSIDE THE US AND CANADA ONLY

[SARS-CoV-2 and COVID-19 background](#)

What is CoVID-19 and what are its symptoms?

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The disease was initially identified in December 2019 in Wuhan, Hubei province, China, and has since spread globally [1]. As of 9 July 2020, there are more than 11.8 million cases reported worldwide, resulting in more than 545,000 fatalities [2].

Symptoms of COVID-19 vary in severity from no symptoms at all (being asymptomatic) to symptoms such as fever, cough, sore throat, loss of the sense of smell, general weakness and fatigue and muscular pain and in the most severe cases, severe pneumonia, acute respiratory distress syndrome, sepsis and septic shock, all potentially leading to death [3].

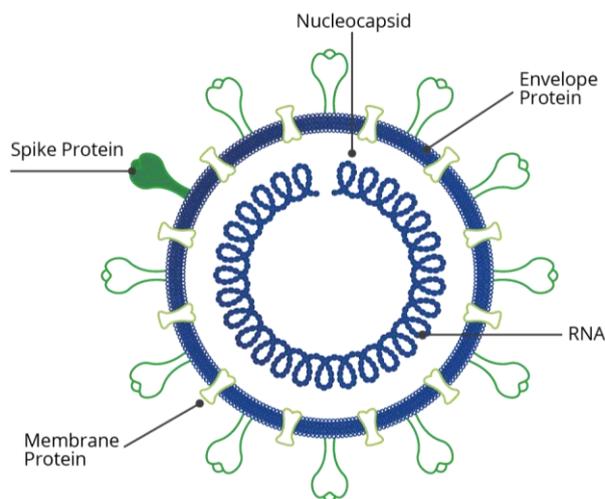
The SARS-CoV-2 Virus

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the pathogen responsible for COVID-19. It is a strain of severe acute respiratory syndrome-related coronavirus (SARSr-CoV) and has close genetic similarity to bat coronaviruses, suggesting it emerged from a bat-borne virus.[4]

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The protein make-up of SARS-CoV-2

SARS-CoV-2 has four structural proteins, known as the S (spike), E (envelope), M (membrane), and N (nucleocapsid) proteins; the N protein holds the RNA genome, and the S, E, and M proteins together create the viral envelope. The spike protein, is the protein responsible for allowing the virus to attach to and fuse with the membrane of a host cell.[5]



The S1 and S2 proteins are derived from the SARS-CoV-2 spike protein: they are responsible for the binding and fusion of the virus to the host cell. The Receptor Binding Domain (RBD) is the domain of the S1 proteins that directly binds to the ACE2 receptor. As the protein on the viral surface that is responsible for entry into the host cell, the spike protein and its antigens are the main antigen target of neutralising antibodies.[9]

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Immune response against SARS-CoV-2

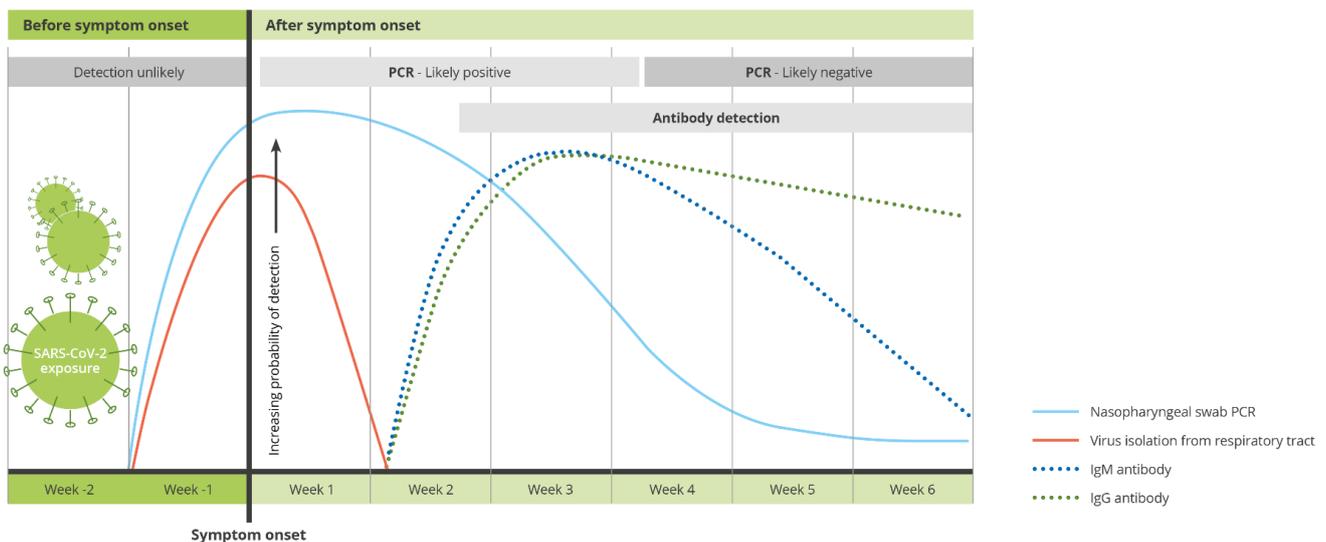
Timing of Immune response to SARS-CoV-2

Timing of seroconversion after exposure to SARS-CoV-2 provides key information to determine the time window in which serology tests can provide clinically useful information. A recent analysis of published literature [6] demonstrates that there is currently no definitive consensus on timing of seroconversion. In a recent study on 285 patients [10], the proportion of patients with positive virus-specific IgG reached 100% approximately 17–19 days after symptom onset.

Difference in IgG and IgM seroconversion

Seroconversion rates are an important aspect to determine usefulness of serology testing. Two studies [14, 15] report median seroconversion timing for IgG to be roughly two days later than IgM.

The estimated variation over time in diagnostic tests for detection of SARS-CoV-2 Infection relative to symptom onset can be depicted for illustrative purposes as follows :





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Should IgG and IgM tested in a combined fashion?

Combined detection of IgM and IgG can be used to assess the immune status of patients

exposed to and infected by SARS-CoV-2.

The use of IgG and IgM in combination can aid to shorten the diagnostic window improving the detection of seroconversion up to day 15 from PCR positivity.

[Serology: use and limitations](#)

Does a positive result to a serology test mean that a patient is not infective anymore?

Recent publications [8] show that 50% of severe COVID-19 cases and 23% of mild cases were positive to viral RNA >20 days post onset. In the same study 100% of patients showed seroconversion to IgG by day 14. Since it is plausible for a patient to be positive to both viral RNA and IgG, a positive IgG result should not be interpreted as a sign that a patient has stopped being infective.

Does a positive result to a serology test mean that a patient is protected from the disease?

Presence of antibodies against a pathogen, and particularly presence of neutralizing antibodies, is considered a sign of protection for many diseases. The effect of neutralizing antibodies must however be demonstrated for each disease, before any assumptions can be made both on their putative protective effect and its duration. Currently, no published data is available to determine if neutralizing IgG antibodies against SARS-CoV-2 protect patients against re-infection.

In consideration of the points above the results coming from any serology test against SARS-CoV-2 should not be used to presume protection against SARS-CoV-2 reinfection.



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Does a negative result to the LIAISON[®] SARS-CoV-2 IgG or IgM test mean that a patient is not infective or has not been exposed to the SARS-CoV-2 virus?

Current data [6,7] shows that IgG antibodies appear in the majority of patients between 7-14 days after onset of symptoms, and in some limited cases could take longer. Due to the time needed for seroconversion, the test could provide a negative result in infected patients, if performed during the incubation period and in the early stages of infection. A negative result could also indicate the absence or a very low level of IgG antibodies against SARS-CoV-2.

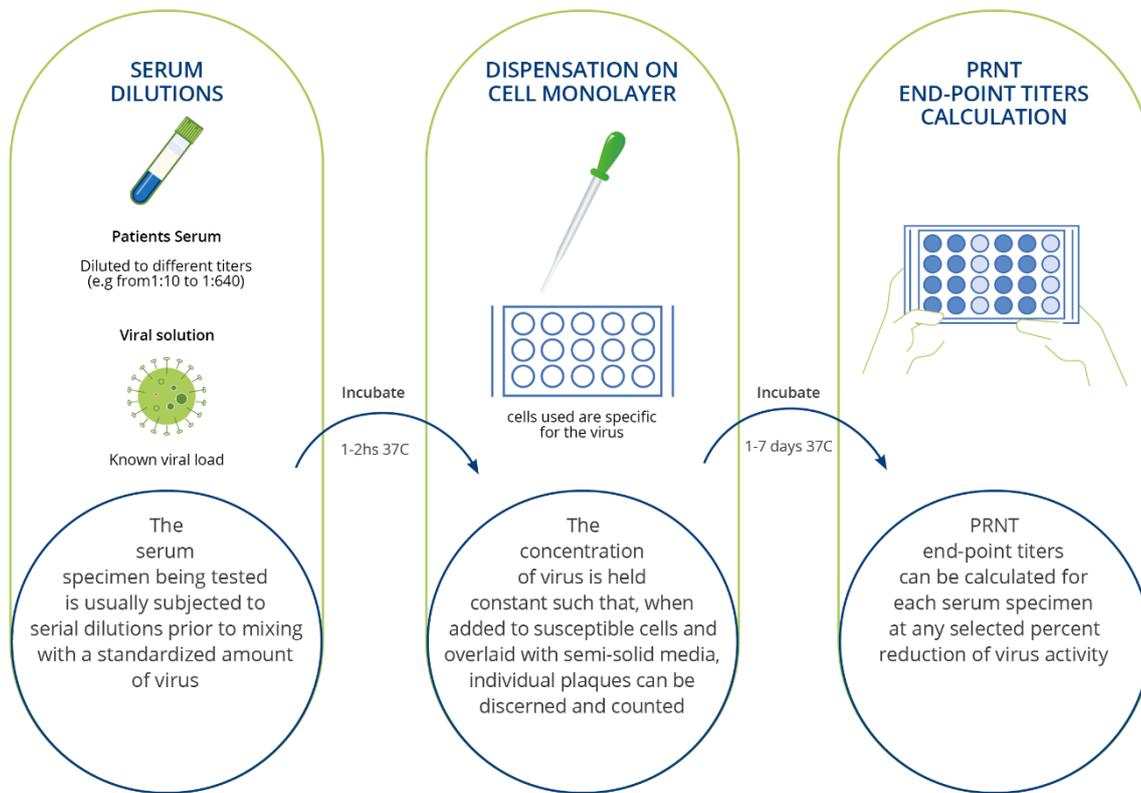
As a consequence, negative serology results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions. Moreover, negative serology results still imply that local rules on social distancing should be followed.

What is the Plaque Reduction Neutralization Test (PRNT)?

The Plaque Reduction Neutralization Test (PRNT) is used to quantify the titer of neutralizing antibody for a virus. Live virus is added to serial dilutions of patient serum and then cultured in a cell line on an agar plate. Over several days, patient antibodies with neutralizing capacity will prevent the virus from creating “plaques,” or small areas of no cell growth, on the plates. Researchers can quantify the neutralizing capacity of patient antibodies by comparing the serial dilution plates and the control plates.

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A visual description from [12] is shown here below:





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[LIAISON[®] SARS-CoV-2 S1/S2 IgG test: key facts](#)

Which SARS-CoV-2 antigens does the LIAISON[®] test use?

The LIAISON[®] SARS-CoV-2 tests uses magnetic beads coated with S1 & S2 Antigens. The antigens used in the tests are expressed in human cells to achieve proper folding, oligomer formation, and glycosylation, providing material similar to the native spikes. The two antigens being used in LIAISON[®] SARS-CoV-2 tests, S1 and S2, are derived from the virus' spike protein. When the virus contacts the host cells, a serine protease cuts the spike protein into the two domains: the S1 domain, containing the receptor binding domain, and the S2 domain which is responsible for the fusion of the viral capsid with the cell. By coating the magnetic beads with S1 and S2 together, protein folding is likely to more closely resemble natural configurations, ensuring higher immunogenic specificity.

The S1 and S2 proteins are both targets to neutralizing antibodies. By using these antigens in our test, the likelihood of concordance to a neutralization assay is increased significantly.[9]

Does the test show cross reactivity to other strains of Coronavirus?

The test was evaluated and showed no cross-reactivity against HuCoV OC43, HuCoV HKU1 and a number of samples for HuCoV where the strain had not been further characterized.

Does the test show any Biotin interference?

Assessment of potential Biotin interference on the LIAISON[®] SARS-CoV-2 S1/S2 IgG test could not detect any interfering effect up to 3500 ng/ml.

Does the test provide data on Neutralizing antibodies?

The LIAISON[®] SARS-CoV-2 S1/S2 IgG test support the study of the immune status of infected patient by providing an indication of the presence of neutralizing IgG antibodies against SARS-CoV-2.



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The test was evaluated for concordance with Plaque Reduction Neutralization Test (PRNT) by testing 304 samples collected during the outbreak from subjects whose PRNT result was available. 180 were PRNT negative and 124 were PRNT positive (i.e. titer above 1:40). Based on the evaluation the LIAISON® SARS-CoV-2 S1/S2 IgG test showed a 97.8% Negative agreement and 94.4% positive agreement with PRNT. For full data on the concordance with PRNT, please consult the Instructions for Use.

What is the advantage of neutralizing antibodies?

Neutralization tests determine the functional ability of antibodies to prevent infection of virus in vitro [16]. However, as pointed out by WHO on April 24th 2020 [13], the evidence on antibody responses to SARS-CoV-2 infection is being continuously monitored. Most of the studies show that people who have recovered from infection have antibodies to the virus.

[LIAISON® SARS-CoV-2 IgM test: key facts](#)

What is the antigen target for the IgM assay and why?

The LIAISON® SARS-CoV-2 IgM uses the S1-RBD as target antigen on the solid phase. More than 10 antigens were evaluated during the feasibility study and S1-RBD provided the best combination of Specificity and Sensitivity for IgM antibodies detection.

Why could be useful to test IgM antibodies to SARS-CoV-2?

IgM testing could help to stratify patients to evaluate new vs previous infection. A combined testing with IgM and IgG antibodies could help in shorten the diagnostic infection window, increasing Sensitivity for the diagnosis of COVID-19.



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As a Health Care Professional, can I purchase the LIAISON® SARS-CoV-2 S1/S2 IgG and IgM test?

Diagnostic laboratories interested in purchasing the LIAISON® SARS-CoV-2 S1/S2 IgG and IgM test should contact our local representative. For worldwide contacts, please [see here](#). Please note that the LIAISON® tests should be performed by trained Health Care Professionals, in the proper diagnostic laboratory environment, and exclusively on the LIAISON® XL analyser.

As a private citizen, can I purchase the LIAISON® SARS-CoV-2 S1/S2 IgG and IgM tests?

The LIAISON® tests are not a test for home use, therefore it is not sold to the public. It should be performed by trained Health Care Professionals in the proper laboratory environment on the LIAISON® XL analyser.

Could the LIAISON® SARS-CoV-2 S1/S2 IgG and IgM tests be run on any kind of laboratory machine?

No, It should be performed by trained Health Care Professionals in the proper laboratory environment on the LIAISON® XL analyser

Can I send my samples to DiaSorin to be tested?

DiaSorin does not perform in-house testing of clinical samples, rather it supplies diagnostic laboratories with the tests and instruments required to analyse samples.

If you believe you may have contracted COVID-19 or if you suspect that you have been in contact with someone who has COVID-19, you should contact your local healthcare service for guidance.

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