

LIAISON® SARS-CoV-2 IgM ([REF] 311480)

For Emergency Use Authorization Only.

Caution: U.S. Federal Law restricts this device to sale by or on the order of a licensed practitioner.

For *in vitro* diagnostic use only.

Samples should be collected from individuals with 8 days to 30 days post symptom onset. Samples should not be tested less than 8 days post symptom onset. Negative samples collected before 8 days post symptom onset should be reflexed to direct detection of the virus. Negative samples collected 8 days or more post symptom onset should be reflexed to a test that detects and reports SARS-CoV-2 IgG.

1. INTENDED USE

The DiaSorin LIAISON® SARS-CoV-2 IgM is a chemiluminescent immunoassay (CLIA) intended for the qualitative detection of IgM antibodies to SARS-CoV-2 in human serum and plasma samples (sodium heparin, lithium heparin, and dipotassium EDTA). The DiaSorin LIAISON® SARS-CoV-2 IgM is intended for use as an aid in identifying individuals with an adaptive immune response to SARS-CoV-2, indicating acute or recent infection.

At this time, it is unknown for how long antibodies persist following infection and if the presence of antibodies confers protective immunity. The DiaSorin LIAISON® SARS-CoV-2 IgM 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 IgM antibodies. IgM 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.

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 DiaSorin LIAISON® SARS-CoV-2 IgM may occur due to cross-reactivity from pre-existing antibodies or other possible causes.

The DiaSorin LIAISON® SARS-CoV-2 IgM is only for use under the Food and Drug Administration's Emergency Use Authorization.

2. SUMMARY AND EXPLANATION OF THE TEST

Coronavirus disease (COVID-19) is an infectious disease caused by a newly discovered coronavirus. At the end of December 2019, Chinese public health authorities reported several cases of acute respiratory syndrome in Wuhan City, Hubei province, China. The initial outbreak in Wuhan spread rapidly, affecting other parts of China. Cases were then detected in several other countries. Since late February, the majority of cases reported are from outside China, with an increasing majority of these reported from EU/EEA countries and the US. The Director General of the World Health Organization declared COVID-19 a global pandemic on 11 March 2020⁽¹⁾.

The causative virus of the COVID-19 is called Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). It is a new strain of coronavirus that has not been previously identified in humans. It spreads primarily through contact with an infected person through respiratory droplets generated when a person coughs or sneezes, or through droplets of saliva or discharge from the nose. Infection with SARS-CoV-2 can cause mild symptoms including a runny nose, sore throat, cough and fever. However, it can be more severe for some people and can lead to pneumonia or breathing difficulties. The elderly and people with pre-existing medical conditions (such as, diabetes and heart disease) appear to be more vulnerable to becoming severely ill with the virus. Based on previous studies on SARS, an incubation period from three to fourteen days after onset of symptoms may be expected.

The incubation period for COVID-19 is thought to range from 2-14 days following exposure, with most cases showing symptoms approximately 4-5 days after exposure⁽²⁾. The interval during which an individual with COVID-19 is infectious has not yet been clearly established. Definite COVID-19 diagnosis entails SARS-CoV-2 detection by nucleic acid amplification technology (NAAT)^(3, 4, 5).

Serological assays can contribute to identifying individuals recently or previously exposed to the virus and assessing the extent of exposure of a population⁽⁶⁾.

As for the detection of IgG, detection of IgM antibodies against SARS-CoV-2 can be used to assess an adaptive immune response of patients affected by COVID-19.

Most people infected with the COVID-19 virus will experience mild to moderate respiratory illness and recover without requiring special treatment. Older people, and those with underlying medical problems like cardiovascular disease, diabetes, chronic respiratory disease or cancer are more likely to develop serious illness.

3. PRINCIPLE OF THE PROCEDURE

The method for qualitative determination of specific IgM to SARS-CoV-2 is an indirect chemiluminescence immunoassay (CLIA). SARS-CoV-2 spike receptor-binding domain (RBD) antigen is used for coating magnetic

particles (solid phase). During the first incubation, the SARS-CoV2 IgM antibodies present in calibrators, samples or controls bind to the solid phase. During the second incubation, mouse monoclonal IgG antibodies to human IgM linked to an isoluminol derivative, N-(4-Amino-Butyl)-N-Ethyl-Isoluminol (ABEI isoluminol-antibody conjugate), react with SARS-CoV2 IgM already bound to the solid phase. After each incubation, the unbound material is removed with a wash cycle. Subsequently, the starter reagents are added and a flash chemiluminescence reaction is thus induced. The light signal, and hence the amount of isoluminol-antibody conjugate, is measured by a photomultiplier as relative light units (RLU) and indicates the presence or absence of antibodies to SARS-CoV2 present in calibrators, samples or controls.

4. MATERIALS PROVIDED

Reagent integral

Magnetic particles (2.63 mL)	[SORB]	One (1) vial. Magnetic particles coated with RBD antigen (mammalian cells), BSA, phosphate buffer, < 0.1% sodium azide.
Calibrator 1 (0.6 mL)	[CAL 1]	One (1) vial. BSA, Phosphate buffer, detergents, ProClin® 300, preservatives, an inert yellow dye.
Calibrator 2 (0.6 mL)	[CAL 2]	One (1) vial. Anti-SARS-CoV-2 Human IgM monoclonal antibody, BSA, phosphate buffer, detergents, ProClin® 300, preservatives, an inert blue dye.
Specimen Diluent (22 mL)	[DIL SPE]	One (1) vial. Goat serum to human IgG (adsorbent reagent), BSA, phosphate buffer, ProClin® 300, preservatives.
Assay Buffer (14 mL)	[BUF]	BSA, phosphate buffer, EDTA, detergents, ProClin® 300, preservatives, an inert yellow dye.
Conjugate (25 mL)	[CONJ]	Mouse monoclonal IgG to human IgM conjugated to an isoluminol derivative, BSA, phosphate buffer, non-specific IgG, ProClin® 300, preservatives.
Number of tests		110

All reagents are supplied ready to use. The order of reagents reflects the layout of containers in the Reagent Integral.

ProClin® is a trademark of the Dow Chemical Company (Dow) or an affiliated company of Dow.

Materials required but not provided

LIAISON® XL Cuvettes ([REF] X0016).

LIAISON® XL Disposable Tips ([REF] X0015) or LIAISON® Disposable Tips ([REF] X0055).

LIAISON® XL Starter Kit ([REF] 319200) or LIAISON® EASY Starter Kit ([REF] 319300).

LIAISON® Wash/System Liquid ([REF] 319100).

LIAISON® XL Waste Bags ([REF] X0025).

LIAISON® XL Cleaning Tool ([REF] 310995)

Additional required materials:

LIAISON® Control SARS-CoV-2 IgM ([REF] 311481).

5. WARNINGS AND PRECAUTIONS


- For Emergency Use Authorization Only.
- For *in vitro* diagnostic use.
- For professional use only.
- 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.
- This test has been authorized only for the presence of IgM antibodies against SARS-CoV-2, not for any other viruses or pathogens.
- 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.
- Observe the normal precautions required for handling all laboratory reagents.
- Do not eat, drink, smoke or apply cosmetics during the assay.
- Do not pipette by mouth.
- Strict adherence to the LIAISON® SARS-CoV-2 IgM assay instructions is necessary to obtain accurate results.
- Avoid direct contact with potentially infectious substances by wearing appropriate personal protective equipment such as laboratory coats, goggles, and disposable gloves. Wash hands thoroughly after removal of gloves.
- Avoid splashing or aerosolization of samples or reagents. All drops and spills must be wiped up with an appropriate disinfectant such as a sodium hypochlorite solution with 0.5% active chlorine, and all soiled materials must be disposed of as infected waste.
- Visually inspect the integral vials for leaking at the membrane seals or elsewhere. If the vials are found to be leaking, discard them and the local customer service should be notified immediately.
- All waste associated with biological samples, biological reagents and disposable materials used for the assay must be considered potentially infectious and therefore should be disposed of in accordance with the national, state or local regulations and guidelines of the agencies holding jurisdiction over the laboratory.
- The LIAISON® XL Analyzer should be cleaned and decontaminated on a routine basis. See the LIAISON® XL Analyzer

- Operator's Manual for the cleaning and decontamination procedures.
- Any materials for reuse must be appropriately sterilized in compliance with the local laws and guidelines. Check the effectiveness of the sterilization/decontamination cycle.
- Previously frozen test samples, once thawed, must be thoroughly mixed prior to testing.
- Do not pool the contents of different vials of the same reagent (even if the reagents are from the same lot).
- Do not use kits or components beyond the expiration date indicated on the label.

Chemical Hazard and Safety Information

Reagents in this kit are classified in accordance with the US OSHA Hazard Communication Standard; individual US State Right-to-Know laws; Canadian Centre for Occupational Health and Safety Controlled Products Regulations; and European Union EC Regulation 1272/2008 (CLP) (for additional information see Safety Data Sheet available on www.diasorin.com).

Pursuant to EC Regulation 1272/2008 (CLP), hazardous reagents are classified and labeled as follows:

REAGENTS:	[CAL 1], [CAL 2], [DIL SPE], [BUF], [CONJ]
CLASSIFICATION:	Skin sens. 1 H317
SIGNAL WORD:	Warning
SYMBOLS / PICTOGRAMS:	 GHS07 Exclamation mark
HAZARD STATEMENTS:	H317 May cause an allergic skin reaction.
PRECAUTIONARY STATEMENTS:	P261 Avoid breathing dust/fume/gas/mist/vapours/spray. P280 Wear protective gloves/protective clothing/eye protection/face protection. P363 Wash contaminated clothing before reuse.
CONTAINS: (only substances prescribed pursuant to Article 18 of EC Regulation 1272/2008).	reaction mass of: 5-chloro-2-methyl-4-isothiazolin-3-one [EC no. 247-500-7] and 2-methyl-2H-isothiazol-3-one [EC no. 220-239-6] (3:1) (ProClin® 300).

Reagent containing sodium azide (Magnetic Particles [SORB])

Sodium azide may react with lead or copper plumbing to form highly explosive metal azides. Immediately after disposal, flush with a large volume of water to prevent azide build-up. For further information, refer to "Decontamination of Laboratory Sink Drains to Remove Azide Salts", in the Manual Guide-Safety Management No. CDC-22 issued by the Centers for Disease Control and Preventions, Atlanta, GA, 1976.

Pursuant to EC Regulation 1272/2008 (CLP), [SORB] is labeled as EUH210, safety data sheets available on request.

For additional information, see Safety Data Sheets available on www.diasorin.com.

6. REAGENT PREPARATION

REAGENT INTEGRAL

Please note the following important reagent handling precautions.

Resuspension of magnetic particles

Magnetic particles must be completely resuspended before the Reagent Integral is placed on the LIAISON® XL Analyzer. Follow the steps below to ensure complete resuspension:

- Before the seal is removed, rotate the small wheel at the magnetic particle vial compartment until the color of the suspension has changed to brown.
- Gentle and careful side-to-side mixing may assist in the resuspension of the magnetic particles (avoid foam formation).
- Visually check the bottom of the magnetic particle vial to confirm that all settled magnetic particles have been resuspended.
- Carefully wipe the surface of each septum to remove residual liquid.
- Repeat all steps as necessary until the magnetic particles are completely resuspended.

Foaming of Reagents

In order to ensure optimal performance of the Reagent Integral, foaming of all reagents should be avoided. Follow the steps below to prevent foaming of reagents:

- Visually inspect the reagents, calibrators in particular (located in position two and three following the magnetic particle vial), to ensure there is no foaming present before using the Reagent Integral.
- If foam is present after resuspension of the magnetic particles, place the integral on the LIAISON® XL Analyzer and allow the foam to dissipate.
- The Reagent Integral is ready for use once the foam of all reagents has dissipated and the integral is positioned onboard the LIAISON® XL Analyzer and mixing.

Loading of Reagent Integral into the Reagent Area

- The LIAISON® XL Analyzer is equipped with a built-in solid-state magnetic device which aids in complete resuspension of microparticles prior to placement of the Reagent Integral into the reagent area of the instrument. Refer to the LIAISON® XL Analyzer operator's manual for details.
 - Insert the Reagent Integral into the dedicated slot.
 - Allow the Reagent Integral to remain in the solid-state magnetic device for at least 30 seconds (up to several minutes). Repeat as necessary.
- Place the Reagent Integral into the reagent area of the LIAISON® XL Analyzer with the label facing left and let it stand for

15 minutes before using. The analyzer automatically stirs and completely resuspends the magnetic particles. Follow the analyzer operator's manual to load the specimens and start the run.

CONTROLS

Refer to the LIAISON® Control SARS-CoV-2 IgM Instructions for Use section for proper preparation and handling instructions.

7. REAGENT INTEGRAL STORAGE AND STABILITY

Upon receipt, the Reagent Integral must be stored in an upright position to facilitate resuspension of the Magnetic Particles. Refer to Reagent Integral Preparation (Section 6) for resuspension instructions.

- **Sealed:** Stable at 2-8°C until the expiry date.
- **Opened on board or at 2-8°C:** Stable up to one week.
- Use storage rack provided with the LIAISON® XL Analyzer for upright storage of Reagent Integral.
- Do not freeze.
- Keep upright for storage to facilitate later proper resuspension of magnetic particles.
- Keep away from direct light.

8. SPECIMEN COLLECTION AND PREPARATION

The correct specimen type must be used in the assay. Following matrices have been tested and may be used:

- serum;
- sodium and lithium heparin plasma;
- dipotassium EDTA plasma.

Blood should be collected aseptically by venipuncture and the serum or plasma separated from clot, red cells or gel separator carefully following the tube manufacturers' instructions and according to good laboratory practices.

Centrifugation conditions of collection tubes may vary depending on the manufacturer. A minimum of 1,000g for 10 minutes is reported. Use of centrifugation conditions should be evaluated and validated by the laboratory.

Package and label specimens in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances.

Specimens may be shipped on dry ice (frozen), on wet ice (for 2°-8°C), following the sample storage limitations described below.

Uncontrolled transport conditions (in terms of temperature and time) may cause inaccurate analytical results. During validation studies, specimen collection tubes commercially available at the time of testing were used. Therefore, not all collection tubes from all manufacturers have been evaluated. Blood collection devices from various manufacturers may contain substances which could affect the test results in some cases (Bowen et al., Clinical Biochemistry, 43, 4-25, 2010). It is the responsibility of the individual laboratory to use all available references and/or its own studies to determine specific stability criteria for its laboratory⁽¹¹⁾.

A dedicated study on storage limitations was performed on serum or plasma specimens removed from clot, red cells or gel separator. The following storage conditions showed no significant differences:

- 2°- 8°C for 4 days, otherwise they should be aliquoted and stored deep-frozen (-20°C or below);
- Up to 3 freeze-thaw cycles, however multiple freeze thaw cycles should be avoided.

If samples are stored frozen, mix thawed samples well before testing.

Further centrifugation of specimens previously removed from red cells, clot or gel separator is recommended (suggested between 3,000 and 10,000 g for 10 minutes) to guarantee the consistency of results whenever one of the following conditions is identified:

- Samples previously centrifuged and stored at 2-8°C
- Samples with particulate matter, fibrin, turbidity, lipaemia or erythrocyte debris;
- Samples frozen and thawed;
- Samples requiring repeat testing.

Specimens with a lipid layer on the top should be transferred into a secondary tube, taking care to transfer only the clarified material.

Grossly haemolyzed or lipaemic samples as well as samples containing particulate matter or exhibiting obvious microbial contamination should not be tested. Heat inactivation of the specimens may affect the test results. Check for and remove air bubbles before assaying.

The minimum volume required for a single determination is 164 µL of specimen (14 µL specimen + 150 µL dead volume).

9. CALIBRATION

Testing of assay specific calibrator allows the detected relative light unit (RLU) values to set the cut-off.

Each calibration solution allows 4 calibrations to be performed.

Recalibration in triplicate is mandatory whenever at least one of the following conditions occurs:

- A new lot of Starter Kit is used.
- The previous calibration was performed more than 1 week before.
- A new lot of Reagent Integral is used.
- The analyzer has been serviced.
- Control values lie outside the expected ranges.

10. ASSAY PROCEDURE

Strict adherence to the analyzer operator's manual ensures proper assay performance. Each test parameter is identified via information encoded in the Reagent Integral Radio Frequency IDentification transponder (RFID Tag). In the event that the RFID Tag cannot be read by the analyzer, the integral cannot be used. Do not discard the reagent integral; contact your local DiaSorin technical support for instruction.

The analyzer operations are as follows:

1. Dispense specimens (calibrator or control), coated magnetic particles, specimen diluent and assay buffer into the reaction cuvettes
2. Incubate and wash
3. Dispense the Conjugate into the reaction cuvettes
4. Incubate and wash
5. Add the Starter Reagents and measure the light emitted.

Warning - Maintenance with the LIAISON® XL Cleaning Tool ([REF] 310995) must be performed (refer to pertinent instruction for use for details)

11. QUALITY CONTROL

The LIAISON® Control SARS-CoV-2 IgM ([REF] 311481) is recommended for the determination of quality control requirements for this assay and should be run in singlicate to monitor the assay performance.

Quality control is recommended once per day of use, or in accordance with local, state, and/or federal regulations or accreditation requirements and your laboratory's quality control procedures. It is recommended the user refer to CLSI document C24-A3 and 42 CFR 493.1256(c) for guidance on appropriate quality control practices (7).

The range of concentrations of each control is reported on the certificate of analysis and indicates the limits established by DiaSorin for control values that can be obtained in reliable assay runs.

The performance of other controls should be evaluated for compatibility with this assay before they are used. Appropriate value ranges should be established for all quality control materials used.

Quality control could be performed by running the LIAISON® Control SARS-CoV-2 IgM:

- at least once per day of use,
- whenever the kit is calibrated,
- whenever a new lot of Starter Reagents is used.

Control values must lie within the expected ranges: whenever one of the controls lies outside the expected ranges, calibration should be repeated and controls retested. If control values obtained after successful calibration lie repeatedly outside the predefined ranges, the test should be repeated using an unopened control vial. If control values lie outside the expected ranges, patient results must not be reported.

12. INTERPRETATION OF RESULTS

The analyzer automatically reads the light signal emitted from the chemiluminescence reaction and calculates an Index value and grades the results. For details, refer to the analyzer operator's manual.

Sample results should be interpreted as follows:

LIAISON® SARS-CoV-2 IgM assay		
Index	Results	Rules and interpretation
< 1.10	Negative	A result below the 1.10 Index may indicate the absence or level of IgM antibodies to SARS-CoV-2 below the limit of detection of the test. A negative result can also be seen in samples taken during an acute infection prior to seroconversion.
≥ 1.10	Positive	A result above or equal to the 1.10 Index generally indicates the presence of IgM antibodies to SARS-CoV-2 and generally indicates exposure to SARS-CoV-2.

Test results are reported qualitatively as positive or negative. If acute SARS-CoV-2 infection is suspected, direct molecular testing should be performed.

13. LIMITATIONS OF THE PROCEDURE

1. For prescription use only
2. For *in vitro* diagnostic use only
3. For Emergency Use Authorization Only
4. Performance has only been established with the specimens listed in the Intended Use. Other specimen types have not been evaluated and should not be used with this assay.
5. This test is for qualitative detection of anti-SARS-CoV-2 IgM antibody in human serum or plasma and does not measure the quantity of the antibodies.
6. It is not known at this time if the presence of antibodies to SARS-CoV-2 confers immunity to reinfection.
7. A skillful technique and strict adherence to the instructions are necessary to obtain reliable results.
8. Bacterial contamination or heat inactivation of the specimens may affect the test results.
9. Results from antibody testing should not be used to diagnose or exclude acute SARS-CoV-2 infection or to inform infection status. A molecular assay should be used to evaluate symptomatic patients for acute COVID-19.
10. Anti-SARS-CoV-2 antibodies may not be detectable in patients with recent infections (7 days or less) or patients who have been exhibiting symptoms for less than 3 days.
11. The individual immune response following SARS-CoV-2 infection varies considerably and might give different results with assays from different manufacturers. Results of assays from different manufacturers should not be used interchangeably.
12. Samples from individuals who exhibit COVID-19 symptoms for less than 8 days should not be tested.
13. A positive result may not indicate previous SARS-CoV-2 infection. Consider other information, including clinical history, local disease prevalence, and results of a second but different 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.
14. A positive result should be confirmed with another available method and interpreted in conjunction with the patient's clinical

information.

15. Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions. False positive may occur due to cross-reactivity from pre-existing antibodies or other possible causes. Samples with positive results should be confirmed with alternative testing method(s) and clinical findings. A negative result can occur if the quantity of the anti-SARS-CoV-2 antibodies present in the specimen is below the detection limits of the assay, or the antibodies that are detected are not present during the stage of disease in which a sample is collected.
16. Results from immunocompromised patients should be interpreted with caution.
17. This test should not be used for screening of donated blood.
18. Do not dilute specimens before testing

Conditions of Authorization for the Laboratory

The LIAISON® SARS-CoV-2 IgM Letter of Authorization, along with the authorized Fact Sheet for Healthcare Providers, the authorized Fact Sheet for Patients, and authorized labelling 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> or at www.diasorin.com.

Authorized laboratories using the LIAISON® SARS-CoV-2 IgM (“your product” in the conditions below), must adhere to the Conditions of Authorization indicated in the Letter of Authorization as listed below:

- A. Authorized laboratories using your product will include with result reports of your product, all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.
- B. Authorized laboratories using your product will use your product as outlined in the Instructions for Use. Deviations from the authorized procedures, including the authorized instruments, authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and authorized materials required to use your product are not permitted.
- C. Authorized laboratories that receive your product will notify the relevant public health authorities of their intent to run your product prior to initiating testing.
- D. 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.
- E. 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 DiaSorin Inc. (via DiaSorin S.p.A. or DiaSorin Inc. at www.diasorin.com) any suspected occurrence of false reactive or false non-reactive results and significant deviations from the established performance characteristics of your product of which they become aware.
- F. All laboratory personnel using your product must be appropriately trained in automated immunoassay 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.
- G. DiaSorin 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.”

14. SPECIFIC PERFORMANCE CHARACTERISTICS

14.1. Analytical specificity

Analytical specificity may be defined as the ability of the assay to accurately detect specific analyte in the presence of potentially interfering factors in the sample matrix (e.g., anticoagulants, haemolysis, effects of sample treatment), or cross-reactive antibodies.

Interference.

Controlled studies of potentially interfering substances showed no interference to each substance listed below with the LIAISON® SARS-CoV-2 IgM assay, at the indicated concentration.

Substances	Tested concentrations
Biotin	3500 ng/mL
Triglycerides	3000 mg/dL
Hemoglobin	1000 mg/dL
Unconjugated bilirubin	40 mg/dL
Conjugated bilirubin	40 mg/dL
Cholesterol total	500 mg/dL
Acetaminophen	500 mg/mL
Ibuprofen	500 mg/mL
Total Protein (high)	≥ 120 g/L
Total Protein (low)	≤ 60 g/L
Total IgM	5.5 mg/dL

Cross-reactions.

The cross-reactivity study for the LIAISON® SARS-CoV-2 IgM assay was designed to evaluate potential cross-reactivity from antibodies to other viruses that may cause symptoms similar to SARS-CoV-2 infection, other organisms that may cause infectious diseases, as well as from other conditions that may result from atypical immune system activity. Samples for the evaluation were collected before October 2018, prior to the SARS-CoV-2 pandemic. Three specimens out of 190 assessed specimens resulted Positive with the LIAISON® SARS-CoV-2 IgM assay. The results are summarized in the following table.

Condition	Number of tested samples	LIAISON® XL Positive results
Anti-nuclear auto-antibodies (ANA)	10	0
Anti-HBV	10	0
Anti-HCV	10	0
Anti-Influenza A	10	0
Anti-Influenza B	10	0
Anti-RSV	10	0
Anti-Mycoplasma pneumoniae	10	1
HAMA	10	1
Anti-Chlamydia pneumoniae	10	0
Mycobacterium tuberculosis	10	0
Anti-Borrelia burgdorferi	10	0
Anti-CMV	10	0
Anti-EBV	10	0
Anti-HSV 1/2	10	1
Anti-Parvovirus B19	10	0
Rheumatoid factor	10	0
Anti-Rubella Virus	10	0
Anti-VZV	10	0
Anti-HIV	10	0
Total	190	3

Additionally in the clinical evaluation, a total of 2,473 negative samples collected prior to December 2019, including 400 samples collected within the US, were tested with an overall specificity of 99.3%.

14.2. Precision

A five-day precision study was performed by using a coded panel of 6 serum samples prepared by either spiking or diluting samples as necessary to obtain negative, low positive and moderate positive samples. Kit Controls sets were also included in the study. The panel samples and kit controls were tested with the LIAISON® SARS-CoV-2 IgM assay in 6 replicates per run, 3 runs per day for 5 operating days on one LIAISON® XL Analyzer, on 2 kit lots. The CLSI document EP5-A3 was consulted in the preparation of the testing protocol.

The results refer to the groups of samples investigated and are not guaranteed specifications, as differences may exist between laboratories and locations.

Sample	N	Mean (Index)	Intra-Run		Between-Run		Between-Day		Between-Lot		Overall	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
RS1031	180	0.0527	0.003	5.9	0.002	3.8	0.002	3.2	0.005	10.2	0.007	12.8
RS1032	180	2.90	0.066	2.3	0.094	3.2	0.109	3.8	0.216	7.5	0.268	9.2
RS1033	180	2.61	0.064	2.5	0.079	3.0	0.086	3.3	0.197	7.5	0.237	9.1
COVM-01-U1	180	0.824	0.036	4.4	0.043	5.2	0.023	2.8	0.049	6.0	0.078	9.5
COVM-01-U2	180	0.830	0.036	4.3	0.041	4.9	0.009	1.1	0.054	6.6	0.077	9.3
COVM-01-U3	180	1.62	0.067	4.2	0.071	4.4	0.032	2.0	0.122	7.5	0.159	9.8
COVM-01-U4	180	1.90	0.071	3.7	0.055	2.9	0.037	1.9	0.127	6.7	0.160	8.4
COVM-01-U5	180	3.88	0.151	3.9	0.192	4.9	0.038	1.0	0.340	8.8	0.420	10.8
COVM-01-U6	180	4.45	0.126	2.3	0.159	3.6	0.087	2.0	0.361	8.1	0.423	9.5

14.3. Antibody Class Specificity

Upon treatment with DTT, five SARS-CoV-2 patient samples (initially positive for both IgG and IgM) remained positive for IgG when tested with the LIAISON® SARS-CoV-2 S1/S2 IgG assay and became negative for IgM when tested with the LIAISON® SARS-CoV-2 IgM assay. Upon affinity purification to remove IgG, five SARS-CoV-2 patient samples (initially positive for both IgG and IgM) became negative for IgG when tested with the LIAISON® SARS-CoV-2 S1/S2 IgG assay and remained positive for IgM when tested with the LIAISON® SARS-CoV-2 IgM assay. This study confirms the LIAISON® SARS-CoV-2 IgM assay is specific for the IgM class of antibodies.

15. SUMMARY OF CLINICAL PERFORMANCE

15.1. Positive percent agreement (PPA)

The positive percent agreement (PPA) between the LIAISON® SARS-CoV-2 IgM assay and the PCR comparator was determined by investigating 223 samples collected from 223 European patients. Infection with SARS-CoV-2 was confirmed by RT-PCR test at the time of the diagnosis.

LIAISON® SARS-CoV-2 IgM tests were performed on samples collected at the time of admission and thereafter up to 30 days. The group included patients hospitalized with moderate symptoms, patients admitted to the ICU with severe symptoms and patients not hospitalized without or with mild symptoms.

The following table describes LIAISON® SARS-CoV-2 IgM clinical sensitivity in three groups, i.e. the early samples (≤ 7 days after diagnosis), the samples between 8 and 14 days after diagnosis, and the later samples (15 – 30 days after diagnosis).

	LIAISON® SARS-CoV-2 IgM		Total	PPA (Wilson 95% CI)
	Negative	Positive		
≤ 7 days	36	65	101	64.4% (54.6% - 73.0%)
8-14 days	4	37	41	90.2% (77.5% - 96.1%)
15 – 30 days	6	75	81	92.6% (84.8% - 96.6%)

15.2. Negative percent agreement (NPA)

2473 presumed SARS-CoV-2 negative samples collected before the COVID19 outbreak from a European laboratory routine (n=1072), a US laboratory routine (n=400) and European blood donors (n= 1001) were tested LIAISON® SARS-CoV-2 IgM assays resulting in a NPA of 99.3% (2455 / 2473, 95% CI: 98.9% – 99.5%).

15.3. Seroconversion study

A longitudinal study to evaluate seroconversion was conducted using a total of 268 samples collected over the course of time from 223 COVID-19 European patients. The table below represents the study design and results of serial bleeds by days from symptom onset:

Days from Symptom Onset	1 st serial measurement		2 nd serial measurement		>2 nd serial measurement		Total Bleeds
	Number of Samples Tested	IgM Positive Results	Number of Samples Tested	IgM Positive Results	Number of Samples Tested	IgM Positive Results	
≤ 7	101	65	4	3	0	0	
8 to 14	41	37	5	5	1	1	
15 to 30	81	75	20	19	15	15	
TOTAL	223		29		16		268

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For Customer Service in the U.S. and Canada call toll free: 1-800-328-1482.

LIAISON® Control SARS-CoV-2 IgM ([REF] 311481)

1. INTENDED USE

The DiaSorin LIAISON® SARS-CoV-2 IgM controls (negative and positive) are intended for use as assayed quality control samples to monitor the performance of the DiaSorin LIAISON® SARS-CoV-2 IgM assay. The performance characteristics of DiaSorin LIAISON® SARS-CoV-2 IgM controls have not been established for any other assays or instrument platforms.

For Emergency Use Authorization Only.

Caution: U.S. Federal Law restricts this device to sale by or on the order of a licensed practitioner.

For *in vitro* diagnostic use only.

2. MATERIALS PROVIDED

Negative control (2 x 0.9 mL)	[CONTROL]-]	Two (2) vials. Human serum non-reactive for SARS-CoV-2 IgM antibodies, with ProClin® 300, preservatives.
Positive control (2 x 0.9 mL)	[CONTROL +]	Two (2) vials. Human IgM monoclonal antibody diluted in human serum with ProClin® 300, preservatives.

ProClin® is a trademark of the Dow Chemical Company (Dow) or an affiliated company of Dow.

All reagents are supplied ready to use. The range of values of each control is reported on the certificate of analysis and indicates the limits established by DiaSorin for control values that can be obtained in reliable assay runs. Each laboratory is responsible for adopting different limits to meet individual requirements.

The certificate of analysis bar codes gives specific information on the lot of controls and should be read by the hand-held bar code scanner of the LIAISON® XL Analyzer prior to loading the control vials on board. For details, refer to the analyzer operator's manual.

3. WARNINGS AND PRECAUTIONS

- For prescription use only
- For Emergency Use Authorization Only.
- For *in vitro* diagnostic use.
- 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.
- This test has been authorized only for the presence of IgM antibodies against SARS-CoV-2, not for any other viruses or pathogens.
- 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.
- Controls are not kit lot specific and may be safely interchanged even with different Reagent Integral lots.
- All materials used to produce the components provided in this kit have been tested for the presence of HBsAg, anti-HCV, anti-HIV-1, anti-HIV-2 and found to be non-reactive.
- As, however, no test method can offer absolute assurance that pathogens are absent, all specimens of human origin should be considered potentially infectious and handled with care.
- Observe the normal precautions required for handling all laboratory reagents.
- Disposal of all waste material should be in accordance with local guidelines.


4. SAFETY PRECAUTIONS

- Do not eat, drink, smoke or apply cosmetics in the assay laboratory. Do not pipette by mouth.
- Avoid direct contact with potentially infected material by wearing laboratory clothing, protective goggles, and disposable gloves. Wash hands thoroughly at the end of each assay.
- Avoid splashing or forming an aerosol. All drops of biological reagent must be removed with a sodium hypochlorite solution with 0.5% active chlorine, and the means used must be treated as infected waste.
- All samples and reagents containing biological materials used for the assay must be considered as potentially able to transmit infectious agents. The waste must be handled with care and disposed of in compliance with the laboratory guidelines and the statutory provisions in force in each Country. Any materials for reuse must be appropriately sterilized in compliance with the local laws and guidelines. Check the effectiveness of the sterilization/decontamination cycle.
- Do not use kits or components beyond the expiration date given on the label.

Chemical Hazard and Safety Information

Reagents in this kit are classified in accordance with the US OSHA Hazard Communication Standard; individual US State Right-to-Know laws; Canadian Centre for Occupational Health and Safety Controlled Products Regulations; and European Union EC Regulation 1272/2008 (CLP) (for additional information see Safety Data Sheet available on www.diasorin.com).

Pursuant to EC Regulation 1272/2008 (CLP) hazardous reagents are classified and labeled as follows:

REAGENTS:	[CONTROL]-, [CONTROL]+
CLASSIFICATION:	Skin sens. 1 H317
SIGNAL WORD:	Warning
SYMBOLS / PICTOGRAMS:	 GHS07 Exclamation mark
HAZARD STATEMENTS:	H317 May cause an allergic skin reaction.
PRECAUTIONARY STATEMENTS:	P261 Avoid breathing dust/fume/gas/mist/vapours/spray. P280 Wear protective gloves/protective clothing/eye protection/face protection. P363 Wash contaminated clothing before reuse.
CONTAINS: (only substances prescribed pursuant to Article 18 of EC Regulation 1272/2008).	reaction mass of: 5-chloro-2-methyl-4-isothiazolin-3-one [EC no. 247-500-7] and 2-methyl-2H -isothiazol-3-one [EC no. 220-239-6] (3:1). (ProClin® 300).

5. STORAGE AND STABILITY

Upon receipt, the controls must be stored at 2-8°C in an upright position to prevent adherence of the solution to the vial cap. Do not freeze. When controls are stored sealed and kept upright, they are stable at 2-8°C up to the expiry date. Once opened controls are stable up to four weeks when properly stored at 2-8°C. Avoid bacterial contamination of controls. The controls should not be used past the expiry date indicated on the vial labels.

6. PREPARATION OF REAGENTS

- Place the control vials in type C racks on the LIAISON® XL analyzer. Each control vial allows at least 20 tests to be performed.
- The dead volume is 400 µL.
- At the time of use, equilibrate controls to room temperature (20-25°C) before opening the vials and keep them on board the instrument only for the amount of time required for quality control testing.
- After use, stopper the vials promptly and store them at 2-8°C in an upright position.
- During handling, use appropriate precautions to avoid bacterial contamination of controls.

7. LIMITATIONS

Control values for assays other than the LIAISON® SARS-CoV-2 IgM assay have not been established. If users wish to use this control material with other assays, it is their responsibility to establish appropriate ranges.

The performance of other controls should be evaluated for compatibility with this assay before they are used. Appropriate reference ranges should be established for all quality control materials used.

If control values obtained after successful calibration lie repeatedly outside the expect ranges, the test should be repeated using an unopened control vial.

8. ASSIGNED VALUES

The ranges of SARS-CoV-2 IgM concentration in the controls are printed on the certificate of analysis. They have been established after taking into account run variability, in order to guarantee accuracy of analytical results and to obtain indications on stability or deterioration of reagents.

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