



Changes: §1, 5, 13;
Deletions: -

LIAISON® SARS-CoV-2 S1/S2 IgG ([REF] 311460)

For Emergency Use Authorization Only.

For *in vitro* diagnostic use only.

For prescription use only.

1. INTENDED USE

The LIAISON® SARS-CoV-2 S1/S2 IgG is a chemiluminescent immunoassay (CLIA) intended for the qualitative detection of IgG antibodies to SARS-CoV-2 in human serum, and plasma (sodium heparin, lithium heparin, and potassium EDTA). The LIAISON® SARS-CoV-2 S1/S2 IgG is intended for use as an aid in identifying individuals with an adaptive immune response to SARS-CoV-2, indicating recent or prior infection. At this time, it is unknown for how long antibodies persist following infection and if the presence of antibodies confers protective immunity. The LIAISON® SARS-CoV-2 S1/S2 IgG should not be used to diagnose or exclude 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.

The LIAISON® SARS-CoV-2 S1/S2 IgG is to be used on the LIAISON® XL Analyzer.

Results are for the detection of SARS-CoV-2 antibodies. 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.

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 LIAISON® SARS-CoV-2 S1/S2 IgG may occur due to cross-reactivity from pre-existing antibodies or other possible causes.

The LIAISON® SARS-CoV-2 S1/S2 IgG 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. (1,2) As of April 20, 2020, 2,475,841 cases of COVID-19 were reported worldwide.

The causative virus of the COVID-19 is 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. (3)

The presence of IgG antibodies to SARS-CoV-2 is indicative of an immune response to infection; however, it is unknown whether the presence of IgG antibodies to SARS-CoV-2 confers protective immunity or for how long after infection IgG antibodies will remain detected. Patients can remain infectious in the presence of IgG if specimens are obtained during acute infection (5)

Currently molecular testing is available using reverse transcription-polymerase chain reaction (RT-PCR) for detecting viral RNA for early identification of SARS-CoV-2.

The coronavirus spike (S) glycoprotein is a class I viral fusion protein on the outer envelope of the virion that plays a critical role in viral infection by recognizing host cell receptors and mediating fusion of the viral and cellular membranes. Coronavirus entry into host cells is mediated by the transmembrane spike (S) glycoprotein that forms homotrimers protruding from the viral surface. S comprises two functional subunits responsible for binding to the host cell receptor (S1 subunit) and fusion of the viral and cellular membranes (S2 subunit). (6)

The spike and nucleocapsid proteins are major immunogenic components of CoVs and are produced in abundant quantities during acute infection. (7)

3. PRINCIPLE OF THE PROCEDURE

The method for qualitative determination of IgG anti-S1 and IgG anti-S2 specific antibodies to SARS-CoV-2 is an indirect chemiluminescence immunoassay (CLIA). The specific recombinant S1 and S2 antigens are used for coating magnetic particles (solid phase) and mouse monoclonal antibodies to human IgG are linked to an isoluminol derivative (isoluminol-antibody conjugate). During the first incubation, the SARS-CoV-2 IgG antibodies present in calibrators, samples or controls bind to the solid phase through the recombinant S1 and S2 antigens. During the second incubation the antibody conjugate reacts with IgG to SARS-CoV-2 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 is indicative of the presence of IgG to SARS-CoV2 in calibrators, samples or controls.

4. MATERIALS PROVIDED

Reagent Integral

Magnetic particles (2.63 mL)	[SORB]	One (1) vial. Magnetic particles coated with biotinylated recombinant S1 and biotinylated recombinant S2 antigens (obtained in mammalian cells), biotinylated BSA, streptavidin, BSA, phosphate buffer, < 0.1% sodium azide.
Calibrator 1 (1.2 mL)	[CAL 1]	One (1) vial. Human serum/plasma containing low SARS-CoV-2 IgG levels, stabilized in TRIS buffer, 0.2% Proclin® 300, preservatives, an inert yellow dye.
Calibrator 2 (1.2 mL)	[CAL 2]	One (1) vial. Human serum/plasma containing high SARS-CoV-2 IgG levels, stabilized in TRIS buffer, 0.2% Proclin® 300, preservatives.
Specimen Diluent (23 mL)	[DIL SPE]	One (1) vial. BSA, phosphate buffer, detergent, EDTA, 0.2% ProClin® 300, sheep serum, preservatives.
Conjugate (25 mL)	[CONJ]	One (1) vial. Mouse monoclonal IgG to human IgG conjugated to an isoluminol derivative, BSA, phosphate buffer, 0.2% ProClin® 300, preservatives, an inert blue dye.
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)

Additional required materials:

LIAISON® Control SARS-CoV-2 S1/S2 IgG ([REF] 311461)

5. WARNINGS AND PRECAUTIONS

- For use under an Emergency Use Authorization Only.
- For *in vitro* diagnostic use only.
- For prescription 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 the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C 263a, to perform moderate or high complexity tests.
- This test has been authorized only for the detection of IgG 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* 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 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 S1/S2 IgG 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.
- All human serum and plasma units 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. 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.
- 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], [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/vapourous/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 colour 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.
 - a. Insert the Reagent Integral into the dedicated slot.
 - b. 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® SARS-CoV-2 S1/S2 IgG Control Set 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:** stability up to two weeks.
- 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;
- potassium EDTA.

Blood should be collected aseptically by venipuncture and the serum or plasma separated from clot, red cells or gel separator, after centrifugation, carefully following the tube manufacturers' instructions and according to good laboratory practices (8).

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).

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 2 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 removed from red cells, clot or gel separator (suggested between 3,000 and 10,000 g for 10 minutes) is recommended 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 170 µL of specimen (20 µL specimen + 150 µL dead volume).

9. CALIBRATION

Test of assay specific calibrators allows the detected relative light unit (RLU) values to adjust the assigned master curve. Each calibration solution allows four 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 two weeks before.

- Each time a new lot of 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 (or calibrator or control), coated magnetic particles, specimen diluent into the reaction cuvettes
2. Incubate and wash
3. Dispense Conjugate into the reaction cuvettes
4. Incubate and wash
5. Add the Starter Reagents and measure the light emitted.

11. QUALITY CONTROL

The LIAISON® Control SARS-CoV-2 S1/S2 IgG ([REF] 311461) 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.

Quality control could be performed by running the LIAISON® Control SARS-CoV-2 S1/S2 IgG:

- 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 calculates SARS-CoV-2 S1/S2 IgG antibody concentrations expressed as arbitrary units (AU/mL) and grades the results. For details, refer to the analyzer operator's manual.

Sample results should be interpreted as follows:

LIAISON® SARS-CoV-2 S1/S2 IgG assay		
AU/mL	Results	Interpretation of the Results
< 15.0	Negative	A negative result may indicate absence or level of IgG antibodies to SARS-CoV-2 below the limit of detection of this test. A negative result can also be seen in samples taken during an acute infection prior to IgG seroconversion.
≥ 15.0	Positive	A positive result indicates the presence of IgG antibodies to SARS-CoV-2 and generally indicates exposure to SARS-CoV-2.

Test results are reported qualitatively as positive or negative.

13. LIMITATIONS OF THE PROCEDURE

1. A skillful technique and strict adherence to the instructions are necessary to obtain reliable results.
2. Bacterial contamination or heat inactivation of the specimens may affect the test results.
3. Specimens from patients receiving therapeutic doses of Biotin (Vitamin H, B7 or B8) may interfere in immunoassays based on biotinylated reagents. Interference was not observed testing Biotin serum concentration up to 3500 ng/mL with LIAISON® SARS-CoV-2 S1/S2 IgG assay (for details, refer to §14).
4. Use of the LIAISON® SARS-CoV-2 S1/S2 IgG is limited to laboratory personnel who have been trained. Not for home use.
5. 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.
6. Negative results do not preclude SARS-CoV2 infection and should not be used as the sole basis for patient management decisions. False-positive results for IgG antibodies may occur due to cross-reactivity from pre-existing antibodies or other possible causes.
7. 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 the antibodies that are detected are not present during the stage of disease in which a sample is collected.
8. Results from antibody testing should not be used to diagnose or exclude acute SARS-CoV-2 infection or to determine infection status.
9. Detection of IgG antibodies against SARS-CoV-2 at present is not yet established to determine long term immunity to the virus or to protect the patient against re-infection by the virus.
10. 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 a second but different serology test to confirm an immune response.
11. The results obtained with this test should only be interpreted in conjunction with clinical findings, and the results from other laboratory tests and evaluations. This is especially important if the patient has had recent exposure to COVID-19, or

clinical presentation indicates that COVID-19 is likely and diagnostic tests for other causes of illness (e.g., other respiratory illness) are negative. In this case, direct testing for the SARS-CoV-2 virus (e.g. PCR testing) should be considered.

12. This test should not be used for screening of donated blood.
13. 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. This device should not be used for the screening of donated blood.
15. The performance of this device 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.
16. The performance of this test was established based on the evaluation of a limited number of clinical specimens collected from February to April of 2020 from multiple sites in Italy. Clinical performance has not been established with 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.

Conditions of Authorization for the Laboratory

The LIAISON® SARS-CoV-2 S1/S2 IgG 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/in-vitro-diagnostics-euas> or at www.diasorin.com.

Authorized laboratories using the LIAISON® SARS-CoV-2 S1/S2 IgG (“your product” in the conditions below), must adhere to the Conditions of Authorization indicated in the Letter of Authorization are 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/OHT-7-OIR/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov) and DiaSorin S.p.A. or DiaSorin Inc. at www.diasorin.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.
- 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 S.p.A., 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 and 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 in the LIAISON® SARS-CoV-2 S1/S2 IgG assay, at the indicated concentration.

Substances	Tested concentrations
Triglycerides	3000 mg/dL
Hemoglobin	1000 mg/dL
Unconjugated bilirubin	40 mg/dL
Conjugated bilirubin	40 mg/dL
Cholesterol total	400 mg/dL
Acetaminophen	500 mg/mL
Ibuprofen	500 mg/mL

The LIAISON® SARS-CoV-2 S1/S2 IgG assay demonstrated up to a 16% negative Bias in SARS-CoV-2 IgG positive specimens with biotin concentrations of 3500 ng/mL.

Cross-reactions.

The cross-reactivity study for the LIAISON® SARS-CoV-2 S1/S2 IgG assay was designed to evaluate potential cross-reactivity to antibodies to other viruses that may cause symptoms similar to SARS-CoV-2 infection, to other organisms that may cause infectious diseases, as well as to other conditions that may result in atypical immune system activity. Samples for the evaluation were collected before October 2019, prior to the SARS-CoV-2 pandemic. Three (3) specimens out of 168 assessed specimens resulted Positive with the LIAISON® SARS-CoV-2 S1/S2 IgG assay. The results are summarized in the following tables.

Non-SARS Human Coronavirus Condition	Number of tested samples	LIAISON® XL Positive results
Anti-Human CoVOC43	3	0
Anti-Human CoVHKU1	1	0
Anti-Human CoV unknown strain	4	0
Total	8	0

Condition	Number of tested samples	LIAISON® XL Positive results
Anti-nuclear autoantibodies (ANA)	10	0
Anti-HBV	10	1
Anti-HCV	10	0
Anti-Influenza A	10	1
Anti-Influenza B	10	0
Anti-respiratory syncytial virus	10	0
Anti-borrelia burgdorferi	10	0
Anti-Mycoplasma pneumoniae	10	0
Anti-EBV	10	0
Anti-CMV	10	0
Anti-HSV-1/2	10	0
HAMA	10	0
Anti-Parvovirus B19	10	0
Rheumatoid factor	10	1
Anti-Rubella	10	0
Anti-VZV	10	0
Total	160	3

14.2 Precision

A five day precision study was performed by using a coded panel of 6 plasma samples prepared by either spiking or diluting samples as necessary to obtain negative, low positive and moderate positive samples. Kit Controls were also included in the study. The panel samples and kit controls were tested with LIAISON® SARS-CoV-2 S1/S2 IgG assay in 6 replicates per run, 3 runs per day for five operating days on one LIAISON® XL Analyzer. The CLSI document EP5-A3 was consulted in the preparation of the testing protocol.

			Within run		Between run		Between day		Overall	
Data	N	Mean (AU/mL)	SD	CV %	SD	CV %	SD	CV %	SD	CV %
RS1011 Neg	90	626*	22.14	3.5	26.44	4.2	47.89	7.6	59.0	9.4
RS1013 Neg	90	884*	46.58	5.3	20.58	2.3	97.89	11.1	110	12.5
RS1012 Pos	90	28.1	0.94	3.3	0.51	1.8	1.04	3.7	1.49	5.3
RS1014 Pos	90	28.3	0.75	2.6	0.03	0.1	0.64	2.3	0.99	3.5
COVG-1-U1	90	5.45	0.14	2.5	0.06	1.0	0.00	0.00	0.15	2.7
COVG-1-U2	90	6.72	0.23	3.4	0.13	1.9	0.00	0.0	0.26	3.9
COVG-1-U3	90	11.1	0.34	3.0	0.09	0.8	0.15	1.3	0.38	3.4
COVG-1-U4	90	20.2	0.54	2.7	0.29	1.4	0.27	1.3	0.67	3.3
COVG-1-U5	90	40.1	1.14	2.8	0.28	0.7	0.00	0.0	1.17	2.9
COVG-1-U6	90	64.1	1.68	2.6	0.70	1.1	0.35	0.5	1.86	2.9

* AU/mL values for the Negative Controls fall below the assay range and were evaluated based on RLUs instead of AU/mL.

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

15. SUMMARY OF CLINICAL PERFORMANCE

15.1 Clinical study

The positive percent agreement (PPA) between the LIAISON® SARS-CoV-2 S1/S2 IgG assay and the PCR comparator was determined by investigating 135 samples collected over the course of time from 76 European patients. Infection with SARS-CoV-2 was confirmed by RT-PCR test at the time of the diagnosis.

The LIAISON® SARS-CoV-2 S1/S2 IgG test was performed on samples collected at the time of admission and thereafter up to 36 days for 44 patients hospitalized with moderate symptoms and 11 admitted to the ICU with severe symptoms.

Twenty-one single samples were from RT-PCR confirmed COVID-19 patients who were admitted to the ICU with known sample collection dates relative to PCR diagnosis.

The following table describes positive percent agreement by time of sampling following a PCR positive result.

Summary of the IgG positive results with the LIAISON® SARS-CoV-2 S1/S2 IgG assay from 76 patients SARS-CoV-2 PCR positive admitted in 3 hospitals:

Days from Diagnosis	First Serial Measurement		Second Serial Measurement		Third Serial Measurement ⁴		Total IgG Results	PPA (95%CI)
	Samples tested	Samples with IgG + Results	Samples tested	Samples with IgG + Results	Samples tested	Samples with IgG + Results		
≤ 5 days	44	11/44	-	-	-	-	11/44 (25%)	25.00% (14.57% to 39.44%)
6-14 days	18	16/18	30	27/30 ¹⁻²	1	1/1	44/49 (89.80%)	89.80% (78.24% to 95.56%)
≥15 days	14	14/14	19	18/19 ³	8	8/8 ⁴	40/41 (97.56%)	97.56% (87.40% to 99.57%)
Total Subjects	76	-	49	-	9	-	-	-

¹After 6-14 days from diagnosis (PCR+ result), 17 out of the 19 IgG positive subjects had PCR negative results

²One patient had a sample taken at day 6 and at day 12 from diagnosis. Both were IgG+.

³After 15 days from PCR diagnosis (PCR + result), 5 out of 6 IgG positive subjects had PCR negative results

⁴After 36 days from diagnosis (PCR+ result), one patient had a fourth sample taken that was IgG+

15.2 Negative Percent Agreement (NPA)

One thousand ninety (n=1090) presumed SARS-CoV-2 negative samples from a European laboratory routine (n=90) and European blood donors (n=1000) were collected prior to COVID-19 and tested with the LIAISON® SARS-CoV-2 S1/S2 IgG. From the samples tested, 1082 out of 1090 were negative resulting in a NPA of 99.3% (95% CI: 98.6 – 99.6%).

REFERENCES:

1. European Centre for Disease Prevention and Control (ECDC). Novel Coronavirus. Available from: <https://www.ecdc.europa.eu/en/novel-coronavirus-china> (last page update March 24 2020)
2. European Centre for Disease Prevention and Control (ECDC). Geographical distribution 2019.
3. Wang G, Jin X. The progress of 2019 Novel Coronavirus (2019-nCoV) event in China. *J Med Virol*. doi: 10.1002/jmv.25705
4. World_Health_Organization. Laboratory testing for coronavirus disease (COVID-19) in suspected human cases; ad interim – March 19, 2020.
Available from: <https://www.ecdc.europa.eu/en/geographical-distribution-2019-ncov-cases> (last page update March 24 2020)
5. Kelvin Kai-Wang To, Owen Tak-Yin Tsang et al.: Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. March 23, 2020 *Lancet Infectious Diseases*
6. Structure, Function, and Antigenicity of the SARS-CoV-2 Spike Glycoprotein. Walls, Park, Tortorici, Wall, McGuire, Veesler. *Cell* 180, 1–12, March 19, 2020^a 2020 Elsevier Inc. Correspondence: dveesler@uw.edu - <https://doi.org/10.1016/j.cell.2020.02.058>
7. Fan Wu et al, Neutralizing antibody responses to SARS-CoV-2 in a COVID-19 recovered patient cohort and their implications *medRxiv* 2020.03.30.20047365; doi: <https://doi.org/10.1101/2020.03.30.20047365>
8. Clinical and Laboratory Standards Institute (CLSI) H18-A4, Vol.30, No.10, Procedures for the Handling and Processing of Blood Specimens for Common Laboratory Tests; Approved Guideline – Fourth Edition
9. Grimsey, Paul, et al.: Population pharmacokinetics of exogenous biotin and the relationship between biotin serum levels and in vitro immunoassay interference. 2017 *International journal of Pharmacokinetics* 2.4: 247-256.
10. Piketty, Marie-Liesse, et al.: High-dose biotin therapy leading to false biochemical endocrine profiles: validation of a simple method to overcome biotin interference. *Clinical Chemistry and Laboratory Medicine (CCLM)* 2017 55.6: 817-825

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

LIAISON® Control SARS-CoV-2 S1/S2 IgG ([REF] 311461)

1. INTENDED USE

The LIAISON® SARS-CoV-2 S1/S2 IgG controls (negative and positive) are intended for use as assayed quality control samples to monitor the performance of the LIAISON® SARS-CoV-2 S1/S2 IgG assay. The performance characteristics of LIAISON® SARS-CoV-2 S1/S2 IgG controls have not been established for any other assays or instrument platforms.

For Emergency Use Authorization Only.

For *in vitro* diagnostic use only.

For Prescription Use Only.

2. MATERIALS PROVIDED

Negative control (2 x 0.9 mL)	[CONTROL-]	Two (2) vials. Human serum non-reactive for SARS-CoV-2 S1/S2 IgG antibodies, 0.2% ProClin®300, preservatives.
Positive control (2 x 0.9 mL)	[CONTROL+]	Two (2) vials. Human serum/plasma reactive for SARS-CoV-2 S1/S2 IgG antibodies, 0.2% 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

- This test has not been FDA cleared or approved
- This test has been authorized for emergency use by FDA under an EUA for use by authorized laboratories;
- This test has been authorized only for the detection of IgG 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* diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.
-
- For use under an Emergency Use Authorization Only.
- For *in vitro* diagnostic use.
- 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 S1/S2 IgG 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 S1/S2 IgG 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.