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Changes: §
Deletions: §

LIAISON® CMV IgG ([REF] 310740)

1. INTENDED USE

The LIAISON® CMV IgG assay uses chemiluminescent immunoassay (CLIA) technology on the LIAISON® Analyzer family* for the qualitative determination of IgG antibodies to human cytomegalovirus (hCMV) in human serum. It is intended to be used as an aid in the determination of serological status to CMV.
Caution: U.S. Federal Law restricts this device to sale by or on the order of a licensed practitioner.

This assay is not FDA-cleared for use in testing (i.e. screening) blood or plasma donors. The performance characteristics of this assay have not been established for cord blood or specimens from neonates, infants or pre-transplant patients.

2. SUMMARY AND EXPLANATION OF THE TEST

Human cytomegalovirus (hCMV) is a herpes virus. It is ubiquitous, species-specific, and spread by close human contact (1).
Primary infection may be acquired through different transmission routes and in different periods of life (e.g., congenital, perinatal and post-natal infections). Following primary infection, hCMV enters a latency phase during which the virus can be found in B lymphocytes. Subsequent reactivation of viral replication (secondary infection) may take place concomitantly with changes in the relationship between host and virus. Reinfection with exogenous virus can occur in subjects with deficiency of cellular immunity even when antibodies to hCMV are already present (2).
hCMV infection may be transmitted transplacentally (congenital) or at birth (perinatal). If seronegative women contract primary hCMV infection during pregnancy, the infection is transmitted to the fetus in about 40% of the cases and sequelae may be spontaneous abortion, stillbirth or neonatal malformation. The clinical picture of congenital hCMV infection may be mild to severe and includes psychomotor retardation, deafness, retinochoroiditis, microcephaly, hydrocephalus, cardiac disease, hepatitis, hepatosplenomegaly, or thrombocytopoenia (3).
Most individuals (40-90%) acquire primary hCMV infection during childhood or adulthood. Post-natal infections are transmitted through close contact with infected biological fluids (urine, saliva, breast milk, semen, cervical secretions, feces), infected blood products, and, occasionally, organ transplants. In immunocompetent individuals, the clinical picture of post-natal hCMV infection is usually mild or asymptomatic. The most common signs include fever, malaise, and increased serum transaminase levels without jaundice (1, 4).
By contrast in immunocompromised patients (organ transplant recipients, patients with AIDS, lymphoproliferative diseases, or cancer), symptoms may be severe because of disseminated and/or visceral infection, and may include splenomegaly, pneumonia, hemolytic anemia, myocarditis and encephalitis. In these patients the disease may be fatal (4, 5).
The immune response to hCMV involves synthesis of IgM antibodies some weeks after infection by hCMV, and later, IgG antibodies. Levels of IgM to hCMV usually increase for some weeks and decrease slowly thereafter, in four to six months. Occasionally, IgM may circulate for years. IgG antibodies rise gradually and persist for the rest of the host life. The specific IgG assay is useful in distinguishing subjects who have been exposed to the virus from those who have not (1).

3. PRINCIPLE OF THE PROCEDURE

The method for qualititative determination of specific IgG to hCMV is an indirect chemiluminescence immunoassay (CLIA). All assay steps (with the exception of magnetic particle resuspension) and incubations are performed by the Analyzer. The principal components of the test are magnetic particles (solid phase) coated with hCMV and a conjugate of mouse monoclonal antibody to human IgG linked to an isoluminol derivative (isoluminol-antibody conjugate). During the first incubation, hCMV antibodies present in calibrators, samples or controls bind to the solid phase. During the second incubation, the antibody conjugate reacts with hCMV IgG that is already bound to the solid phase. After each incubation, 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 hCMV IgG antibodies present in calibrators, samples or controls.

*(LIAISON® and LIAISON® XL)

4. MATERIALS PROVIDED

Reagent Integral

Magnetic particles (2.3 mL)	Magnetic particles coated with inactivated hCMV antigen (AD 169 strain) derived from infected MRC-5 cells, BSA, phosphate buffer, < 0.1% sodium azide.
Calibrator 1 (2.3 mL)	Human serum/defibrinated plasma containing low hCMV IgG levels, BSA, phosphate buffer, with ProClin® 300 as a preservative and an inert yellow dye. The calibrator concentration (U/mL*) is referenced to the proposed WHO International Standard preparation (1995) and is encoded in the Reagent Integral bar code.
Calibrator 2 (2.3 mL)	Human serum/defibrinated plasma containing high hCMV IgG levels, BSA, phosphate buffer, with ProClin® 300 as a preservative and an inert blue dye. The calibrator concentration (U/mL*) is referenced to the proposed WHO International Standard preparation (1995) and is encoded in the Reagent Integral bar code.
Specimen diluent (28 mL)	BSA, phosphate buffer, with ProClin® 300 as a preservative and an inert yellow dye.
Conjugate (23 mL)	Mouse monoclonal antibodies to human IgG conjugated to an isoluminol derivative, BSA, phosphate buffer, with ProClin® 300 and gentamicin sulfate as preservatives.
Number of tests	100

ProClin® is a registered trademark of Rohm and Haas Co.

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

* Calibration of the LIAISON® CMV IgG assay is not referenced to any established international standard.

Materials required but not provided (system related)

LIAISON® XL Analyzer	LIAISON® Analyzer
LIAISON® XL Cuvettes ([REF] X0016). LIAISON® XL Disposable Tips ([REF] X0015). LIAISON® XL Starter Kit ([REF] 319200). – LIAISON® Wash/System Liquid ([REF] 319100). LIAISON® XL Waste Bags ([REF] X0025). –	LIAISON® Module ([REF] 319130). – LIAISON® Starter Kit ([REF] 319102) or LIAISON® XL Starter Kit ([REF] 319200). LIAISON® Light Check ([REF] 319101). LIAISON® Wash/System Liquid ([REF] 319100). LIAISON® Waste Bags ([REF] 450003). LIAISON® Cleaning Kit ([REF] 310990).

Additionally required materials

LIAISON®Control CMV IgG([REF] 310741).

5. WARNINGS AND PRECAUTIONS

- For in vitro diagnostic use.
- The human blood source material used to produce the components provided in this kit derives from donations found to be non-reactive for HBsAg, antibodies to HCV, HIV-1 and HIV-2 when tested by an FDA-approved method and found to be non-reactive for syphilis when tested by a serological test. Because no test method can offer complete assurance that laboratory specimens are pathogen-free, specimens should be handled at the BSL 2 as recommended for any potentially infectious human serum or blood specimen in the CDC-NIH manual, Biosafety in Microbiological and Biomedical Laboratories, 5th Edition, Feb. 2007, and CLSI Approved Guideline M29-A3, Protection of Laboratory Workers from Occupationally Acquired Infections (6, 7, 8).
- Some reagents contain sodium azide as a preservative. Because sodium azide may form explosive lead or copper azide in plumbing, it is recommended that drains be thoroughly flushed with water after disposal of solutions containing sodium azide.
- Do not eat, drink, smoke or apply cosmetics in the assay laboratory.
- Do not pipette solutions by mouth.
- Avoid direct contact with all potentially infectious materials by using protective clothing such as lab coats, protective glasses and disposable gloves. Wash hands thoroughly at the end of each assay.
- Avoid splashing or forming an aerosol. Any reagent spills should be washed with a 5% sodium hypochlorite solution and disposed of as though potentially infectious.

- All samples, biological reagents and materials used in the assay must be considered potentially able to transmit infectious agents. They should therefore be disposed of in accordance with the prevailing regulations and guidelines of the agencies holding jurisdiction over the laboratory, and the regulations of each Country. Disposable materials must be incinerated; liquid waste must be decontaminated with sodium hypochlorite at a final concentration of 5% for at least half an hour. Any materials to be reused must be autoclaved using an overkill approach (USP 24, 2000, p. 2143). A minimum of one hour at 121°C is usually considered adequate, though the users must check the effectiveness of their decontamination cycle by initially validating it and routinely using biological indicators.
- Reagents containing ProClin® 300 may cause allergic reactions. Avoid prolonged contact with skin. Wash thoroughly after handling.
- The LIAISON® Analyzer family should be cleaned and decontaminated on a routine basis. See the Operator's Manual for the procedures.
- Strict adherence to the instructions are necessary to obtain reliable results.

6. PREPARATION OF REAGENT INTEGRAL

Please note the following important reagent handling precautions:

Resuspension of magnetic particles

Magnetic particles must be completely resuspended before the Integral is placed on the instrument. Follow the steps below to ensure complete suspension:
Before the seal is removed, rotate the small wheel at the magnetic particle compartment until the colour of the suspension has changed to brown. Gentle and careful side-to-side mixing may assist in the suspension of the magnetic particles (avoid foam formation). Visually check the bottom of the magnetic particle vial to confirm that all settled magnetic particles have resuspended. Carefully wipe the surface of each septum to remove residual liquid. Repeat as necessary until the magnetic particles are completely resuspended.

Foaming of reagents

In order to ensure optimal performance of the Integral, foaming of reagents should be avoided. Adhere to the recommendation below to prevent this occurrence:
Visually inspect the reagents, calibrators in particular (position two and three following the magnetic particle vial), to ensure there is no foaming present before using the Integral. If foam is present after resuspension of the magnetic particles, place the Integral on the instrument and allow the foam to dissipate. The Integral is ready to use once the foam has dissipated and the integral has remained onboard and mixing.

Loading of Integral into the reagent area

LIAISON® Analyzer

- Place the Integral into the reagent area of the Analyzer with the bar code label facing left and let it stand for 30 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.

LIAISON® XL Analyzer

- LIAISON® XL Analyzer is equipped with a built-in solid-state magnetic device which aids in the dispersal of microparticles prior to placement of a Reagent Integral into the reagent area of the Analyzer. Refer to the 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 Integral into the reagent area of the 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 CMV IgG 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 magnetic particles. See Reagent Integral Preparation for resuspension instructions. When the Reagent Integral is stored sealed, the reagents are stable at 2-8°C up to the expiration date. Do not freeze. The Reagent Integral must not be used past the expiration date indicated on the kit and Reagent Integral labels. After removing the seals, the Reagent Integral is stable for eight weeks when stored at 2-8°C in a refrigerator or on board the Analyzer.

8. SPECIMEN COLLECTION AND PREPARATION

This assay can only test human serum samples. Blood should be collected aseptically by venipuncture, allowed to clot, and the serum separated from the clot as soon as possible. Grossly hemolyzed, icteric or lipemic samples as well as samples containing particulate matter or exhibiting obvious microbial contamination are not recommended and should not be tested. Do not heat-inactivate sera. Check for and remove air bubbles before assaying. If the assay is performed within two days of sample collection, the samples may be kept at 2-8°C; otherwise they should be dispensed in aliquots and stored deep-frozen (–20°C or below). If samples are stored frozen, mix thawed samples well before testing. Samples should not be repeatedly frozen and thawed. Self-defrosting freezers are not recommended for sample storage. The minimum volume required is 170 µL per specimen (20 µL specimen + 150 µL dead volume). For shipping, specimens should be frozen at –20°C or below and shipped with dry ice. Temperature level during entire shipment should be no greater (warmer) than –20°C. Pack specimens in compliance with government regulations covering the transportation of etiologic agents (9).

9. ASSAY PROCEDURE

Strict adherence to the relevant Analyzer operator's manual ensures proper assay performance.

LIAISON® Analyzer. Each test parameter is identified via the bar codes on the reagent integral label. In case the barcode cannot be read, the cartridge cannot be used and must be discarded. For details, refer to the Analyzer operator's manual.

LIAISON® XL Analyzer. Each test parameter is identified via information encoded in the reagent integral Radio Frequency IDentification transponder (RFID Tag). In case the RFID Tag cannot be read, the cartridge cannot be used and must be discarded. For details, refer to the Analyzer operator's manual.

The Analyzer operations are as follows:

1. Dispense calibrators, controls or specimens into the reaction module.
2. Dispense coated magnetic particles.
3. Dispense specimen diluent.
4. Incubate.
5. Wash with Wash/System liquid.
6. Dispense conjugate into the reaction module.
7. Incubate.
8. Wash with Wash/System liquid.
9. Add the Starter Kit and measure the light emitted.

Procedural details for the test may be viewed directly from the Analyzer's assay definition displays.

10. 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 Reagent Integral or of Starter Kit is used.
- The previous calibration was performed more than two weeks before.
- The Analyzer has been serviced.
- The values of the recommended LIAISON® controls lie outside the expected ranges.

Refer to the relevant Analyzer Operator's Manual or relevant Analyzer Quick Guide for calibration instructions.

LIAISON® Analyzer: Calibrator values are stored in the bar codes on the integral label.

LIAISON® XL Analyzer: Calibrator values are stored in the Radio Frequency IDentification transponder (RFID Tag).

11. QUALITY CONTROL

Quality control is performed once per day of use or in conformance with local, state and/or federal regulations or accreditation requirements and your laboratory's quality control procedures. It is recommended that the user refer to CLSI document, C24-A2, and 42 CFR 493.1256 for guidance on appropriate quality control practices.

The recommended LIAISON® CMV IgG quality control material contains only a 5% serum matrix. It will not adequately control the DiaSorin LIAISON® CMV IgG assay for serum specimens. The user must provide quality control material for serum specimens. Alternative materials for the control of serum specimens include commercial quality control materials or your laboratory's own pooled serum specimens. Choose control levels that check assay performance at all clinically relevant points (e.g., assay cutoff). The recommendation is to run a positive and negative control close (± 50%) to the assay's decision point. It is the responsibility of the user to validate the use of alternative control materials with this assay and to establish appropriate control ranges.

The LIAISON® CMV IgG negative and positive controls are intended to monitor for substantial reagent failure and the positive control will not ensure precision at the assay cutoff. If control results lie within the expected ranges provided on the certificate of analysis, the test is valid. If the control results lie outside the expected ranges, the test is invalid and patient results cannot be reported. Assay calibration should be performed if a control failure is observed and controls and samples must be retested.

12. INTERPRETATION OF RESULTS

The Analyzer automatically calculates hCMV IgG antibody concentrations expressed as U/mL and grades the results. For details, refer to the relevant Analyzer Operator's Manual.

The cutoff for the LIAISON® CMV IgG assay was determined during European clinical trials in which 1086 samples were run at three different sites. The samples consisted of either single samples or serial panels drawn from different selected populations (subjects never infected by CMV, patients affected by primary CMV infection, subjects with past CMV infection, patients with persistent CMV IgM, subjects with CMV reactivation, patients affected by autoimmune diseases, patients affected by other infectious diseases, pregnant women, and transplant recipients). Based on available clinical and laboratory data, the samples were classified as expected positive or negative for CMV IgG and evaluated with the LIAISON® CMV IgG assay. A positive cutoff of 0.7 U/mL with an equivocal zone of 0.6-0.69 U/mL was determined to provide the best sensitivity and specificity for the tested clinical samples.

Calibrators and controls may give different RLU or dose results on LIAISON® and LIAISON® XL.

Warning - If the sample result displays "Invalid RLU" and an exclamation mark (!) flag, the result obtained lies below the assay signal range. The sample must be retested. If the sample result upon retest still displays "Invalid RLU", call DiaSorin Technical Support.

Sample results should be interpreted as follows:

U/mL Value	Result	Interpretation
Below 0.6	Negative	Absence of detectable CMV IgG antibodies. A negative result generally indicates that immunity has not been acquired. If exposure to CMV is suspected despite a negative finding, a second sample should be collected and tested no less than one or two weeks later.
Between 0.6 and 0.69	Equivocal	The equivocal sample should be repeat tested. In case the result remains in this range after repeat testing, a second sample should be collected.
Equal to or above 0.7	Positive	Presence of detectable CMV IgG antibodies. A positive result generally indicates either recent or past exposure to the CMV.

Note - The magnitude of the measured result, above the cutoff, is not indicative of the amount of antibody present.

The presence of CMV IgM should also be determined to assess the stage of CMV infection. Diagnosis of infectious diseases should not be established on the basis of a single test result, but should be determined in conjunction with clinical findings and other diagnostic procedures as well as in association with medical judgment.

Diseases such as Epstein-Barr viral syndrome, toxoplasmosis and hepatitis may cause symptoms similar to CMV infection and must be excluded before confirmation of diagnosis.

13. LIMITATIONS OF THE PROCEDURE

1. The test should be performed on serum only. The use of whole blood or plasma specimens has not been established.
2. The clinical diagnosis must be interpreted with clinical signs and symptoms of the patient. The results from this kit are not by themselves diagnostic and should be considered in association with other clinical data and patient symptoms.
3. Results from immunosuppressed patients should be interpreted with caution.
4. Screening of the general population should not be performed. The positive predictive value depends on the likelihood of the virus being present. Testing should only be performed on patients with clinical symptoms or when exposure is suspected.
5. Integrals may not be exchanged between Analyzer types (LIAISON® and LIAISON® XL). Once an Integral has been introduced to a particular Analyzer type, it must always be used on that Analyzer until it has been exhausted. Due to traceability issues resulting from the above statement, patient follow-ups may not be conducted between Analyzer types. These must be accomplished on one particular Analyzer type (either LIAISON® or LIAISON® XL).

14. EXPECTED VALUES

The LIAISON® CMV IgG assay was tested with prospectively collected samples from subjects sent to the laboratory for hCMV testing (n = 320) and from pregnant women (n = 202) to evaluate the prevalence of IgG antibodies to CMV in these populations. The subjects sent to the laboratory for hCMV testing were 52.2% female (167), 31.9% male (102), 15.9% unknown (51) and represented the mid-Atlantic and Northeastern U.S. The pregnant woman population was also collected from the mid-Atlantic and Northeastern U.S. areas.

The distribution of results for IgG antibodies to hCMV in the routine testing population as determined by the LIAISON® CMV IgG Assay is summarized in the following table.

Subjects	N	Negative	Equivocal	Positive	Prevalence
Total	320	136	1	183	57.2%
Gender					
Female	167	62	0	105	62.9%
Male	102	45	0	57	55.9%
Unknown	51	29	1	21	41.1%
Age (years)					
< 10	7	3	0	4	57.1%
10-19	27	19	0	8	29.6%
20-29	46	26	0	20	43.5%
30-39	62	29	0	33	53.2%
40-49	48	15	0	33	68.8%
50-59	47	16	1	30	63.8%
60-69	14	3	0	11	78.6%
≥ 70	23	6	0	17	73.9%
Unknown	46	19	0	27	58.7%

The distribution of results for IgG antibodies to CMV in the pregnant woman population as determined by the LIAISON® CMV IgG assay is summarized in the following table.

Subjects	N	Negative	Equivocal	Positive	Prevalence
Total	202	26	0	176	87.1%
Age (years)					
16-19	22	4	0	18	81.8%
20-29	86	9	0	77	89.5%
30-39	86	12	0	74	86.1%
40-42	8	1	0	7	87.5%
Trimester					
First	31	4	0	27	87.1%
Second	127	17	0	110	86.6%
Third	44	5	0	39	88.6%

15. SPECIFIC PERFORMANCE CHARACTERISTICS

Agreement
A total of 622 samples were tested – 522 prospectively and 100 retrospectively collected. The prospective samples represented 320 samples from subjects sent to the laboratory for CMV testing and 202 samples from pregnant women. The retrospective samples represented 100 samples from patients with serologic results suggesting acute infection with CMV. The testing was performed at a plasma center in California, a physician's office laboratory in Michigan, and at DiaSorin. All samples were tested with the LIAISON® CMV IgG Assay and an enzyme immunoassay ELISA.

Subjects Sent to the Laboratory for CMV Testing

LIAISON® CMV IgG	CMV IgG ELISA			Total
	Negative	Equivocal	Positive	
Negative (< 0.6 U/mL)	136	0	0	136
Equivocal (0.6-0.69 U/mL)	1	0	0	1
Positive (≥ 0.7 U/mL)	4	1	178	183
Total	141	1	178	320

Condition	Percent Agreement	Exact 95% confidence interval
Positives Negatives	100.0% (178/178) 96.45% (136/141)	97.95-100.0% 91.92-98.84%
Overall	98.13% (314/320)	95.96-99.31%

Pregnant Women

LIAISON® CMV IgG	CMV IgG ELISA			Total
	Negative	Equivocal	Positive	
Negative (< 0.6 U/mL)	25	0	1	26
Equivocal (0.6-0.69 U/mL)	0	0	0	0
Positive (≥ 0.7 U/mL)	1	0	175	176
Total	26	0	176	202

Condition	Percent Agreement	Exact 95% confidence interval
Positives Negatives	99.43% (175/176) 96.15% (25/26)	96.88-99.99% 80.36-99.90%
Overall	99.01% (200/202)	96.47-99.88%

Retrospective Samples: Suspected CMV Acute Infection

LIAISON® CMV IgG	CMV IgG ELISA			Total
	Negative	Equivocal	Positive	
Negative (< 0.6 U/mL)	0	0	0	0
Equivocal (0.6-0.69 U/mL)	0	0	0	0
Positive (≥ 0.7 U/mL)	0	0	100	100
Total	0	0	100	100

Condition	Percent Agreement	Exact 95% confidence interval
Positives Negatives	100.0% (100/100) N/A	96.38-100.0% N/A
Overall	100.0% (100/100)	96.38-100.0%

N/A = not applicable.

Precision

An assay reproducibility study was conducted at two external U.S. laboratories and at DiaSorin. A coded panel comprised of 9 frozen repository samples was prepared by DiaSorin and provided to each site for testing by the LIAISON® CMV IgG assay. The panel contained 9 serum samples prepared to represent low- to mid-positive analyte levels. All samples were divided into aliquots and stored frozen prior to testing. The same samples were tested at all three sites, in three replicates per run for ten runs. The results are summarized below.

ID#	N	Mean (U/mL)	Within-run S.D.	Within-run %CV	Between-run S.D.	Between-run %CV	Between-site S.D.	Between-site %CV	Overall S.D.	Overall %CV
CGS1	90	0.91	0.04	4.84	0.11	9.39	0.06	6.55	0.11	12.29
CGS2	90	6.09	0.57	9.69	1.24	14.57	0.85	13.93	1.34	22.07
CGS3	90	1.59	0.10	6.05	0.14	8.21	0.07	4.60	0.16	10.31
CG1	90	1.15	0.04	3.76	0.12	5.36	0.12	10.35	0.12	10.88
CG2	90	0.94	0.04	3.95	0.09	6.01	0.08	8.13	0.09	9.86
CG3	90	0.84	0.04	5.01	0.09	7.24	0.08	9.41	0.10	11.46
CG4	90	0.68	0.02	3.60	0.05	5.34	0.05	6.76	0.06	8.43
CG5	90	0.68	0.03	4.63	0.06	5.12	0.06	8.47	0.07	9.88
CG6	90	1.17	0.07	6.02	0.06	5.17	0.03	2.20	0.09	7.68

Cross-reactions. The cross-reactivity studies for the LIAISON® CMV IgG assay were designed to evaluate potential interference from IgG immunoglobulins directed against closely-related members of the herpes virus family (EBV, HSV, VZV), from other organisms that may cause symptoms similar to CMV (Hepatitis A virus, Parvovirus B19) and from other conditions that may result from atypical immune system activity [antinuclear antibodies (ANA), rheumatoid factor (RF)]. Samples for these studies were selected using commercially available devices.

Organism / condition	Number of Samples	Positive LIAISON® Result
EBV (VCA) IgG	25	0/25
HSV IgG	2	0/2
VZV IgG	1	0/1
Hepatitis A Ig	1	0/1
Parvovirus B19 IgG	11	0/11
ANA Ig	3	0/3
RF	3	0/3
Total	**46**	**0/46**

None of the 46 total specimens tested from the disease panel was positive. There was no conclusive evidence of cross-reactivity observed, however due to the limited availability of certain samples, the possibility of cross-reactivity cannot be excluded.

WARNING: Assay interference due to circulating antibodies against HIV, Hepatitis A, Hepatitis B and Hepatitis C viruses has not been evaluated. *The user is responsible for establishing cross-reactivity performance with* these infectious agents.

CDC Panel
A CDC Reference Panel for standardizing analysis of IgG antibodies to CMV were tested and evaluated using the DiaSorin LIAISON® CMV IgG assay. The following information is from a serum panel obtained from the CDC and tested by DiaSorin. The results are presented as a means to convey further information on the performance of this assay with a masked, characterized serum panel. The Reference Panel contained 100 blind samples consisting of 50 split pairs representing individuals having antibodies to CMV and those absent of antibodies to CMV. Results were submitted to the CDC for their interpretation and evaluation. This does not imply an endorsement of the assay by the CDC.
The panel consists of 66% positive and 34% negative samples. The DiaSorin LIAISON® CMV IgG assay demonstrated 100% agreement with the CDC reported results (by IHA and EIA). Of the results obtained by DiaSorin, there was 100% (66/66) agreement with the positive specimens and 100% (34/34) agreement with the negative specimens.

Substances That Do Not Interfere
Controlled studies of potentially interfering substances showed that the assay performance was not affected by hemolysis (at 1000 mg/dL hemoglobin), lipemia (at 3000 mg/dL triglycerides) or icterus (at 20 mg/dL bilirubin).

16. REFERENCES

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LIAISON® Control CMV IgG ([REF] 310741)

1. INTENDED USE

The LIAISON® CMV IgG Controls (negative, positive) are used for monitoring substantial reagent failure of the LIAISON® CMV IgG chemiluminescent immunoassay (CLIA).
The LIAISON® CMV IgG quality control material contains only a 5% serum matrix and may not adequately control the DiaSorin LIAISON® CMV IgG assay for serum specimens.
The performance of the LIAISON® CMV IgG Controls has not been established with any other CMV assay or instrument platforms different from LIAISON® and LIAISON® XL.
LIAISON® Analyzer: The certificate of analysis gives specific information on the lot of controls, which should be manually entered in the Analyzer software prior to loading the control vials on board. For details, refer to the Analyzer Operator's Manual.
LIAISON® XL Analyzer: The certificate of analysis bar codes give 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.

Warning: United States federal law restricts this device to sale by or on the order of a physician.

2. MATERIALS PROVIDED

Negative control (0.7 mL)	Human serum/defibrinated plasma not reactive for CMV IgG antibodies, diluted in PBS buffer, BSA, with ProClin® 300 as a preservative.
Positive control (0.7 mL)	Human serum/defibrinated plasma reactive for CMV IgG antibodies, diluted in PBS buffer, BSA, with ProClin® 300 as a preservative and an inert yellow dye.

ProClin® is a registered trademark of Rohm and Haas Co.

All reagents are supplied ready to use. The reference range 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.

3. WARNINGS AND PRECAUTIONS

For in vitro diagnostic use.
Controls are not kit lot specific and may be interchanged among different kit lots.
The human blood source material used to produce the components provided in this kit derives from donations found to be non-reactive for HBsAg, antibodies to HCV, HIV-1 and HIV-2 when tested by an FDA-approved method and found to be non-reactive for syphilis when tested by a serological test. 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.
The controls are not calibrators and should not be used for assay calibration.

4. SAFETY PRECAUTIONS

Do not eat, drink, smoke or apply cosmetics in the assay laboratory.
Do not pipette solutions by mouth.
Avoid direct contact with all potentially infectious materials by using protective clothing such as lab coats, protective glasses, and disposable gloves. Wash hands thoroughly at the end of each assay.
Avoid splashing or forming an aerosol. Any reagent spills should be washed with a 5% sodium hypochlorite solution and disposed of as though potentially infectious.
All samples, biological reagents and materials used in the assay must be considered potentially able to transmit infectious agents. They should therefore be disposed of in accordance with the prevailing regulations and guidelines of the agencies holding jurisdiction over the laboratory, and the regulations of each Country. Disposable materials must be incinerated; liquid waste must be decontaminated with sodium hypochlorite at a final concentration of 5% for at least half an hour. Any materials to be reused must be autoclaved using an overkill approach (USP 24, 2000, p. 2143). A minimum of one hour at 121°C is usually considered adequate, though the users must check the effectiveness of their decontamination cycle by initially validating it and routinely using biological indicators.
Reagents containing ProClin® 300 may cause allergic reactions. Avoid prolonged contact with skin. Wash thoroughly after handling.

5. STORAGE AND STABILITY

Upon receipt, the controls must be stored at 2-8°C. When controls are stored sealed, they are stable at 2-8°C up to the expiration date on the vial. The controls should not be used past the expiration date indicated on the vial labels. Once opened controls are stable for four weeks when properly stored at 2-8°C between uses. Avoid bacterial contamination of controls. The minimum specimen volume required is 220 µL (20 µL specimen + 200 µL dead volume).
Allow controls to reach room temperature prior to use. Return controls to the refrigerator immediately after each use.

SYMBOLS USED WITH IVD DEVICES

 Consult instructions for use.

IVD In vitro diagnostic.

LOT Lot No.

Use by:

+ 8°C

+ 2°C Temperature limitation.

Caution, consult accompanying documents.

REF Catalogue number.

Manufacturer.

CE mark in accordance to 98/79/ECC.

Σ XX For XX tests

CONT	Kit contents
SORB	Magnetic particles
CONJ	Conjugate
CAL 1	Calibrator
CAL 2	Calibrator
DIL SPE	Specimen diluent
CONTROL –	Negative control
CONTROL +	Positive control

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

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6. QUALITY CONTROL

Quality control should be performed once per day of use, or according to guidelines or requirements of local regulations or accredited organizations. It is recommended that the user refer to CLSI document, C24-A2, and 42 CFR 493.1256 for guidance on appropriate quality control practices.

LIAISON® controls are intended to monitor for substantial reagent failure. Whenever controls lie outside the expected ranges provided on the certificate of analysis, calibration should be repeated and controls and samples retested. Do not report patient results until control results are within expected ranges.

A skillful technique and strict adherence to the instructions of the LIAISON® CMV IgG kit are necessary to obtain reliable results.

7. LIMITATIONS

LIAISON® controls contain a 5% serum matrix and may not adequately control the LIAISON® CMV IgG assay for serum specimens. The user must provide alternative quality control material for serum specimens, which may consist of commercial quality control materials or your laboratory's own pooled serum. Choose control levels that check assay performance at all clinically relevant points (e.g., assay cutoff). The recommendation is to run a positive and negative control close (±50%) to the assay's decision point. It is the responsibility of the user to validate the use of alternative control materials with this assay and to establish appropriate control ranges.

The LIAISON® CMV IgG positive control will not ensure precision at the assay cutoff.

Control values for assays other than LIAISON® CMV 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.