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Changes: §
Deletions: §

LIAISON® VCA IgG (310510)

1. INTENDED USE

The LIAISON® VCA IgG assay uses chemiluminescent immunoassay (CLIA) technology on the LIAISON® Analyzer family* for the qualitative determination of specific IgG antibodies to Epstein-Barr virus (EBV) viral capsid antigen (VCA) p18 synthetic peptide in human serum. When performed in conjunction with other EBV markers, this assay can be used as an aid in the clinical laboratory diagnosis of Epstein-Barr Viral Syndrome in patients with signs and symptoms of EBV infection such as infectious mononucleosis.

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

Assay performance characteristics have not been established for immunocompromised or immunosuppressed patients, cord blood, neonatal specimens, or infants. Assay performance characteristics have not been established for the diagnosis of nasopharyngeal carcinoma, Burkitt's lymphoma, and other EBV-associated lymphomas.

2. SUMMARY AND EXPLANATION OF THE TEST

Epstein-Barr virus (EBV) is responsible for infectious mononucleosis (IM) and is implicated in Burkitt's lymphoma and nasopharyngeal carcinoma. Diagnosis of IM is based upon clinical manifestations which generally include sore throat, fever, lymphadenopathy, and malaise in conjunction with hematological evidence for lymphocytosis and serological evidence for the presence of heterophile antibody and/or EBV antibodies to specific proteins. Clinical manifestations similar to IM can also be induced by a number of other pathogenic infectious agents including Cytomegalovirus, *Toxoplasma gondii*, Hepatitis viruses, Human Immunodeficiency Virus (HIV), and others (1). The term mononucleosis syndrome is often applied until the specific etiologic agent is identified. Confirmation of an acute diagnosis of EBV IM is generally sought by a positive heterophile antibody test (agglutination by patient's serum with horse or sheep red blood cells). However, difficulties in diagnosis arise when the heterophile test is negative or when clinical manifestations are atypical (2). Heterophile-negative IM has been demonstrated in 10 to 20% of adults with an even greater percentage in children with acute IM infections (2, 3). For these individuals, IM diagnosis may be confirmed by identification of antibodies to specific EBV protein antigens which include Viral Capsid Antigen (VCA) and Early Antigen Diffuse [EA(D)]. The presence of VCA IgM antibody usually suffices for diagnosis of IM. However, verification should be sought with additional clinically relevant information (4). Serologic testing for EBV infection is possible because characteristic time-dependent antibody responses occur. Most (> 80%) symptomatic IM patients show near-peak antibody levels of VCA IgG and IgM when first examined. VCA IgM antibodies usually disappear in 2-3 months while IgG antibodies persist indefinitely. Most patients transiently develop antibodies to EA(D), but IgG antibodies against Epstein-Barr Nuclear Antigen (EBNA) appear several weeks or months after the onset of disease and persist for years or even life (5, 6). During IM infections, a rise in VCA IgG level is indicative of an acute stage of infection. The presence of VCA IgG antibodies in healthy individuals indicates immunological exposure to EBV either as silent primary infection or past exposure (7). Because of the complex relationship that exists between the EBV virus/host reaction and clinical manifestation, tracking of EBV antibody patterns may assist in diagnosis of EBV infection. Individual levels of specific antibodies are not necessarily indicative of disease state but can be of diagnostic significance when tracked as an antibody response profile. Antibody response profiles for the different EBV antigens demonstrate a characteristic pattern for silent primary or persistent latent EBV infections, as well as for each of the EBV-associated diseases (8).

*(LIAISON® and LIAISON® XL)

3. PRINCIPLE OF THE PROCEDURE

The method for qualititative determination of specific IgG to EBV viral capsid antigen (VCA) is an indirect chemiluminescence immunoassay (CLIA). All assay steps (with the exception of magnetic particle resuspension) and incubations are performed by the LIAISON® Analyzer. The principal components of the test are magnetic particles (solid phase) coated with EBV VCA p18 synthetic peptide and a conjugate of mouse monoclonal antibody to human IgG linked to an isoluminol derivative (isoluminol-antibody conjugate). During the first incubation, VCA IgG antibodies present in calibrators, samples or controls bind to the solid phase. During the second incubation, the antibody conjugate reacts with VCA IgG antibodies that are 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 EBV VCA IgG antibodies present in calibrators, samples or controls.

4. MATERIALS PROVIDED

Reagent Integral

Magnetic particles (2.3 mL)	Magnetic particles coated with VCA p18 synthetic peptide, BSA, phosphate buffer, < 0.1% sodium azide.
Calibrator 1 (3.2 mL)	Human serum/defibrinated plasma containing low EBV VCA IgG levels, BSA, phosphate buffer, with ProClin® 300 as a preservative. The calibrator concentration (U/mL) is referenced to an in-house antibody preparation and is encoded in the Reagent Integral bar code.
Calibrator 2 (3.2 mL)	Human serum/defibrinated plasma containing high EBV VCA IgG levels, BSA, phosphate buffer, with ProClin® 300 as a preservative, and an inert blue dye. The calibrator concentration (U/mL) is referenced to an in-house antibody preparation and is encoded in the Reagent Integral bar code.
Specimen diluent (2 x 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 preserv-atives.
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.

Materials required but not provided (system related)

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

Additionally required materials

LIAISON® Control VCA IgG (code 310511).

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 (9, 10, 11).

- 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 should be cleaned and decontaminated on a routine basis. See the Operator's Manual for the procedures.

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® Analyzers

- 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 Analyzers

- 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.

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 LIAISON® 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 or lipemic samples as well as samples containing particulate matter or exhibiting obvious microbial contamination are not recommended and should not be tested. 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 (12).

9. ASSAY PROCEDURE

Strict adherence to the Analyzer Operator's Manual ensures proper assay performance.

LIAISON® Analyzers. 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 Analyzers. 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.
- Control values lie outside the expected ranges.

Refer to the analyzer operator's manual or LIAISON® Quick Guide for calibration instructions.

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

LIAISON® XL analyzers: 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® VCA IgG quality control material contains a 5% serum matrix. It may not adequately control the DiaSorin LIAISON® VCA 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® VCA 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 control vial labels, 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 EBV VCA IgG antibody concentrations expressed as U/mL and grades the results. For details, refer to the Analyzer Operator's Manual.

The cutoff for the LIAISON® VCA IgG assay was determined during European clinical trials in which 1133 samples were tested at four separate sites. The samples were drawn from several different populations, including seronegative subjects, subjects with primary EBV infection, past EBV infection, suspected chronic EBV infection and reactivated EBV infection and from an apparently healthy adult population. Based on available clinical and laboratory data, the samples were classified as expected positive or negative for VCA IgG and evaluated with the LIAISON® VCA IgG assay. A cutoff of 20 U/mL was determined to provide the best balance of sensitivity and specificity for the tested clinical samples. An equivocal zone of 18.0-21.9 U/mL was applied to the assay to account for normal measurement imprecision.

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:

Unit Value	Result	Interpretation
< 18.0 U/mL	Negative	Absence of detectable VCA IgG antibodies. If exposure to Epstein-Barr virus is suspected despite a negative finding, a second sample should be collected and tested no less than one to two weeks later.
18.0 to 21.9 U/mL	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 and tested no less than one or two weeks later.
≥ 22.0 U/mL	Positive	Presence of detectable VCA IgG antibodies. A positive result indicates current or past exposure to Epstein-Barr virus.

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

The accurate distinction of a primary infection from seronegative status or past infection is a key concern of EBV diagnostics. The presence of other EBV serological markers (e.g. VCA IgM, EBNA-1 IgG) should be determined to assess the immunological status to infection with EBV. Based on the results of three commonly-used antibody tests (VCA IgG, VCA IgM, EBNA-1 IgG), distinct serological profiles have been described in the medical literature (13).

Condition	VCA IgG	VCA IgM	EBNA-1 IgG
EBV seronegative	–	–	–
Acute infection	+	+	–
Past infection	+	–	+
Indeterminate			
VCA IgG only	+	–	–
VCA IgM only	–	+	–
EBNA IgG only	–	–	+
Convalescent	+	+	+

Because some individuals are reported to exhibit long-lasting VCA IgM antibodies, the convalescent pattern may represent a transient period late in the primary infection stage or may persist well into the past infection stage. Thus, it is considered an indeterminate pattern (13). For samples that exhibit indeterminate patterns, further diagnostic testing may be required. In all cases, 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.

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 use of icteric or lipemic sera, or sera exhibiting hemolysis or microbial growth should be avoided.
3. Do not heat-inactivate sera.
4. 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.
5. Results from immunosuppressed patients should be interpreted with caution.
6. Diseases such as cytomegalovirus, toxoplasmosis and hepatitis may cause symptoms similar to infectious mononucleosis and must be excluded before confirmation of diagnosis.
7. The combined use of EBV serological markers and clinical data is recommended when the diagnosis of EBV infection is based on a single serum specimen. A single result cannot be used for diagnosis. Accurate interpretation of EBV infection is based on results of EA(D) IgG, VCA IgM, VCA IgG, EBNA IgG, EBNA IgM and heterophile antibodies.
8. The performance characteristics have not been established for patients with nasopharyngeal carcinoma, Burkitt's lymphoma, EBV-associated lymphadenopathies and other EBV-associated diseases besides EBV-related mononucleosis.
9. 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.
10. 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® VCA IgG assay was tested with prospectively collected samples from subjects sent to the laboratory for EBV testing (n = 823) to evaluate the prevalence of IgG antibodies to VCA in these populations. The subjects sent to the laboratory for EBV testing were 61.7% female (508), 28.1% male (231) and 10.2% unknown (84) and represented the mid-Atlantic and Northeastern U.S.

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

Subjects	N	Negative	Equivocal	Positive	Prevalence
Total	823	97	5	721	87.6%
Gender					
Female	508	56	2	450	88.6%
Male	231	32	3	196	84.8%
Unknown	84	9	0	75	89.3%
Age (years)					
≤ 18	173	36	2	135	78.0%
< 10	29	9	0	20	69.0%
10-19	183	30	2	151	82.5%
20-29	190	28	2	160	84.2%
30-39	95	5	1	89	93.7%
40-49	78	2	0	76	97.4%
50-59	59	2	0	57	96.6%
60-69	32	0	0	32	100.0%
≥ 70	27	3	0	24	88.9%
Unknown	130	18	0	112	86.2%

15. SPECIFIC PERFORMANCE CHARACTERISTICS

Agreement

A total of 893 samples was tested – 823 prospectively and 70 retrospectively collected. The prospective samples represented 823 samples from subjects sent to the laboratory for EBV testing. The retrospective samples represented 70 samples from patients positive for VCA IgM. The testing was performed at three sites – a hospital, a donor laboratory, and at DiaSorin. All samples were tested with the LIAISON® VCA IgG assay and an enzyme immunoassay ELISA.

Retrospective Samples: VCA IgM-positive Samples

Using the results for the retrospective samples in three reference assays (VCA IgG, EBNA-1 IgG and VCA IgM ELISA), the samples were grouped into serological categories. Indeterminate refers to serological patterns that are not consistent with the typical EBV categories; EBV seronegative, acute or past infection. The profiles and number of occurrences are presented in the following table:

Condition	VCA IgG	VCA IgM	EBNA-1 IgG	Total
EBV seronegative	–	–	–	0
Acute infection	+	+	–	9
Past infection	+	–	+	0
Indeterminate				
VCA IgG only	+	–	–	0
VCA IgM only	–	+	–	0
EBNA IgG only	–	–	+	0
Convalescent	+	+	+	61

Based on these serological classifications, the LIAISON® VCA IgG results for the retrospective samples were compared with those obtained with the reference assay (VCA IgG ELISA).

Condition	Percent Agreement	95% confidence interval
EBV seronegative	N/A	N/A
Acute infection	100.0% (9/9)	71.7-100.0%
Past infection	N/A	N/A
Indeterminate	100.0% (61/61)	95.2-100.0%
Overall	100.0% (70/70)	95.8-100.0%

Prospective samples: Subjects Sent to the Laboratory for EBV Testing
Using the results for the prospective samples in three reference assays (VCA IgG, EBNA-1 IgG and VCA IgM ELISA), the samples were grouped into serological categories. Indeterminate refers to serological patterns that are not consistent with the typical EBV categories; EBV seronegative, acute or past infection. Four samples tested in the LIAISON® VCA IgG assay had insufficient volume for the entire test profile and are omitted from this analysis. The profiles and number of occurrences are presented in the following table:

Condition	VCA IgG	VCA IgM	EBNA-1 IgG	Total
EBV seronegative	–	–	–	62
Acute infection	+	+	–	29
Past infection	+	–	+	573
Indeterminate				
VCA IgG only	+	–	–	67
VCA IgM only	–	+	–	5
EBNA IgG only	–	–	+	10
Convalescent	+	+	+	73

Based on these serological classifications, the LIAISON® VCA IgG results for the prospective samples were compared with those obtained with the reference assay (VCA IgG ELISA).

Condition	Percent Agreement	95% confidence interval
EBV seronegative	98.4% (61/62)	91.3-100.0%
Acute infection	82.8% (24/29)	64.2-94.2%
Past infection	98.3% (563/573)	96.8-99.2%
Indeterminate	89.7% (139/155)	83.8-94.0%
Overall	96.1% (787/819)	94.5-97.3%

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

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
VGS1	90	266.6	9.86	3.68	23.56	7.23	12.98	4.87	25.19	9.45
VGS2	90	52.9	1.89	3.83	3.75	5.43	2.81	5.32	4.35	8.22
VGS3	90	145.5	7.55	5.78	11.69	7.41	4.71	3.23	15.37	10.56
VG1	90	31.6	0.71	2.31	2.94	6.36	2.64	8.35	2.99	9.45
VG2	90	52.2	1.09	2.06	2.88	5.43	0.97	1.86	3.07	5.89
VG3	90	61.0	1.17	1.92	3.75	5.64	2.05	3.35	3.86	6.32
VG4	90	69.2	1.58	2.31	4.56	5.38	3.28	4.74	4.79	6.92
VG5	90	58.0	1.21	2.11	3.07	4.08	2.47	4.26	3.27	5.63
VG6	90	49.6	1.23	2.46	3.05	5.76	1.46	2.94	3.25	6.55

Cross-reactions. The cross-reactivity studies for the LIAISON® VCA IgG assay were designed to evaluate potential interference from IgG immunoglobulins directed against closely-related members of the herpes virus family (HSV-1, HSV-2, VZV, CMV, HHV6), from other organisms that may cause symptoms similar to EBV (*Toxoplasma gondii*, rubella virus) and from other conditions that may result from atypical immune system activity [rheumatoid factor (RF)]. Samples for these studies were selected using commercially available devices.

Organism / condition	Number of Samples	Positive LIAISON® Result
CMV IgG	16	0/16
VZV IgG	7	0/7
HSV-1 IgG	18	2/18
HSV-2 IgG	3	0/3
HHV6 IgG	3	0/3
Toxoplasma gondii IgG	8	1/8
Rubella virus IgG	30	0/30
RF	4	0/4
Total	**89**	**4/89**

Four specimens out of 89 total specimens tested from the disease panel were positive. There was no evidence of extensive cross-reactivity with any other condition, however due to the limited availability of certain samples, the possibility of cross-reactivity cannot be excluded. The user is advised to perform other EBV serology assays to confirm EBV-associated infectious mononucleosis.

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

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), icterus (at 20 mg/dL bilirubin).

16. REFERENCES

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1. INTENDED USE

The LIAISON® VCA IgG Controls (negative, positive) are used for monitoring substantial reagent failure of the LIAISON® VCA IgG chemiluminescent immunoassay (CLIA).
The LIAISON® VCA IgG quality control material contains a 5% serum matrix and may not adequately control the DiaSorin LIAISON® VCA IgG assay for serum specimens.
The performance of the LIAISON® VCA IgG Controls has not been established with any other EBV assay or instrument platforms different from LIAISON® and LIAISON® XL.

LIAISON® Analyzers: 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 Analyzers: 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 (0.9 mL)	Human serum/defibrinated plasma not reactive for VCA IgG antibodies, diluted in PBS buffer, BSA, with ProClin® 300 as a preservative.
Positive control (0.9 mL)	Human serum/defibrinated plasma reactive for VCA 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.

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 sample + 200 µL dead volume).
Allow controls to reach room temperature prior to use. Return controls to the refrigerator immediately after each use.

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 control vial labels, 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® VCA IgG kit are necessary to obtain reliable results.

7. LIMITATIONS

LIAISON® controls contain a 5% serum matrix and may not adequately control the LIAISON® VCA 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® VCA IgG positive control will not ensure precision at the assay cutoff.

Control values for assays other than LIAISON® VCA 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.

SYMBOLS USED WITH IVD DEVICES

 Consult instructions for use.

In vitro diagnostic.

Lot No.

 Use by:

+ 8°C

 Temperature limitation.

+ 2°C

 Caution, consult accompanying documents.

Catalogue number.

 Manufacturer.

 CE mark in accordance to 98/79/ECC.

 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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