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The symbols glossary is provided electronically and can be found in the Dialog section at www.diasorin.com using the part and lot numbers associated with the corresponding IVD product.

LIAISON® XL murex Anti-HBs ([REF] 318220)

1. INTENDED USE

The LIAISON® XL murex Anti-HBs is an *in vitro* chemiluminescent immunoassay (CLIA) for the qualitative and quantitative determination of antibody to hepatitis B surface antigen (anti-HBs) in human adult and pediatric (2 – 21 years) serum and plasma (lithium and sodium heparin and K_2 EDTA) including separator tubes, on the LIAISON® XL Analyzer. Assay results in conjunction with other hepatitis B virus (HBV) serological markers and clinical information may be used as an aid in the diagnosis of HBV infection in patients with symptoms of hepatitis or who may be at risk for HBV infection. The assay results may be used as an aid in the determination of susceptibility to HBV infection in individuals prior to or following HBV vaccination or where vaccination status is unknown.

The assay is not approved for use in screening blood, plasma or tissue donors.

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

2. SUMMARY

Hepatitis B is a liver infection caused by the hepatitis B virus (HBV). HBV is an enveloped deoxyribose nucleic acid (DNA) virus.

HBV is spread when an uninfected person comes into contact with infected blood or body fluids. Most infections occur via contact with infected blood, but semen, saliva and cervical secretions can also be infectious and Mother-to-Child Transmission (MTCT) of HBV remains an important source of incident cases of HBV. The virus can live on surfaces for at least seven days which means it can also be transmitted via objects that have been contaminated with infected body fluids (e.g. used needles) (1).

HBV is a non-cytopathic virus that causes liver damage through immunopathogenesis (2). Common symptoms of HBV infection include malaise, fever, gastroenteritis and jaundice. However, some patients may have chronic HBV infection and be asymptomatic. Most infected adults (>90%) will completely recover from an HBV infection, only experiencing a mild, asymptomatic acute illness. In contrast, ~90% of infants and young children will develop a more severe chronic infection (2; 3). Chronic HBV infection is characterized by the persistence of HBsAg (Hepatitis B surface Antigen) for at least six months and can lead to serious complications such as cirrhosis, hepatocellular carcinoma and liver related mortality. HBV is endemic throughout the world, despite the availability of an efficient vaccine (4, 5, 6).

Diagnosis of HBV infection is achieved through blood or serum detection of viral nucleic acid or serological markers (i.e. proteins produced by the virus or antibodies produced by the host that target viral proteins). Serological tests are commonly used to detect HBV infection status and are the first testing strategy to screen for HBV exposure. Common HBV serological markers include Hepatitis B surface Antigen (HBsAg), antibody to HBsAg (anti-HBs), total antibody to hepatitis B core antigen (HBcAg) (total anti-HBc), immunoglobulin M (IgM) antibody to HBcAg (IgM anti-HBc), hepatitis B e antigen (HBeAg), and antibody to HBeAg (anti-HBe). The detection of these serological markers allows identification of past or ongoing HBV infection, assessment of the clinical phases of the disease, monitoring of antiviral therapy and determination of the immune status of the patient. (7-11).
DiaSorin's LIAISON® XL MUREX Anti-HBs assay detects antibodies directed against the hepatitis B virus surface antigen (HBsAg). This assay can be used to detect a successful response to HBV vaccination, or confirm the resolution of an HBV infection.
Before the onset of clinical illness, HBsAg is detectable in the serum, and its presence persists through the symptomatic phase of illness. Following clinical illness, the titer of HBsAg begins to decline and eventually falls below a detectable level. After HBsAg disappears, anti-HBs appears in the serum, although there is often a gap called the window period between the disappearance of HBsAg and the appearance of anti-HBs (seroconversion).

Anti-HBs generally remains detectable in a HBV-exposed individual indefinitely, engendering immunity to future infections with HBV (12). However, in some patients, anti-HBs can decrease below detectable thresholds, but this does not necessarily correlate with loss of immunity to HBV as levels may quickly reach a detectable threshold following HBV re-exposure. During this period of undetectable anti-HBs, Anti-HBc (total) may be the only detectable serological marker for HBV infection (13).
Detection of anti-HBs is therefore critical in establishing whether complete resolution of the infection has occurred as well as in establishing the acquisition of immunity, whether acquired as a result of natural HBV infection or vaccination. Vaccines based on either human plasma-derived or recombinant HBsAg are in widespread use and have emphasized the requirement for accurate quantification of immunoglobulin concentration. Measurement of anti-HBs in vaccinees is essential to assessing the duration of protection after primary immunization and the need and timing of booster doses. Anti-HBs testing is also crucial in identifying HBV-susceptible individuals in pre-vaccination screening programs.

3. PRINCIPLE OF THE PROCEDURE

The method for qualitative and quantitative determination of anti-HBs is a direct, sandwich chemiluminescence immunoassay (CLIA). Recombinant HBsAg (subtypes *ad* and *ay*) is used for coating magnetic particles (solid phase) and human HBsAg (subtypes *ad* and *ay*) is linked to an isoluminol derivative (isoluminol-HBsAg conjugate). During the

incubation, anti-HBs present in calibrators, samples or controls binds to the solid phase and HBsAg conjugate, thus forming a sandwich. After the 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-HBsAg conjugate, is measured by a photomultiplier as relative light units (RLU) and is indicative of anti-HBs concentration present in calibrators, samples or controls.

4. MATERIALS PROVIDED

Reagent integral

Magnetic particles (2.5 mL)	**[SORB]**	Magnetic particles coated with HBsAg obtained in *mammalian cells* by the recombinant DNA technology (balanced *ad* and *ay* subtypes), BSA, PBS buffer, < 0.1% sodium azide.
Calibrator 1 (2.3 mL)	**[CAL|1]**	Human plasma containing low levels of anti-HBs, fetal calf serum, EDTA, 0.2% ProClin® 300, preservatives. The calibrator concentrations (mIU/mL) are referenced to WHO Second International Standard for anti-hepatitis B surface antigen (anti-HBs) immunoglobulin, human (NIBSC code: 07/164, 2008).
Calibrator 2 (2.3 mL)	**[CAL|2]**	Human plasma containing high levels of anti-HBs, fetal calf serum, EDTA, 0.2% ProClin® 300, preservatives, an inert blue dye. The calibrator concentrations (mIU/mL) are referenced to WHO Second International Standard for anti-hepatitis B surface antigen (anti-HBs) immunoglobulin, human (NIBSC code: 07/164, 2008).
Conjugate (20 mL)	**[CONJ]**	Heat-treated human HBsAg (balanced *ad* and *ay* subtypes), conjugated to an isoluminol derivative, BSA, PBS buffer, EDTA, 0.2% ProClin® 300, preservatives, an inert red dye.
Number of tests		200

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

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

LIAISON® XL 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).

Additionally required materials

LIAISON® XL MUREX Control Anti-HBs ([REF] 318221).

LIAISON® XL MUREX Anti-HBs Verifiers ([REF] 318223).

5. WARNINGS AND PRECAUTIONS

- For *in vitro* diagnostic use only.
- For Prescription Use Only.
- 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 Biosafety Level 2, as recommended for any potentially infectious human serum or blood specimen in the CDCNIH 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.
- Observe the normal precautions required for handling all laboratory reagents.
- Disposal of all waste material should be in accordance with local guidelines.
- Do not eat, drink, smoke or apply cosmetics in the assay laboratory.
- Do not pipette by mouth.
- Strict adherence to the instructions are necessary to obtain reliable results.
- Avoid direct contact with potentially infected material by wearing laboratory coats, 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 10% sodium hypochlorite solution (containing 0.5% active chlorine), and the means used must be treated as infected waste.

- All samples, biological reagents and disposable materials used in the assay must be considered as 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.
- Liquid waste must be decontaminated with sodium hypochlorite at a final concentration of 10% for at least half an hour.
- Any materials to be reused must be appropriately sterilized in compliance with the local laws and guidelines. 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.
- The LIAISON® Analyzer family should be cleaned and decontaminated on a routine basis. See the relevant Operator's Manual for the procedures.
- Do not use kits or components beyond the expiration date given on the label.
- Do not mix reagents from different reagents packs (even for the same reagent).
- Previously frozen samples should be thoroughly mixed after thawing and prior to testing.

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).

Hazardous reagents are classified and labelled as follows:

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

Reagents containing sodium azide

Sodium azide may react with lead or copper plumbing to form highly explosive metal azides. On 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 Prevention, Atlanta, GA, 1976.

Pursuant 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. 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 been 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® 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 the Preparation of Reagent Integral section for resuspension instructions. When the Reagent Integral is stored sealed and kept upright, the reagents are stable at 2-8°C up to the expiration date. Do not freeze. The Reagent Integral should 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 six weeks (6) when stored at 2-8°C in a refrigerator or on board the analyzer.

8. SPECIMEN COLLECTION AND PREPARATION

Either human serum, serum in serum-separating-tube (SST) or plasma may be used. The results obtained on the serum-plasma paired samples indicated that there is equivalence among serum (with and without gel SST), K_2 EDTA, lithium heparin and sodium heparin plasma.

Blood should be collected aseptically by venipuncture, allowed to clot (if applicable), and the serum or plasma separated from the red cells as soon as possible. Samples having particulate matter, turbidity, lipemia, or erythrocyte debris may require clarification by filtration or centrifugation before testing. Grossly hemolyzed or lipemic samples as well as samples containing particulate matter or exhibiting obvious microbial contamination should not be tested.

Check for and remove air bubbles and foam before assaying. A limited time of room temperature storage (between 18 and 30°C) for one (1) day does not influence the assay performance. If the assay is performed within seven (7) days of sample collection, the samples may be kept at 2-8°C; otherwise they should be aliquoted and stored deep-frozen (-20°C or below). If samples are stored frozen, mix thawed samples well before testing. Serum samples are stable through six (6) freeze/thaw cycles, while plasma samples are stable through 1 freeze/thaw cycle. Self-defrosting freezers are not recommended for sample storage.

It is responsibility of the individual laboratory to use all available references and/or its own studies to determinate specific stability criteria for its laboratory.

The minimum specimen volume required for a single determination is 300 µL (150 µL specimen + 150 µL dead volume). Dead volume is the volume left at the bottom of the aliquot tube which the instrument cannot aspirate.

For shipping, use sterile containers and pack specimens in compliance with government regulations covering the transportation of etiologic agents. Ensure that specimens reach their destination within the following specifications:

- Plasma and Serum separated from the clot can be maintained at 2-8°C during transit. Do not exceed the maximum 2-8°C stability of seven (7) days.
- Plasma and Serum separated from the clot can be stored at -20°C or below and shipped with dry ice. Temperature level during entire shipment should be no greater (warmer) than -20°C.

9. 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 calibrators, controls or specimens into the reaction cuvettes.
2. Dispense coated magnetic particles.
3. Dispense conjugate into the reaction cuvettes.
4. Incubate.
5. Wash with Wash/System liquid.
6. Add the Starter Reagents and measure the light emitted.

10. CALIBRATION

Testing assay specific calibrators allows the detected relative light unit (RLU) values to adjust the assigned master curve. Each calibration solution allows four (4) 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 six (6) weeks before.
– The analyzer has been serviced.
– Control values lie outside the expected ranges.

Calibrator values are stored in the Radio Frequency IDentification transponder (RFID Tag)

11. QUALITY CONTROL

Quality control must be performed 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 that the user refer to CLSI document, C24-A3, and 42 CFR 493.1256(c) for guidance on appropriate quality control practices. LIAISON® controls should be run in singlicate to monitor the assay performance. If control values lie within the expected ranges provided on the control vial labels, the test is valid. If control values 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 patient specimens must be retested.

12. LIMITATIONS OF THE PROCEDURE

- A skillful technique and strict adherence to the instructions are necessary to obtain reliable results.
- Bacterial contamination or heat inactivation of the specimens may affect the test results.
- Do not heat-inactivate sera.
- Measured Anti-HBs levels may vary depending from the testing procedure used. Results obtained from a single sample using tests from different manufacturers can therefore differ. If there is a change in the assay procedure used during the monitoring of vaccination protection, then the anti-HBs values obtained upon changing over to the new procedure must be confirmed by parallel measurements with both methods.
- Test results are reported qualitatively and quantitatively as Positive or Negative for the presence of anti-HBs above or below the medical decision point of 10.0 mIU/mL. However, diagnosis of Hepatitis B should be made in conjunction with other serological markers for HBV, clinical findings and other diagnostic procedures.
- Specimens with results above the assay measuring range may not be assayed after dilution.

13. INTERPRETATION OF RESULTS

The analyzer automatically calculates anti-HBs levels expressed as mIU/mL and grades the results.
For details, refer to the analyzer operator's manual.
Assay range. 3 to 500 mIU/mL anti-HBs. Samples that read less than 3.0 will be reported as <3.0 mIU/mL.
Samples that read greater than 500 will be reported as > 500 mIU/mL

Per current CDC guidance individuals with anti-HBs levels greater than 10 mIU/mL after completing an HBV vaccination series are considered protected from hepatitis B.
A positive result indicates recovery from acute or chronic hepatitis B virus (HBV) infection or acquired immunity from HBV vaccination. This assay does not differentiate between a vaccine-induced immune response and an immune response induced by infection with HBV.
Negative results, defined as anti-HBs levels of less than 10.0 mIU/mL, indicate a lack of recovery from acute or chronic hepatitis B or inadequate immune response to HBV vaccination.

The interpretation of results for the LIAISON® XL MUREX Anti-HBs is as follow:

Initial Result LIAISON® XL Anti-HBs assay		
mIU/mL	**Results**	**Retest Procedure**
< 9.0	Negative	No retest is required.
9.0 < x < 11.0	Equivocal	Retest in duplicate with the LIAISON® XL Anti-HBs assay.
≥ 11.0	Positive	No retest is required.

Final Result LIAISON® XL Anti-HBs assay		
Result After Retest	**Final Result**	**Clinical Interpretation of the Final Results**
Both retest results are <10 IU/mL	Negative	Anti-HBs concentration detected at < 10 mIU/mL. Individual is considered to be not immune to infection with HBV.
2 results out of 3 <10 IU/mL	Negative	Anti-HBs concentration detected at < 10 mIU/mL. Individual is considered to be not immune to infection with HBV.
2 results out of 3 ≥10 IU/mL	Positive	Anti-HBs concentration detected at ≥ 10 mIU/mL. Individual is considered to be immune to infection with HBV.
Both retest results are ≥10 IU/mL	Positive	Anti-HBs concentration detected at ≥ 10 mIU/mL. Individual is considered to be immune to infection with HBV.

- Samples with anti-HBs levels equal to or above 11.0 mIU/mL are considered Positive.
- Samples with anti-HBs levels below 9.00 mIU/mL are considered Negative.
- Samples with anti-HBs levels ranging between 9.00 mIU/mL and 11.0 mIU/mL should be graded as Equivocal. Equivocal samples must be retested in duplicate in order to confirm the initial result. Samples that are repeatedly equal

to or above 10.0 mIU/mL (i.e. at least 2 out of 3 results) should be considered as Positive for Anti-HBs. Samples that are repeatedly below 10.0 mIU/mL (i.e. at least 2 out of 3 results) should be considered as Negative for Anti-HBs.

The result should be assessed in conjunction with the patient's medical history, clinical examination and other hepatitis B serology markers to determine disease status.

14. SPECIFIC PERFORMANCE CHARACTERISTICS

14.1 Summary of clinical performance

The LIAISON® XL MUREX Anti-HBs clinical study population consisted of a total of 3082 specimens of whom 2826 were collected prospectively from individuals at increased risk of HBV infection due to lifestyle, behavior, occupation, disease state or known exposure event, or from individuals with signs and symptoms of a hepatitis infection (asymptomatic and symptomatic). A demographic summary of the overall risk specimen population by race, age and sex is provided in the following tables:

Demographics of Clinical Study Samples by Gender

	Adult				Pediatric (2-21)				Unknown Age			
	Prospective		Retrospective		Prospective		Retrospective		Prospective		Retrospective	
Gender	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Female	1643	61.7%	54	26.2%	98	60.9%	2	6.9%	1	50.0%	0	0.0%
Male	1017	38.2%	151	73.3%	61	37.9%	27	93.1%	1	50.0%	0	0.0%
Unknown	3	0.1%	1	0.5%	2	1.2%	0	0.0%	0	0.0%	21	100.0%
Total	**2663**	**100.0%**	**206**	**100.0%**	**161**	**100.0%**	**29**	**100.0%**	**2**	**100.0%**	**21**	**100.0%**

Demographics of Clinical Study Samples by Race

	Adult				Pediatric (2-21)				Unknown Age			
	Prospective		Retrospective		Prospective		Retrospective		Prospective		Retrospective	
Race	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
American Indian/ Alaskan Native	2	0.1%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Asian	21	0.8%	4	1.9%	3	1.9%	0	0.0%	0	0.0%	0	0.0%
Black/ African American	832	31.2%	57	27.7%	64	39.8%	4	13.8%	0	0.0%	0	0.0%
Native Hawaiian or Other Pacific Islander	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
White	1664	62.5%	141	68.4%	89	55.3%	25	86.2%	2	100.0%	21	100.0%
Unknown	6	0.2%	1	0.5%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Other	138	5.2%	3	1.5%	5	3.1%	0	0.0%	0	0.0%	0	0.0%
Total	**2663**	**100.0%**	**206**	**100.0%**	**161**	**100.0%**	**29**	**100.0%**	**2**	**100.0%**	**21**	**100.0%**

HBV serological classification for prospective and retrospective specimens is presented in the next table. Classification was based on test results of the FDA approved hepatitis-B assays listed below to determine the disease state for serological characterization. The following HBV markers were evaluated: HBsAg (and HBsAg Confirmatory test), Anti-HBs, Anti-HBc IgM, Anti-HBc, Anti-HBe and HBeAg.

Serological Classification by FDA-Approved HBV Panel

HBV Classification	HBsAg	HBeAg	Anti-HBc	Anti-HBc IgM	Anti-HBe	Anti-HBs	Prospective (n)	Retrospective (n)
Acute	R	NR	NR	NR	NR	NR	12	97
Acute	R	R	NR	NR	NR	NR		
Acute	R	R	R	R	NR	NR		
Acute	R	R	R	R	R	NR		
Acute	R	R	R	R	EQV	NR		
Acute	R	NR	R	EQV	R	NR		
Acute	R	NR	R	R	EQV	NR		
Acute	R	EQV	R	R	R	NR		
Acute	R	NR	R	R	NR	NR		
Acute	R	R	R	EQV	NR	NR		
Acute	R	R	R	R	NR	R		
Acute	R	R	R	R	EQV	R		
Acute	R	R	R	R	R	EQV		
Late Acute	R	NR	R	R	R	NR	2	32
Late Acute	R	NR	R	R	R	R		
Chronic	R	NR	NR	NR	R	NR	76	68
Chronic	R	NR	R	NR	NR	R		
Chronic	R	R	R	NR	NR	R		
Chronic	R	R	R	NR	NR	NR		
Chronic	R	EQV	R	NR	NR	NR		
Chronic	R	NR	R	NR	R	NR		
Chronic	R	NR	R	NR	NR	NR		
Chronic	R	NR	R	NR	R	R		
Chronic	R	EQV	R	NR	NR	NR		
Early Recovery	NR	NR	R	R	R	NR	48	9
Early Recovery	NR	NR	R	EQV	R	R		
Early Recovery	NR	NR	R	R	NR	NR		
Early Recovery	NR	NR	R	NR	R	NR		
Early Recovery	NR	NR	R	NR	NR	NR		
Early Recovery	NR	NR	R	R	NR	R		
Early Recovery	NR	NR	R	R	R	R		
Recovery	NR	NR	R	NR	R	R	131	36
Recovery	NR	NR	NR	NR	R	R		
Recovery	NR	NR	R	NR	EQV	R		
Immune Due to Natural Infection	NR	NR	R	NR	NR	R	104	3
Immune Due to Natural Infection	NR	NR	R	NR	NR	EQV		
HBV Vaccine Response	NR	NR	NR	NR	NR	R	1144	8
HBV Vaccine Response	NR	NR	NR	NR	NR	EQV		
Not Previously Infected	NR	NR	NR	NR	NR	NR	1302	1
Not Interpretable	NR	NR	NR	NR	R	NR	7	2
Not Interpretable	NR	NR	NR	R	NR	NR		
Not Interpretable	NR	R	NR	NR	NR	NR		
Not Interpretable	NR	R	NR	NR	NR	R		
Not Interpretable	NR	R	R	R	NR	EQV		
Not Interpretable	NR	R	R	R	NR	R		
Not Interpretable	R	NR	NR	NR	NR	R		

Based on the HBV classifications, the LIAISON® XL MUREX Anti-HBs results for the 2826 prospective and 256 retrospective specimens were compared to a reference Anti-HBs assay. The following tables show this comparison and percent agreement with 95% exact confidence intervals with the reference anti-HBs assay results.

Cumulative Clinical Agreement (Combined Prospective & Retrospective*)
LIAISON® XL MUREX Anti-HBs vs Reference Assay by Characterization.

HBV Classification	Reference Anti-HBs assay						Total
	Reactive		Eqv		Non reactive		
	LIAISON® XL MUREX Anti-HBs		LIAISON® XL MUREX Anti-HBs		LIAISON® XL MUREX Anti-HBs		
	Positive	Negative	Positive	Negative	Positive	Negative	
Acute	2	2	0	1	0	104	109
Late Acute	1	1	0	0	0	32	34
Chronic	3	1	0	0	1	139	144
Early Recovery	8	0	0	0	9	40	57
Recovery	163	4	0	0	0	0	167
Immune Due to Natural Infection	103	0	3	1	0	0	107
HBV Vaccine Response	1106	14	16	16	0	0	1152
Not Previously Infected	0	0	0	0	29	1274	1303
Not Interpretable	3	0	0	1	0	5	9
Total	**1389**	**22**	**19**	**19**	**39**	**1594**	**3082**

*An analysis of study data showed no significant difference in assay performance between prospective and retrospective specimens.

Cumulative Clinical Agreement (Combined Prospective & Retrospective)
LIAISON® XL MUREX Anti-HBs vs Reference Assay by Characterization.

HBV Classification	Positive Percent Agreement (PPA)	Negative Percent Agreement (NPA)
Acute	2/5 (40.0%) 95% CI: 11.8% to 76.9%	104/104 (100.0%) 95% CI: 96.4% to 100.0%
Late Acute	1/2 (50.0%) 95% CI: 9.5% to 90.5%	32/32 (100.0%) 95% CI: 89.3% to 100.0%
Chronic	3/4 (75.0%) 95% CI: 30.1% to 95.4%	139/140 (99.3%) 95% CI: 96.1% to 99.9%
Early Recovery	8/8 (100.0%) 95% CI: 67.6% to 100.0%	40/49 (81.6%) 95% CI: 68.6% to 90.0%
Recovery	163/167 (97.6%) 95% CI: 94.0% to 99.1%	N/A
Immune Due to Natural Infection	103/104 (99.0%) 95% CI: 94.8% to 99.8%	0/3 (0.0%) 95% CI: 0.0% to 56.2%
HBV Vaccine Response	1106/1136 (97.4%) 95% CI: 96.3% to 98.1%	0/16 (0.0%) 95% CI: 0.0% to 19.4%
Not Previously Infected	N/A	1274/1303 (97.8%) 95% CI: 96.8% to 98.4%
Not Interpretable	3/4 (75.0%) 95% CI: 30.1% to 95.4%	5/5 (100.0%) 95% CI: 56.6% to 100.0%
Total	1389/1430 (97.1%) 95% CI: 96.1% to 97.9%	1594/1652 (96.5%) 95% CI: 95.5% to 97.3%

Pediatric Cumulative Clinical Agreement (Combined Prospective & Retrospective*)
LIAISON® XL MUREX Anti-HBs vs Reference Assay by Characterization.

HBV Classification	Reference Anti-HBs assay						Total
	Reactive		Eqv		Non reactive		
	LIAISON® XL MUREX Anti-HBs		LIAISON® XL MUREX Anti-HBs		LIAISON® XL MUREX Anti-HBs		
	Positive	Negative	Positive	Negative	Positive	Negative	
Acute	0	0	0	0	0	20	20
Late Acute	0	0	0	0	0	7	7
Chronic	0	0	0	0	1	6	7
Early Recovery	0	0	0	0	0	1	1
Recovery	4	1	0	0	0	0	5
Immune Due to Natural Infection	3	0	0	0	0	0	3
HBV Vaccine Response	57	2	3	1	0	0	63
Not Previously Infected	0	0	0	0	6	78	84
Not Interpretable	0	0	0	0	0	2	2
Total	**64**	**3**	**3**	**1**	**7**	**114**	**192**

Pediatric Cumulative Clinical Agreement (Combined Prospective & Retrospective)
LIAISON® XL MUREX Anti-HBs vs Reference Assay by Characterization.

HBV Classification	Positive Percent Agreement (PPA)	Negative Percent Agreement (NPA)
Acute	N/A	20/20 (100.0%) 95% CI: 83.9% to 100.0%
Late Acute	N/A	7/7 (100.0%) 95% CI: 64.6% to 100.0%
Chronic	N/A	6/7 (85.7%) 95% CI: 48.7% to 97.4%
Early Recovery	N/A	1/1 (100.0%) 95% CI: 20.7% to 100.0%
Recovery	4/5 (80.0%) 95% CI: 37.6% to 96.4%	N/A
Immune Due to Natural Infection	3/3 (100.0%) 95% CI: 43.8.8% to 100.0%	NA
HBV Vaccine Response	57/60(95.0) 95% CI: 86.3% to 98.0%	0/3 (0.0%) 95% CI: 0.0% to 56.2%
Not Previously Infected	N/A	78/84(92.9%) 95% CI: 85.3% to 96.7%
Not Interpretable	N/A	2/2 (100.0%) 95% CI: 34.2% to 100.0%
Total	64/68 (94.1%) 95% CI: 85.9% to 97.7%	114/124 (91.9%) 95% CI: 85.8% to 95.6%

14.2. Pediatric samples

Pediatric samples were tested to determine if these types of samples provide equivalent results to adult human serum.
A total of thirty (30) negative pediatric patient samples were collected for this study. The pediatric samples encompassed the age range of two (2) months to twenty-one (21) years. Ten (10) negative pediatric samples were spiked with IgG anti-HBs high positive sample to obtain high negative samples. Ten (10) pediatric samples were spiked with IgG anti-HBs high positive sample to obtain high low positive samples. Ten (10) pediatric samples were spiked with IgG anti-HBs high positive sample to obtain moderate positive samples. Adult negative pool samples were used as controls, by spiking with IgG anti-HBs high positive sample to achieve the same three (3) levels of samples: high negative, low positive and moderate positive samples. Averaged results for each pediatric sample were compared to results obtained on adult samples. The results of the study suggest that pediatric samples react in the same manner as adult samples.

14.3. Within Laboratory Precision with LIAISON® XL Analyzer

A twenty (20) day reproducibility/precision study was performed by using a coded panel that was prepared by either spiking or diluting samples as necessary to obtain negative, low positive and mid positive samples. Kit Controls and Calibration Verifiers were also included in the 20-day study. The panel samples, kit controls and Cal Verifiers were tested on three (3) LIAISON® XL MUREX Anti HBs kit lots in two (replicates) per run, two (2) runs per day for twenty (20) operating days on one (1) LIAISON® XL Analyzer for a total of 240 results. The CLSI document EP5-A3 was consulted in the preparation of the testing protocol.

LIAISON® XL MUREX Anti-HBs Assay All 3 Lots Combined											
Sample ID	Mean	Repeatability		Between-Run		Between-Day		Between-Lot		Within Laboratory	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Ctrl Neg #RS-764	*977	32.198	3.30%	7.269	0.70%	24.653	2.50%	20.068	2.10%	45.826	4.70%
Ctrl Neg #RS-765	*940	27.365	2.90%	13.132	1.40%	18.266	1.90%	17.476	1.90%	39.501	4.20%
Ctrl Neg #RS-766	*941	25.578	2.70%	17.607	1.90%	19.764	2.10%	20.353	2.20%	42.061	4.50%
Ctrl Pos #RS-767	51.9	0.825	1.60%	0.905	1.70%	0.694	1.30%	5.428	10.50%	5.608	10.80%
Ctrl Pos #RS-768	56.4	0.908	1.60%	1.012	1.80%	0.641	1.10%	4.215	7.50%	4.475	7.90%
Ctrl Pos #RS-769	53.7	0.89	1.70%	1.169	2.20%	0.578	1.10%	3.967	7.40%	4.269	8.00%
Cal Ver #RS-784 A	7.56	0.236	3.10%	0.154	2.00%	0.181	2.40%	0.95	12.60%	1.007	13.30%
Cal Ver #RS-784 B	20.1	0.396	2.00%	0.248	1.20%	0.364	1.80%	2.47	12.30%	2.54	12.60%
Cal Ver #RS-784 C	72.6	1.022	1.40%	0.681	0.90%	0.857	1.20%	6.809	9.40%	6.972	9.60%
Cal Ver #RS-784 D	237	2.973	1.30%	3.572	1.50%	2.681	1.10%	27.599	11.60%	28.116	11.90%
Cal Ver #RS-785 A	6.94	0.214	3.10%	0.103	1.50%	0.146	2.10%	0.658	9.50%	0.715	10.30%
Cal Ver #RS-785 B	18.3	0.412	2.30%	0.339	1.90%	0.375	2.10%	1.662	9.10%	1.786	9.80%
Cal Ver #RS-785 C	75.1	0.87	1.20%	1.042	1.40%	0.885	1.20%	4.376	5.80%	4.666	6.20%
Cal Ver #RS-785 D	238	3.747	1.60%	2.507	1.10%	3.324	1.40%	19.32	8.10%	20.116	8.50%
Cal Ver #RS-786 A	7.15	0.223	3.10%	0.08	1.10%	0.203	2.80%	0.7	9.80%	0.767	10.70%
Cal Ver #RS-786 B	19.4	0.371	1.90%	0.371	1.90%	0.289	1.50%	1.736	8.90%	1.836	9.50%
Cal Ver #RS-786 C	77.3	1.038	1.30%	0.935	1.20%	1.122	1.50%	5.436	7.00%	5.723	7.40%
Cal Ver #RS-786 D	251	4.106	1.60%	2.782	1.10%	3.584	1.40%	23.625	9.40%	24.404	9.70%
AHBS-1-U1	*1024	27.177	2.70%	18.492	1.80%	18.06	1.80%	22.522	2.20%	43.749	4.30%
AHBS-1-U2	7.32	0.205	2.80%	0.124	1.70%	0.135	1.80%	1.116	15.30%	1.149	15.70%
AHBS-1-U3	16.9	0.386	2.30%	0.618	3.70%	0.000	0.00%	1.841	10.90%	1.98	11.70%
AHBS-1-U4	26.9	0.457	1.70%	0.405	1.50%	0.556	2.10%	3.967	14.80%	4.052	15.10%
AHBS-1-U5	35.2	0.608	1.70%	0.675	1.90%	0.313	0.90%	2.234	6.40%	2.432	6.90%
AHBS-1-U6	76	1.385	1.80%	0.41	0.50%	1.062	1.40%	4.744	6.20%	5.071	6.70%
AHBS-1-U7	122	1.77	1.40%	1.288	1.10%	1.693	1.40%	14.523	11.90%	14.784	12.10%
AHBS-1-U8	289	4.745	1.60%	5.408	1.90%	3.25	1.10%	38.677	13.40%	39.475	13.60%

* Samples outside the reading range of the assay, precision calculations are based on signal (RLU)

14.4. Reproducibility

A 5-day reproducibility/precision study was conducted at two (2) external laboratories and one (1) internal Diasorin laboratory. Each site used a different lot of LIAISON® XL MUREX Anti-HBs assay. The coded panel used in the 5-day study was the same panel used in the 20-day study. The coded panel, one (1) lot of kit controls and one (1) lot of Calibration Verifiers were tested at all three (3) sites, using six (6) replicates per run in one (1) runs per day for five (5) operating days. The CLSI document EP15-A3 was consulted in the preparation of the testing protocol. The mean, standard deviation, and coefficient of variation (%CV) of the results were computed for each of the tested specimens across sites.

*Precision calculations are based on signal (RLU).

Sample ID	N	Mean	Repeatability		Between-Day/Runs		Within Laboratory Precision		Between sites/lots		Reproducibility	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Ctrl Neg* (all 3 lots)	90	780.611	28.577	3.7%	13.741	1.8%	31.710	4.1%	51.133	6.6%	60.167	7.7%
Ctrl Pos (all 3 lots)	90	53.777	1.313	2.4%	0.811	1.5%	1.543	2.9%	1.862	3.5%	2.418	4.5%
Cal Ver A (all 3 lots)	90	7.278	0.217	3.0%	0.082	1.1%	0.232	3.2%	0.227	3.1%	0.325	4.5%
Cal Ver B (all 3 lots)	90	19.269	0.527	2.7%	0.279	1.4%	0.596	3.1%	1.044	5.4%	1.202	6.2%
Cal Ver C (all 3 lots)	90	74.560	1.345	1.8%	1.253	1.7%	1.838	2.5%	1.200	1.6%	2.195	2.9%
Cal Ver D (all 3 lots)	90	242.422	4.881	2.0%	3.828	1.6%	6.203	2.6%	13.707	5.7%	15.045	6.2%
AHBS-1-U1*	90	847.011	22.506	2.7%	14.415	1.7%	26.727	3.2%	54.888	6.5%	61.049	7.2%
AHBS-1-U2	90	7.119	0.260	3.6%	0.248	3.5%	0.359	5.0%	0.264	3.7%	0.445	6.3%
AHBS-1-U3	90	16.532	0.531	3.2%	1.198	7.2%	1.311	7.9%	0.892	5.4%	1.585	9.6%
AHBS-1-U4	90	25.670	1.265	4.9%	2.254	8.8%	2.585	10.1%	0.981	3.8%	2.765	10.8%
AHBS-1-U5	90	33.063	1.140	3.4%	2.018	6.1%	2.317	7.0%	1.000	3.0%	2.524	7.6%
AHBS-1-U6	90	72.782	2.392	3.3%	4.628	6.4%	5.210	7.2%	2.950	4.1%	5.987	8.2%
AHBS-1-U7	90	113.361	4.672	4.1%	8.672	7.7%	9.850	8.7%	8.769	7.7%	13.188	11.6%
AHBS-1-U8	90	282.244	8.281	2.9%	10.400	3.7%	13.294	4.7%	20.494	7.3%	24.429	8.7%

14.5. Standardization

The LIAISON® XL MUREX Anti-HBs assay is standardized against the WHO Second International Standard for anti-hepatitis B surface antigen (anti-HBs) immunoglobulin, human (NIBSC code: 07/164, 2008), and assay demonstrated linearity between 3 and 500 mIU/mL.

14.6. Linearity by dilution test

Linearity was evaluated by preparing dilutions of the WHO Second International Standard for anti-HBs (NIBSC code: 07/164) in anti-HBs negative serum and plasma matrices, The first sample was prepared to have an observed concentration of above 1000 mIU/m. Samples representing a calibration curve, to cover the whole assay range, were prepared by serial dilution of the first sample.

Data analysis was based on CLSI EP6A2, by regression analysis of the Expected vs. Observed values. The assay demonstrated linearity between 3 and 500 mIU/mL.

14.7. Analytical Sensitivity as Seroconversion Panel Performance

Ten (10) commercially available HBV seroconversion panels were tested using LIAISON® XL MUREX Anti-HBs and a commercially available FDA-approved comparator assay to determine the sensitivity of the assay. The results are summarized in the following table:

PANEL ID	Number of Specimens	LIAISON® XL MUREX Anti-HBs		Comparator assay		Difference in number of Days	Difference in number of Blood draws
		Last Bleed (Draw) with negative Result	First Bleed (Draw) with positive Result	Last Bleed (Draw) with non-reactive Result	First Bleed (Draw) with reactive Result		
HBV-001	20	166	186	202	n.a.	n.a.	-2
HBV-002	20	74	79	88	107	-28	-3
6281	12	43	50	50	54	-4	-1
6507	14	70	84	98	127	-43	-2
6509	12	84	98	98	112	-14	-1
6510	12	84	98	98	112	-14	-1
6511	12	112	126	126	140	-14	-1
6516	12	28	42	42	87	-45	-3
6529	12	42	56	85	98	-42	-3
6534	12	29	43	43	57	-14	-1

*n.a. indicates a positive result was not achieved.

The sensitivity of the LIAISON® XL MUREX Anti-HBs was comparable to the comparator assay in the ten (10) seroconversion panels tested.

14.8. Matrix Comparison

Twenty Five (25) paired sets of matched serum (with and without gel SST) and plasma (K_2 EDTA, lithium and sodium heparin) were tested to determine if these sample types provide equivalent results on the LIAISON® XL MUREX Anti-HBs assay. Each sample was divided into three aliquots. Two sets of aliquots were spiked with an IgG anti-HBs high positive sample to achieve: high negative samples and positive samples spanning the assay range. The third set of aliquots was un-spiked to serve as control samples. Where possible, native samples identified as high negative and low positive during the initial screening, were used instead of spiking these samples. The results obtained on the serum-plasma paired samples indicated that there is equivalence among serum (with and without gel SST), K_2 EDTA, lithium heparin and sodium heparin plasma.

14.9. Potential interfering substances

Controlled studies of potentially interfering substances at five (5) Anti HBs levels showed no interference at the concentration for each substance listed below in the LIAISON® XL MUREX Anti-HBs assay. The testing was based on CLSI-EP07.

Substances	Tested concentrations
Triglycerides	3000 mg/dL
Hemoglobin	1000 mg/dL
Unconjugated bilirubin	20 mg/dL
Conjugated bilirubin	20 mg/dL
Albumin	6000 mg/dL
Cholesterol	350 mg/dL

14.10. Cross-Reactivity

The LIAISON® XL MUREX Anti-HBs assay was evaluated for potential interference with specimens from individuals with medical conditions unrelated to hepatitis B infection and from other conditions that may result from atypical immune system activity (i.e. rheumatoid factor, anti-nuclear antibodies, HAMA). None of the tested cross reactant pathologies returned consistent with a conclusion of Cross reactivity. There is no evidence of cross reactivity with the tested pathologies.

Organism / Condition	N	Comparator Anti HBs assay	LIAISON® XL MUREX Anti-HBs	
			Negative	Positive
Anti-nuclear antibodies (ANA)	10	Negative	10	0
Auto-immune hepatitis	10	Negative	10	0
C. trachomatis	11	Negative	11	0
CMV (IgG / IgM)	11	Negative	11	0
EBV (IgM)	11	Negative	11	0
Fatty liver disease	11	Negative	11	0
HAMA	11	Negative	11	0
Hemodialysis patient	11	Negative	11	0
Hepatitis A Virus (anti-HAV IgM)	11	Negative	11	0
Hepatitis C Virus (anti-HCV)	11	Negative	11	0
Hepatocellular carcinoma	11	Negative	11	0
HIV-1 (anti-HIV-1)	11	Negative	11	0
HIV-2 (anti-HIV-2)	11	Negative	11	0
HSV (IgG / IgM)	11	Negative	11	0
HTLV-1/2 (anti-HTLV)	11	Negative	11	0
IgG monoclonal gammopathy	11	Negative	11	0
IgM monoclonal gammopathy	10	Negative	10	0
Influenza vaccine recipients	11	Negative	11	0
Multiparous pregnancies	10	Negative	10	0
Multiple myeloma	11	Negative	11	0
Multiple transfusion recipients	10	Negative	10	0
N. gonorrhoea	11	Negative	11	0
Pregnancy 1st trimester	10	Negative	10	0
Pregnancy 2nd trimester	10	Negative	10	0
Pregnancy 3rd trimester	11	Negative	11	0
Rheumatoid Factor	11	Negative	11	0
T. pallidum	11	Negative	11	0
T.cruzi (anti-T. cruzi)	11	Negative	11	0

14.11. High–dose hook effect

No High dose hook effect was observed for Anti-HBs concentrations up to 570,000 mIU/mL.

14.12. Limit of Blank (LoB)*

Following the method from CLSI EP17-A, the limit of blank for the LIAISON® XL MUREX Anti-HBs assay is ≤0.6 mIU/mL.

*Limit of Blank, or the highest value likely to be observed with a sample containing no analyte, replaces the term “analytical sensitivity”.

14.13. Limit of Detection (LoD)

Following the method from CLSI EP17-A, the limit of detection for the LIAISON® XL MUREX Anti-HBs assay is 0.970 mIU/mL.

14.14. Limit of Quantitation (LoQ)

Following the method from CLSI EP17-A, the limit of quantitation for the LIAISON® XL MUREX Anti-HBs assay is 3 mIU/mL.

15. REFERENCES

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For Customer Service in the US call toll free 1-800-328-1482.

The symbols glossary is provided electronically and can be found in the Dialog section at www.diasorin.com using the part and lot numbers associated with the corresponding IVD product.

LIAISON® XL murex Control Anti-HBs ([REF] 318221)

1. INTENDED USE

The LIAISON® XL murex Control Anti-HBs (negative and positive) is intended for use as assayed quality control samples to monitor the performance of the LIAISON® XL MUREX Anti-HBs assay. The performance characteristics of LIAISON® XL MUREX Control Anti-HBs have not been established for any other assays or instrument platforms.

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

2. MATERIALS PROVIDED

Negative control (2 x 3.7 mL)	**[CONTROL|-]**	Human serum, without HBs antibodies, 0.2% ProClin® 300 and preservatives.
Positive control (2 x 3.7 mL)	**[CONTROL|+]**	Human plasma Positive for Anti-HBs and negative for HBsAg, 0.2% ProClin® 300 and 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 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. Each laboratory is responsible for adopting different limits to meet individual requirements.

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.

3. WARNINGS AND PRECAUTIONS

- 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.
- 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).

Hazardous reagents are classified and labelled as follow:

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).)

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

4. 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 for twelve (12) weeks when properly stored at 2-8°C between multiple uses. Avoid bacterial contamination of controls. The controls should not be used past the expiry date indicated on the vial labels.

5. PREPARATION OF REAGENTS

- Place the control vials in type C racks on the analyzer. Each control solution allows at least 20 tests to be performed.
- The minimum volume required is 550 µL (150 µL control + 400 µL dead volume).
- 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.

6. TARGET VALUES

The range of concentration 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. If control values obtained after successful calibration lie repeatedly outside the expected ranges, the test should be repeated using an unopened control vial.

7. 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-A3, and 42 CFR 493.1256(c) for guidance on appropriate quality control practices.

LIAISON® XL controls are intended to monitor for reagent failure. Whenever LIAISON® XL 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.

Strict adherence to the instructions of the LIAISON® XL MUREX Anti-HBs kit are necessary to obtain reliable results.

8. LIMITATIONS

Control values for assays other the LIAISON® XL MUREX Anti-HBs assay have not been established.

For Customer Service in the US call toll free 1-800-328-1482.

The symbols glossary is provided electronically and can be found in the Dialog section at www.diasorin.com using the part and lot numbers associated with the corresponding IVD product.

LIAISON® XL MUREX Anti-HBs Verifiers ([REF] 318223)

1. INTENDED USE

The LIAISON® XL MUREX Anti-HBs Verifiers (level 1, 2, 3, and level 4) are assayed quality control materials intended for the quantitative verification of calibration and reportable range of the LIAISON® XL MUREX Anti-HBs assay. The performance characteristics of LIAISON® XL MUREX Anti-HBs Verifiers have not been established in connection with any other assay or instrument platforms.

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

2. MATERIALS PROVIDED

Calibration verifiers: 5 x 1 vials

Verifiers A-D (1 vial each level x 3.7 mL)	**[CONTROL|A]** **[CONTROL|B]** **[CONTROL|C]** **[CONTROL|D]**	Human plasma positive for Anti-HBs and negative for HBsAg, 0.2% ProClin® 300 and 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 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. Each laboratory is responsible for adopting different limits to meet individual requirements.

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.

3. WARNINGS AND PRECAUTIONS

- For *in vitro* diagnostic use.
- Verifiers 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.
- 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).

Hazardous reagents are classified and labelled as follow:

REAGENTS:	[CONTROL|A], [CONTROL|B], [CONTROL|C], [CONTROL|D], [CONTROL|E]
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).)

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

4. 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 for twelve (12) weeks when properly stored at 2-8°C between multiple uses. Avoid bacterial contamination of controls. The controls should not be used past the expiry date indicated on the vial labels.

5. PREPARATION OF REAGENTS

- Place the control vials in type C racks on the analyzer. Each control solution allows at least 20 tests to be performed.
- The minimum volume required is 550 µL (150 µL control + 400 µL dead volume).
- 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.

6. LIMITATIONS

The DiaSorin LIAISON® XL MUREX Anti-HBs Verifiers are designed for use with the LIAISON® XL MUREX Anti-HBs assay. The performance of the DiaSorin LIAISON® XL MUREX Anti-HBs Verifiers has not been established with other assays or other immunoassay analyzers. The LIAISON® XL MUREX Anti-HBs Verifiers are not intended for use as routine quality control materials or as calibration materials. Improper reagent storage or technical errors may result in discordant results.

7. ASSIGNED VALUES

Concentrations and ranges assigned by DiaSorin to each Calibration Verifier are provided on a Certificate of Analysis.
The 4 levels of calibration verifiers (A-D) are intended to span the assay range of the LIAISON® XL MUREX Anti-HBs assay. The target concentrations for each lot of calibration verifiers are assigned at DiaSorin by testing several replicates of each concentration in multiple runs, on multiple instruments using multiple lots of LIAISON® XL MUREX Anti-HBs assay integrals and controls.

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