HƯỚNG DẪN SỬ DỤNG TIẾNG ANH

Tài liệu được xác nhận bằng chữ ký số

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Người đại diện hợp pháp của cơ sở

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Changes: Update of Legal Manufacturer name;
Deletions: -

LIAISON® Anti-HBc (REF 310130)

1. INTENDED USE

The LIAISON® Anti-HBc assay uses chemiluminescent immunoassay (CLIA) technology for the qualitative determination of total antibodies to Hepatitis B core Antigen (Anti-HBc) in human serum and plasma samples included specimens collected post-mortem (non-heart beating).

The assay is intended as an aid in the diagnosis of HBV infection in individuals with or without symptoms of hepatitis. It is also intended as a screening test for blood and hemocomponents donors as well as for organ, tissue and cells post-mortem donors.

The test has to be performed on the LIAISON® Analyzer family.

2. SUMMARY AND EXPLANATION OF THE TEST

Hepatitis is an inflammatory disease of the liver that can severely damage the organ. The disease can result from non-infectious causes or from infectious viral and bacterial agents (4).

Viral hepatitis B is endemic throughout the world (8, 11, 16). The infection is spread primarily through percutaneous contact with infected blood, e.g., sharing of needles by drug addicts or transfusion of blood products that have not been screened for HBV (2, 4, 8, 13). The hepatitis B virus (HBV) is also found in virtually every type of human body fluid and has been known to be spread through oral and genital contact (2, 4, 8, 13). HBV can be transmitted perinatally from mother to child (2).

The incubation period for hepatitis B averages 90 days (range: 40-180 days). Common symptoms include malaise, fever, gastroenteritis, and icterus (5, 8). HBV infection can lead to *(a)* icteric hepatitis; *(b)* subclinical anicteric hepatitis; *(c)* fulminant hepatitis; *(d)* chronic active or persistent hepatitis (4, 8). Over 90% of adult patients with hepatitis B completely recover from acute illness, approximately 1% die of fulminant hepatitis, and approximately 6 to 10% become chronic active or persistent carriers (4, 8, 10).

In acute hepatitis B infection, total and IgM anti-HBc are detectable in serum shortly before clinical symptoms appear and slightly after the occurrence of hepatitis B surface antigen (HBsAg). In cases in which hepatitis B infection resolves, total anti-HBc is also detectable during the *window* period following loss of HBsAg and prior to the development of antibody to HBsAg (anti-HBs). In cases of asymptomatic or subclinical hepatitis B, total anti-HBc detectability follows the same pattern as in acute symptomatic infection. In these cases, however, HBsAg and hepatitis B *e* antigen (HBeAg) are present for only a brief period or may not be detectable. Therefore, in these patients, detection of total anti-HBc and/or total anti-HBs must be relied on as evidence of previous HBV infection (3, 6).

IgG anti-HBc antibodies develop shortly after the onset of hepatitis B infection and persist over time in all patients who have previously been infected with hepatitis B, regardless of the outcome of their infection. However, during the prodromal, acute and early convalescent phases of hepatitis B infection, anti-HBc exists primarily as IgM antibody. IgM antibody diminishes and disappears over time (usually in approximately six months).

In patients with chronic hepatitis B infection or an asymptomatic chronic carrier state, HBsAg appears during the incubation phase of the disease and may persist for years and possibly for life (3, 14). Total anti-HBc also appears during this early phase, rises in titre, and persists over time; the highest titres of total anti-HBc are found in the chronic HBsAg carrier state (9, 14). Thus, in chronic infection, total anti-HBc antibody is detectable in association with other hepatitis B serological markers.

In a small percentage of cases, total anti-HBc diminishes over time and may fall into the undetectable range many years after hepatitis B infection. Total anti-HBc may also be undetectable in the very early phases of acute hepatitis B infection.

Total anti-HBc may also be detectable in the absence of any other hepatitis B markers. This finding may indicate recent infection (patient in the HBsAg/anti-HBs *window*), or infection in the more remote past, in which case anti-HBs may also be detectable (1, 7, 12, 15).

Although it is not possible to discriminate between acute and chronic infection or between recent and remote infection solely with the total anti-HBc assay, results obtained in conjunction with other hepatitis B assays may aid in the determination of the stage of disease caused by HBV or in establishing past exposure to HBV.

3. PRINCIPLE OF THE PROCEDURE

The method for qualitative determination of anti-HBc is a two-step competitive chemiluminescence immunoassay (CLIA). Recombinant HBcAg is used for coating magnetic particles (solid phase) and antibodies to HBcAg (mouse monoclonal) are linked to an isoluminol derivative (isoluminol-antibody conjugate). During the first incubation, anti-HBc present in calibrators, samples or controls binds to a fixed and limited amount of recombinant HBcAg bound to the solid phase. During the second incubation, the antibody conjugate links the solid-phase recombinant HBcAg epitopes still free. After each incubation, the unbound material is removed with a wash cycle.

Subsequently, the starter reagents are added and a flash chemiluminescence reaction is thus induced. The light signal, and hence the amount of isoluminol-antibody conjugate, is measured by a photomultiplier as relative light units (RLU) and is inversely indicative of anti-HBc concentration present in calibrators, samples or controls.

4. MATERIALS PROVIDED

Reagent integral

Magnetic particles (2.3 mL)	SORB	Magnetic particles coated with HBcAg obtained in *E. coli* by the recombinant DNA technology, BSA, phosphate buffer, < 0.1% sodium azide.
Calibrator 1 (1.4 mL)	CAL 1	Calf serum containing high anti-HBc antibody levels, 0.2% ProClin® 300, preservatives.
Calibrator 2 (1.4 mL)	CAL 2	Human serum/plasma without anti-HBc antibodies, 0.2% ProClin® 300, preservatives, an inert blue dye.
Buffer F (11 mL)	BUF F	Acetate buffer.
Conjugate (23 mL)	CONJ	Antibody to HBcAg (mouse monoclonal) conjugated to an isoluminol derivative, human serum/plasma, newborn calf serum, phosphate buffer, EDTA, 0.2% ProClin® 300, preservatives, an inert blue dye.
Number of tests		100

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 Analyzer	**LIAISON® Analyzer**
LIAISON® XL Cuvettes (REF X0016). LIAISON® XL Disposable Tips (REF X0015). LIAISON® XL Starter Kit (REF 319200). – LIAISON® Wash/System Liquid (REF 319100). LIAISON® XL Waste Bags (REF X0025). –	LIAISON® Module (REF 319130). – LIAISON® Starter Kit (REF 319102) or LIAISON® XL Starter Kit (REF 319200). LIAISON® Light Check 12 (REF 319150). LIAISON® Wash/System Liquid (REF 319100). LIAISON® Waste Bags (REF 450003). LIAISON® Cleaning Kit (REF 310990).

Additionally required materials

LIAISON® Anti-HBc controls (negative and positive) (REF 310131).

5. WARNINGS AND PRECAUTIONS

For *in vitro* diagnostic use.

All serum and plasma units used to produce the components provided in this kit have been tested for the presence of HBsAg, anti-HCV, anti-HIV-1, anti-HIV-2 and found to be non-reactive. 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.

6. SAFETY PRECAUTIONS

Do not eat, drink, smoke or apply cosmetics in the assay laboratory.

Do not pipette by mouth.

Avoid direct contact with potentially infected material by wearing laboratory clothing, protective goggles, and disposable gloves. Wash hands thoroughly at the end of each assay.

Avoid splashing or forming an aerosol. All drops of biological reagent must be removed with a sodium hypochlorite solution with 0.5% active chlorine, and the means used must be treated as infected waste.

All samples and reagents containing biological materials used for the assay must be considered as potentially able to transmit infectious agents. The waste must be handled with care and disposed of in compliance with the laboratory guidelines and the statutory provisions in force in each Country. Any materials for reuse must be appropriately sterilized in compliance with the local laws and guidelines. Check the effectiveness of the sterilization/decontamination cycle.

Do not use kits or components beyond the expiration date given on the label.

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

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).

Pursuant to EC Regulation 1272/2008 (CLP), SORB and BUF F are labeled as EUH210 safety data sheets available on request.
For additional information see Safety Data Sheets available on www.diasorin.com.

7. 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.

An incomplete magnetic particles resuspension may cause variable and inaccurate analytical results.

Foaming of reagents

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

Loading of integral into the reagent area

LIAISON® Analyzer

– Place the integral into the reagent area of the analyzer with the bar code label facing left and let it stand for 30 minutes before using. The analyzer automatically stirs and completely resuspends the magnetic particles.
– Follow the analyzer operator's manual to load the specimens and start the run.

LIAISON® XL Analyzer

– LIAISON® XL Analyzer is equipped with a built-in solid-state magnetic device which aids in the dispersal of microparticles prior to placement of a reagent integral into the reagent area of the analyzer. Refer to the analyzer operator's manual for details.
  a. Insert the reagent integral into the dedicated slot.
  b. Allow the reagent integral to remain in the solid-state magnetic device for at least 30 seconds (up to several minutes). Repeat as necessary.
– Place the integral into the reagent area of the analyzer with the label facing left and let it stand for 15 minutes before using. The analyzer automatically stirs and completely resuspends the magnetic particles.
– Follow the analyzer operator's manual to load the specimens and start the run.

8. STORAGE AND STABILITY OF REAGENT INTEGRAL

– **Sealed**: Stable at 2-8°C until the expiry date.
– **Opened on board or at 2-8°C**: Stability eight weeks.
– Use always the same analyzer for a reagent integral already opened.
– Use storage rack provided with the analyzer for upright storage of reagent integral.
– Do not freeze.
– Keep upright for storage to facilitate later proper resuspension of magnetic particles.

Keep away from direct light.

9. SPECIMEN COLLECTION AND PREPARATION

Either human serum or plasma may be used. The anticoagulants citrate, EDTA and heparin have been tested and may be used with this assay. Post- mortem specimens, collected up to 24 hours after death, have been tested and may be also used in the assay. The correct specimen type must be used in the assay.

Follow tube manufacturers' instructions carefully when using collection containers. Blood should be collected aseptically by venipuncture and the serum or plasma separated from clot, red cells or gel separator, after centrifugation.

Centrifugation conditions range from 1,000 to 3,000 g for 10 minutes. Conditions may vary depending on tube manufacturers recommendations. Use of alternate centrifugation conditions should be evaluated and validated by the laboratory.

Before shipping specimens, serum or plasma specimens should be removed from clot, red cells or gel separator. Specimens may be shipped in dry ice (frozen), in wet ice (for 2°-8°C) or at room temperature (20°-25°C), by following sample storage limitations described below.

Uncontrolled transport conditions (in terms of temperature and time) can cause inaccurate analytical results. During validation studies, specimen collection tubes commercially available at the time of testing were used. Therefore not all collection tubes from all manufacturers have been evaluated. Blood collection devices from various manufacturers may contain substances which could affect the test results in some cases (Bowen et al., Clinical Biochemistry, 43, 4-25, 2010).

Concerning storage limitations, if the assay is performed within seven days of sample collection, the samples removed from red cells, clot or gel separator may be kept at 2°-8°C; otherwise they should be aliquoted and stored deep-frozen (–20°C or below). Five samples with different reactivity were stored for seven days at 2°-8°C and underwent five freeze-thaw cycles. The results showed no significant differences; however multiple freeze-thaw cycles should be avoided. If samples are stored frozen, mix thawed samples well before testing.

Samples removed from red cells, clot or gel separator having particulate matter, fibrin, turbidity, lipaemia, or erythrocyte debris, specimens that have been stored at room temperature (20°-25°C), or frozen and thawed, or samples requiring repeat testing, require clarification by further centrifugation (it's recommended 10,000 g for 10') before testing, to improve consistency of results. Specimens with a lipid layer on the top should be transferred in a secondary tube, taking care to transfer only the clarified material. Grossly haemolyzed or lipaemic samples as well as samples containing particulate matter or exhibiting obvious microbial contamination should not be tested. Check for and remove air bubbles before assaying.

Cadaveric specimens should be stored following same indications than for living donors.

The minimum volume required is 260 µL specimen (110 µL specimen + 150 µL dead volume).

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 four weeks before.
– The analyzer has been serviced.
– Control values lie outside the expected ranges.

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

11. ASSAY PROCEDURE

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

LIAISON® Analyzer. Each test parameter is identified via the bar codes on the reagent integral label. In the event that the barcode label 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.

LIAISON® XL Analyzer. 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 module.
2. Dispense buffer F.
3. Dispense coated magnetic particles.
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.

12. QUALITY CONTROL

LIAISON® controls should be run in singlicate to monitor the assay performance. Quality control must be performed by running LIAISON® Anti-HBc controls
(a) at least once per day of use,
(b) whenever a new reagent integral is used,
(c) whenever the kit is calibrated,
(d) whenever a new lot of Starter Reagents is used.

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

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

13. INTERPRETATION OF RESULTS

The analyzer automatically calculates anti-HBc levels expressed as index value and grades the results. For details, refer to the analyzer operator's manual.
Calibrators and controls may give different RLU or dose results on LIAISON® and LIAISON® XL, but patient results are equivalent.

The cut-off value discriminating between the presence and the absence of anti-HBc has an index value of 1. Sample results should be interpreted as follows:
Samples with anti-HBc levels equal to or above an index value of 1 are considered *non-reactive* in the assay.

Samples with anti-HBc levels below an index value of 1 are considered *reactive* in the assay.

Samples with anti-HBc levels ranging within +/- 10% of the cut-off value should be retested in duplicate in order to confirm the initial result. Samples which are repeatedly *reactive* (at least 2 out of 3 results) should be considered *reactive*. Samples which are repeatedly *non-reactive* (at least 2 out of 3 results) should be considered *non-reactive*.

14. 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.

Test results are reported qualitatively as reactive or non-reactive for the presence of anti-HBc. However, 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 judgement.

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 concluded between analyzer types. These must be accomplished on one particular analyzer type (either LIAISON® or LIAISON® XL).

Before testing cadaveric specimens, collection and centrifugation procedures should be carefully applied. After death, haemolysis and other changes (including proteolysis and dilution) occur in blood, which may lead to False Negative and False Positive in testing. In subjects transfused immediately prior to death high percentage of haemodilution can affect the performance of the test due to analyte dilution.

15. SPECIFIC PERFORMANCE CHARACTERISTICS

15.1. Analytical specificity

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

Interference. Controlled studies of potentially interfering substances or conditions showed that the assay performance was not affected by anticoagulants (citrate, EDTA, heparin), haemolysis (up to 100 mg/dL haemoglobin), lipaemia (up to 3000 mg/dL triglycerides), bilirubinaemia (up to 20 mg/dL bilirubin), or by freeze-thaw cycles of samples. Results are not influenced by the use of positive same-day fresh samples as a comparative study in 35 freshly collected specimens demonstrates.

Cross-reactions. As a rule, the presence of potentially cross-reactive antibodies does not interfere in the assay. The antibodies investigated were: *(a)* immunoglobulins to various infectious agents – such as hCMV, HSV, EBV, rubella virus, HCV, HIV, HTLV-I/II, HAV, *Toxoplasma gondii*, *Treponema pallidum* – *(b)* anti-nuclear (ANA) antibodies, human anti-mouse antibodies (HAMA), heterophilic antibodies, hypergammaglobulins, and rheumatoid factor (anti-Fc immunoglobulin) antibodies.

15.2. Analytical sensitivity

Analytical sensitivity may also be expressed as the limit of detection, which is the minimal amount of specific analyte detectable by the assay. It was evaluated by testing serial dilutions of a high-titre anti-HBc positive in-house preparation.
The results show that the limit of detection is below 0.60 PEI U/mL (HBc Reference Material 82 - IgG anti-HBc, Paul-Ehrlich-Institut, Germany).

15.3. Precision with LIAISON® Analyzer

Different samples, containing different concentrations of specific analyte, were assayed to determine repeatability and reproducibility of the assay (i.e., within- and between-assay variability). The variability shown in the tables below did not result in sample misclassification. **The results refer to the groups of samples investigated and are not guaranteed specification as differences may exist between laboratories and locations.**

Repeatability	D	C	B	A
Number of determinations	21	21	21	21
Mean (index value)	0.953	0.604	0.347	0.104
Standard deviation	0.093	0.030	0.043	0.010
Coefficient of variation (%)	9.8	4.9	12.4	9.7

Reproducibility	E	C	B	A
Number of determinations	20	20	20	20
Mean (index value)	0.510	0.456	0.321	0.091
Standard deviation	0.091	0.057	0.039	0.015
Coefficient of variation (%)	17.9	12.4	12.1	16.7

15.4. Precision with LIAISON® XL Analyzer

Different samples, containing different concentrations of specific analyte, were assayed to determine repeatability and reproducibility of the assay (i.e., within- and between-assay variability). The variability shown in the tables below did not result in sample misclassification. **The results refer to the groups of samples investigated and are not guaranteed specification as differences may exist between laboratories and locations.**

Repeatability. Twenty replicates were performed in the same run to evaluate repeatability.

Repeatability	1	2	3	Positive control
Number of determinations	20	20	20	20
Mean (index value)	1.55	0.729	0.524	0.531
Standard deviation	0.090	0.070	0.019	0.025
Coefficient of variation (%)	5.8	9.6	3.7	4.7
Min. index value	1.35	0.563	0.466	0.486
Max. index value	1.75	0.832	0.555	0.590

Reproducibility. Twenty replicates were performed in different days (one or two runs per day) to evaluate reproducibility.

Reproducibility	1	2	3	Positive control
Number of determinations	20	20	20	20
Mean (index value)	1.53	0.703	0.469	0.462
Standard deviation	0.12	0.039	0.035	0.035
Coefficient of variation (%)	7.8	5.6	7.5	7.5
Min. index value	1.34	0.642	0.391	0.391
Max. index value	1.79	0.786	0.540	0.526

15.5. High-dose saturation effect

Whenever samples containing extremely high antibody concentrations are tested in a competitive test, misestimated results may be excluded, because the analytical signals remain consistently low (saturation curve).
Analysis of saturation effect was evaluated by testing one high-titred sample positive for anti-HBc. This sample resulted in an index value around zero that would be expected with high-titred sera, indicating no sample misclassification.

15.6. Performance characteristics of cadaveric specimen testing

Performance characteristics of cadaveric specimens testing was determined by testing, according PEI validation protocol*, post-mortem specimens collected up to 24 hours after death in comparison to living donor specimens. 30 post-mortem samples were tested as unspiked and spiked at 2 levels: low positive and medium/high positive. The same procedure was performed with the same number of normal human serum from living donors, tested in parallel as reference to compare with post-mortem sample results. The results obtained were analyzed through calculation of percentage difference between mean of living donors results and mean of post-mortem results, at each reactivity level. In this study, the obtained percentage difference was equal or below 8,6% for each of the tested reactivity levels (see table below). Paired t-test analysis were performed between post-mortem and living donors specimens, spiked at low and medium/high positive levels, demonstrating not significantly difference on two groups (p value <0.05).

Repeteability was assessed using one post-mortem and one living donor specimens, spiked up to a low-level of reactivity with a human serum reactive for antibodies to hepatitis B core antigen (anti-HBc). Each specimen was assessed in six replicates in the same run. The obtained percent coefficient of variation (CV%) did not exceed 15%. As reported in the table below 4.6% for the cadaveric specimen and 4.8% for the living donor were found in the study. The results refer to the group of investigated samples and are not guaranteed specifications, as differences may exist between laboratories and locations.

	Sample	Test results Means (index value)	Recovery (%) Post-mortem/Living donors	t-test p value	CV% 6 replicates
Neat	Post-Mortem unspiked	2.25	n.a.	n.a	n.a
	Living donors unspiked	2.45			
Low Positive	Post-Mortem spiked	0.448	-8.6	0.244	4.6
	Living donors spiked	0.490			4.8
Medium/high Positive	Post-Mortem spiked	0.265	-6.0	0.201	n.a
	Living donors spiked	0.282			

* Paul Ehrlich Institute - Proposal for the Validation of Anti-HIV-1/2 or HIV Ag/Ab Combination Assays, Anti-HCV-Assays, HBsAg and Anti-HBc Assays for Use with Cadaveric Samples - 08/05/2014

15.7. Diagnostic specificity and sensitivity

BLOOD DONOR POPULATION

Diagnostic specificity was assessed by testing 5010 expected negative specimens from an unselected blood donor population. The specimens were tested by several comparison methods and consensus between them as well as the available clinical and serological data were applied to define the expected results. Three specimens were unresolved by the reference methods and therefore were not included in data analysis.

Specificity with Liaison® analyzers

9 reactive, 15 equivocal and 4983 non-reactive results were obtained at the screening in the expected negative population studied – diagnostic specificity: 99.52% (95% confidence interval: 99.29-99.69%).

15 reactive and 4992 non-reactive results were observed after repeat testing of reactive and equivocal samples in the expected negative population studied – diagnostic specificity 99.70% (95% confidence interval: 99.51-99.83%).

Specificity with Liaison® XL analyzers

3 reactive, 9 equivocal and 4995 non-reactive results were obtained at the screening in the expected negative population studied – diagnostic specificity: 99.76% (95% confidence interval: 99.58-99.88%).

5 reactive and 5002 non-reactive results were observed after repeat testing of reactive and equivocal samples in the expected negative population studied – diagnostic specificity 99.90% (95% confidence interval: 99.76-99.97%).

CLINICAL SAMPLES

Diagnostic specificity and sensitivity were assessed by testing 1339 specimens from different selected populations (subjects never infected by HBV, pregnant women, dialysis patients, transplant recipients, subjects with past HBV infection, HBV vaccinees, patients affected by HBV hepatitis). The specimens were tested by several comparison methods and consensus between them as well as the available clinical and serological data were applied to define the expected results. 20 specimens were unresolved by the reference methods and therefore were not included in the data analysis.

5 reactive, 4 equivocal and 692 non-reactive results were observed at screening in the expected negative population studied - diagnostic specificity: 98.72% (95% confidence interval: 97.57-99.41%).

7 reactive and 694 non-reactive results were observed after repeat testing of equivocal samples in the expected negative population studied - diagnostic specificity: 99.00% (95% confidence interval: 97.95-99.60%).

No non-reactive and 618 reactive results were observed at screening in the expected positive population studied - diagnostic sensitivity: 100% (95% confidence interval: 99.41-100%).

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