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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 HIV Ab/Ag HT ([REF] 318290)

1. INTENDED USE

The LIAISON® XL murex HIV Ab/Ag HT is an *in vitro* chemiluminescent immunoassay for the simultaneous qualitative detection of HIV p24 antigen and antibodies to HIV-1 (Groups M and O) and HIV-2 in human serum (without or with gel-SST) or plasma (lithium and sodium heparin, sodium citrate, and potassium EDTA), on the LIAISON® XL Analyzer. It is intended to be used as an aid in the diagnosis of HIV-1/HIV-2 infection, including acute or primary HIV-1 infection. The assay may also be used as an aid in the diagnosis of HIV-1 and/or HIV-2 infection in pediatric subjects (2-21 years) and in pregnant women.

The assay cannot distinguish between the detection of HIV p24 antigen and HIV-1/HIV-2 antibodies.
The LIAISON® XL murex HIV Ab/Ag HT assay is not intended for screening donors of blood or blood products, or human cells or tissues or cellular and tissue-based products (HCT/Ps), or organ donors for HIV.

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

2. SUMMARY AND EXPLANATION OF THE TEST

The etiological agent of acquired immunodeficiency syndrome (AIDS) has been identified as two types of retrovirus, collectively designated as human immunodeficiency virus (HIV). HIV is transmitted by sexual contact between HIV-infected individuals, exposure to contaminated blood or blood products, and prenatal infection of a fetus or perinatal infection of a newborn from an infected mother. Antibodies to HIV are detected in AIDS patients and in HIV-infected asymptomatic individuals; HIV infection is always detected in AIDS patients and seropositive individuals by cell culture or after amplification of viral RNA and/or proviral DNA.

HIV-1 is classified by phylogenetic analysis into groups M (main or major), N (new, non-M, non-O), O (outlier). The global AIDS pandemic was mainly caused by group M viruses, while group N and O viruses are relatively rare and endemic to West Central Africa. However, group O infections have been identified in Europe and the USA. HIV-1 group M is composed of genetic subtypes (A, B, C, D, F, G, H, J, and K) and circulating recombinant forms (CRFs). HIV-1 subtype B is the predominant subtype in the USA, Europe, Japan, and Australia.

A closely related, but distinct type of immunodeficiency virus is designated human immunodeficiency virus type 2 (HIV-2). Human immunodeficiency virus type 2 is similar to HIV-1 in its structural morphology, genomic organization, cell tropism, in vitro cytopathogenicity, transmission routes, and ability to cause AIDS. HIV-2 is less pathogenic than HIV-1, and HIV-2 infections have a longer latency period with slower progression to full-blown disease, lower viral titers, and lower rates of vertical and horizontal transmission. HIV-2 is endemic to West Africa, but HIV-2 infections, at a lower frequency compared to HIV-1, have been identified in the USA, Europe, Asia, and other regions of Africa.

Serological cross-reactivity between HIV-1 and HIV-2 has been shown to be highly variable from sample to sample. This variability requires the inclusion of antigens to both HIV-1 and HIV-2 for the screening of antibodies to HIV-1 and HIV-2. The presence of HIV-1 and/or HIV-2 antibodies and/or p24 antigen in the blood indicates potential infection with HIV-1 and/or HIV-2. Early after infection with HIV, but prior to seroconversion, HIV antigens may be detected in serum or plasma specimens. The HIV structural protein most often used as the marker of antigenemia is the core protein, p24. The LIAISON® XL murex HIV Ab / Ag HT assay uses HIV p24 monoclonal antibodies to detect HIV p24 antigen prior to seroconversion, thereby decreasing the seroconversion window and improving early detection of HIV infection.

3. PRINCIPLE OF THE PROCEDURE

The assay simultaneously detects but does not differentiate HIV antibodies and HIV p24 antigen. Qualitative determination of specific antibodies to HIV and HIV p24 antigen is a sandwich chemiluminescence immunoassay. HIV-1 recombinant antigen, HIV-1 group O and HIV-2 biotinylated peptides, and biotinylated monoclonal antibodies to HIV p24 antigen are used for coating magnetic particles (solid phase) and are also linked to isoluminol or fluorescein derivatives (isoluminol-antigen/peptides/monoclonal conjugates and fluorescein anti-HIV p24 monoclonal conjugates). The LIAISON® XL MUREX HIV Ab/Ag HT assay consists of two incubation phases. During the first incubation, HIV antibodies present in samples or controls and HIV p24 antigen present in calibrator, samples or controls bind to the solid phase and, for HIV p24 antigen, to anti-HIV p24 monoclonal labelled with fluorescein derivatives. During the second incubation, HIV-1 antigen, HIV-1 group O, HIV-2 peptides, monoclonal anti-HIV p24 antigen and monoclonal anti-fluorescein linked to an isoluminol derivative (isoluminol-antigen conjugate) react with HIV antibodies, HIV p24 antigen and monoclonal anti-HIV p24 antigen labelled with fluorescein derivatives already bound to the solid phase. After each incubation, the unbound material is removed with a wash cycle. Subsequently, the starter reagents are added and a flash chemiluminescence reaction is thus induced. The light signal, and hence the amount of isoluminol-antigen/peptide/monoclonal conjugate, is measured by a photomultiplier as relative light units (RLU) and is indicative of HIV-1/2/O antibodies or HIV p24 antigen presence in calibrator, samples or controls.

4. MATERIALS PROVIDED

Reagent integral

Magnetic particles [SORB] (2.5 mL)	Magnetic particles coated with HIV-1 (group M) gp41 recombinant antigen (obtained in *E. coli)*, HIV-1 group O and HIV-2 biotinylated peptides, biotinylated monoclonal anti-HIV p24 antigen, BSA, PBS buffer, preservatives.
Calibrator [CAL] (2,9 mL)	Human serum and/or plasma with low-level reactivity for anti-HIV-2 and anti-HIV-1 (group M), casein, PBS buffer, 0.2% ProClin® 300, an inert yellow dye.
Assay Buffer 1 [BUF 1] (10.8 mL)	Monoclonal anti-HIV p24 conjugated with fluorescein derivatives, bovine serum, casein, BSA, non-specific IgG (mouse polyclonal), HEPES buffer, detergent, EDTA, 0.2% ProClin® 300, preservatives.
Conjugate [CONJ] (2 x 23 mL)	HIV-1 (group M) gp41 recombinant antigen (obtained in *E. coli*), HIV-1 group O and HIV-2 peptides, monoclonal anti-HIV p24 and monoclonal anti-fluorescein derivative, conjugated to an isoluminol derivative, sheep serum, negative human serum, casein, non-specific IgG (mouse polyclonal), BSA, TRIS buffer, 0.2% ProClin® 300, preservatives.
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 sold separately

The following are required to perform the LIAISON® XL MUREX HIV Ab/Ag HT assay.

LIAISON® XL Analyzer

LIAISON® XL Starter Kit ([REF] 319200) - catalyst in 4% sodium hydroxide solution and 0.12% hydrogen peroxide solution

LIAISON® Wash/System Liquid ([REF] 319100) - (10x) - phosphate buffer solution, < 0.1% sodium azide

LIAISON® XL Cuvettes ([REF] X0016)

LIAISON® XL Disposable Tips ([REF] X0015)

LIAISON® XL Waste Bags ([REF] X0025)

Additional required materials

LIAISON® XL MUREX Control HIV Ab/Ag HT ([REF] 318291)

5. WARNINGS AND PRECAUTIONS

- This test kit is intended for use with the approved matrices. Strict adherence to the instructions is necessary to obtain reliable results.
- All human blood source material used to produce the components provided in this test kit derives from units found to be non-reactive for HBsAg, antibodies to HCV, HIV-1, HIV-2 when tested by an FDA-approved method, except for the positive controls which are reactive for antibodies to HIV-2, HIV-1 group M, or HIV-1 group O. The units positive for HIV antibodies have been obtained from individuals infected with HIV-1 and/or HIV-2. Although these have been inactivated by heat treatment (56 °C for one hour) during the manufacturing process they should be considered as potentially infectious.
- 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.
- Do not pipette by mouth. Do not eat, drink, smoke or apply cosmetics in the assay laboratory.
- Strict adherence to the instructions is necessary to obtain reliable results.
- 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 requirements of local and federal agencies.
- Liquid waste must be decontaminated with sodium hypochlorite at a final concentration of 10% for at least half an hour.
- Any materials for reuse 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 the sterilization/decontamination cycle by initially validating it and routinely using biological indicators.
- The LIAISON® XL Analyzer 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).

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 and European Union EC Regulation 1272/2008 (CLP).
- Hazardous reagents are classified and labelled as follow:

REAGENTS:	CAL, BUFI1, CONJ	CONJ
CLASSIFICATION:	Skin sens. 1 H317	Specific target organ target organ toxicity – repeated exposure category 2 H373
SIGNAL WORD:	Warning	Warning
SYMBOLS / PICTOGRAMS:	 GHS07 Exclamation mark	 GHS08 Health hazard
HAZARD STATEMENTS:	H317 May cause an allergic skin reaction.	H373 May cause damage to organs through prolonged or repeated exposure
PRECAUTIONARY STATEMENTS:	P261 Avoid breathing dust/fume/gas/mist/ vapours/spray. P280 Wear protective gloves/protective clothing/eye protection/face protection. P333+P313- If skin irritation or rash occurs: Get medical advice/attention.	n.a
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)	. Ethylene Glycol

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.

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

6. REAGENT PREPARATION

REAGENT INTEGRAL

Please note the following important reagent handling precautions:

Resuspension of magnetic particles

Magnetic particles must be completely resuspended before the 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 color 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.
An incomplete magnetic particle 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, the calibrator in particular (position two 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. Load the integral into the reagent area once the foam has dissipated.

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).
– 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. Refer to the Reagent Integral Preparation 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 five (5) weeks when stored at 2–8°C or on board the analyzer.

8. SPECIMEN COLLECTION AND PREPARATION

Follow the tube manufacturer's 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 the tube manufacturer's 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 on dry ice (frozen), on wet ice (for 2–8°C) or at room temperature (20°–25°C), by following the sample storage limitations described below.

Uncontrolled transport conditions (in terms of temperature and time) can cause inaccurate analytical results. Blood collection devices from various manufacturers may contain substances which could affect the test results in some cases (Brown et al., Clinical Biochemistry, 43, 45, 2010).

Samples removed from red cells, clot or gel separator having particulate matter, fibrin, turbidity, lipemia, 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 the 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 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 three (3) days does not adversely 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. Samples are stable through seven (7) freeze/thaw cycles. 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 volume required for a single determination is 350 µL specimen (200 µL specimen + 150 µL dead volume).

Dead volume is the volume left at the bottom of the tube which the analyzer cannot aspirate.

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 Assay Buffer.
4. Incubate.
5. Wash with Wash/System liquid.
6. Dispense Conjugate into the reaction cuvettes.
7. Incubate.
8. Wash with Wash/System liquid.
9. Add the Starter Reagents and measure the light emitted.

10. CALIBRATION

Assaying of the calibrator contained in the reagent integral allows the analyzer to set the assay cut-off. The calibrator 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 Starter kit is used.
- The previous calibration was performed more than five (5) weeks before.
- The analyzer has been serviced.
- Control values lie outside the expected ranges.

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, 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 specimens must be retested. 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 additional quality control materials.

12. LIMITATIONS OF THE PROCEDURE

- LIAISON® XL MUREX HIV Ab/Ag HT is for *in vitro* diagnostic use only.
- For prescription use only.
- The LIAISON® XL MUREX HIV Ab/Ag HT assay must be used in accordance with the instructions for use in the package insert to obtain accurate results.
- The LIAISON® XL MUREX HIV Ab/Ag HT assay is not intended for screening donors of blood or blood products, or human cells or tissues or cellular and tissue-based products (HCT/Ps), or organ donors for HIV.
- This assay cannot distinguish between the detection of HIV p24 antigen and HIV-1/HIV-2 antibodies.
- This test is suitable only for investigating single samples, not for diluted specimens, sample pools. Bacterial contamination or heat inactivation of the specimens may affect the test results.
- Serum (without or with gel-SST) or plasma derived from lithium and sodium heparin, sodium citrate, or K2-EDTA (ethylenediaminetetraacetate) as anticoagulants may be used with the LIAISON® XL MUREX HIV Ab/Ag HT assay. Using other types of samples may not yield accurate results.
- A non-reactive test result for HIV p24 antigen and/or HIV antibodies does not exclude the possibility of exposure to or infection with HIV. In fact, either the patient may be unable to synthesize HIV specific antibodies or the circulating levels of p24 antigen and/or HIV specific antibodies may be below the assay detection limit. It is recommended that testing be repeated on a fresh specimen after 1–3 months if clinical judgement indicates a suspected false nonreactive result.
- False non- reactive results may be obtained in individuals infected with HIV-1 and/or HIV-2 who are receiving medication for treatment for HIV infection (ART) or prevention of infection (PrEP or PEP).
- Falsely reactive results cannot be ruled out with any test kit, the percentage of which is related to specimen integrity, the specificity of the test kit, and the HIV prevalence in the population being screened.
- A positive LIAISON® XL MUREX HIV Ab/Ag HT assay result interpretation confirms the presence of specific antibodies to HIV-1 and/or HIV-2 in the sample. HIV and AIDS-related conditions are clinical syndromes caused by HIV-1 and HIV-2 and their diagnosis can only be established clinically.

- A person who has antibodies to HIV-1 or HIV-2 is presumed to be infected with the virus, however, false positive results may be obtained if a person who has participated in an HIV vaccine study may develop antibodies to the vaccine and may or may not be infected with HIV. A comprehensive risk history and clinical judgement should be considered before concluding that an individual is not infected with HIV.

13. INTERPRETATION OF RESULTS

The presence or absence of HIV p24 antigen and/or HIV specific antibodies in the specimens is determined by comparing the chemiluminescence reaction signal to the preliminary cut-off value provided by the assay calibration.
The analyzer automatically calculates the signal-to-cutoff (S/CO) ratios, then interprets the results.
For details, refer to the analyzer operator's manual.

The cutoff discriminating between the reactivity to HIV p24 antigen and/or HIV specific antibodies has a S/CO value of 1.00.

Patient results should be interpreted as follows:

- **Non-Reactive:** Samples with S/CO value of less than 1.00 are considered non-reactive (NR). These samples are considered negative for HIV p24 antigen and HIV specific antibodies and do not require further testing.
- **Reactive:** Samples with S/CO value equal to or greater than 1.00 are considered initially reactive (IR) for HIV p24 antigen and/or HIV specific antibodies.
- All **Initially Reactive** samples should be repeated in duplicate.
  - If S/CO values are equal to or greater than 1.00 in either or both of the repeat replicates, the samples are considered repeatedly reactive (RR) and must be confirmed with supplemental assays.
  - If S/CO values are less than 1.00 in both of the repeat replicates, the samples are considered non-reactive (NR).

14. SPECIFIC PERFORMANCE CHARACTERISTICS

14.1 Summary of clinical performance

A multi-site clinical agreement study was conducted to determine the clinical performance of the LIAISON® XL MUREX HIV Ab/Ag HT assay on samples that would routinely be tested for HIV infection.
The LIAISON® XL MUREX HIV Ab/Ag HT clinical study populations consisted of a total of 1,543 retrospective specimens and 8,035 prospective specimens collected from unique individuals. Two (2) specimens from the prospective population “Individuals at for high risk HIV-2” were excluded from all testing due to potential cross-contamination between samples during aliquoting, reducing the total number of the prospective samples tested to 8,033.

The samples were collected from 15 different countries: Argentina (n=24; 0.3%), Cameroon (n=47; 0.5%), Colombia (n=72; 0.8%), Congo (n=11; <0.1%), Cote d'Ivoire (n=628; 6.6%), Democratic Republic of Congo (69; 0.7%), Dominican Republic (506; 5.3%), Guinea-Bissau (14; 0.1%), Mexico (1; <0.1%), Nigeria (565; 5.9%), Peru (1777; 18.6%), Sierra Leone (1; <0.1%), South Africa (2; <0.1%), Ukraine (1; <0.1%), and the United States (5760; 60.1%). One hundred (100; 1.0%) AIDS specimens with CDC classification were purchased with unknown country of origin. The specimens collected in the United States were from multiple states including California, Florida, Indiana, New Jersey, New York, Pennsylvania, Texas, and Virginia.

A demographic summary of the overall risk specimen population by gender is provided in the following table

Gender	Adult				Pediatric (2-21)				Unknown Age			
	Prospective		Retrospective		Prospective		Retrospective*		Prospective		Retrospective	
	n	%	n	%	N	%	n	%	n	%	n	%
Female	2947	45.4%	407	28.1%	563	38.0%	37	45.1%	7	12.5%	3	23.1%
Male	3549	54.6%	1040	71.9%	918	62.0%	45	54.9%	6	10.7%	10	76.9%
Unknown	0	0.0%	0	0.0%	0	0.0%	0	0.0%	43	76.8%	0	0.0%
Total	**6496**	**100.0%**	**1447**	**100.0%**	**1481**	**100.0%**	**82**	**100.0%**	**56**	**100.0%**	**13**	**100.0%**

The following tables show clinical results of LIAISON® XL MUREX HIV Ab/Ag on prospective populations:

Summary Table of Reactivity in Prospectively Collected US Adults and Subjects of Unknown Age

		LIAISON® XL MUREX HIV Ab/Ag HT			FDA Approved HIV Combo Assay			FDA Approved HIV 1/2 Differentiation Assay Reactive			LIAISON® XL Sensitivity 95% CI	LIAISON® XL Specificity 95% CI
Specimen Population	N	NR	IR	RR	NR	IR	RR	HIV-1	HIV-2	Untypable Cross Reactive		
Low Risk	2015[A]	2009	6	6	2010	6	5	0	0	0	NA	(2009/2015) 99.7% 99.4%-99.9%
Low Risk Fresh*	527	525	3	2	526	1	1	0	0	0	NA	(525/527) 99.6% 98.6%-99.9%
Low Risk Pregnant	367	367	0	0	367	0	0	0	0	0	NA	(367/367) 100.0% 99.0%-100.0%
High Risk	495[B]	478	17	17	475	20	20	16	0	0	(16/16) 100.0% 80.6%-100.0%	(478/479) 99.8% 98.8%-100.0%
High Risk Pregnant	363	351	12	12	354	9	9	4	0	0	(4/4) 100.0% 51.0%-100.0%	(351/359) 97.8% 95.7%-98.9%
TOTAL	3767	3730	38	37	3732	36	35	20	0	0	(20/20) 100.0% 83.9%-100.0%	(3730/3747) 99.5% 99.3%-99.7%

[A] 1980 adults and 35 of unknown age
[B] 493 adults and 2 of unknown age
*Samples collected and not frozen prior to testing.

Summary Table of Reactivity in Prospectively Collected US Pediatric Subjects

		LIAISON® XL MUREX HIV Ab/Ag HT			FDA Approved HIV Combo Assay			FDA Approved HIV 1/2 Differentiation Assay Reactive			LIAISON® XL Sensitivity 95% CI	LIAISON® XL Specificity 95% CI
Specimen Population	N	NR	IR	RR	NR	IR	RR	HIV-1	HIV-2	Untypable Cross Reactive		
Low Risk Pediatric	548	547	1	1	546	3	2	0	0	0	NA	(547/548) 99.8% 99.0%-100.0%
Low Risk Pediatric Fresh*	23	23	0	0	23	0	0	0	0	0	NA	(23/23) 100.0% 85.7%-100.0%
Low Risk Pregnant (≤ 21 yrs)	29	29	0	0	29	0	0	0	0	0	NA	(29/29) 100.0% 88.3%-100.0%
High Risk Pediatric	305	303	3	2	304	1	1	1	0	0	(1/1) 100.0% 20.7%-100.0%	(303/304) 99.7% 98.2%-99.9%
High Risk Pregnant (≤ 21 yrs)	41	40	1	1	41	0	0	0	0	0	NA	(40/41) 97.6% 87.4%-99.6%
TOTAL	946	942	5	4	943	4	3	1	0	0	(1/1) 100.0% 20.7%-100.0%	(942/945) 99.7% 99.1%-99.9%

*Samples collected and not frozen prior to testing.

Summary Table of Reactivity in Prospectively Collected Non-US Adults and Subjects of Unknown Age

		LIAISON® XL MUREX HIV Ab/Ag HT			FDA Approved HIV Combo Assay			FDA Approved HIV 1/2 Differentiation Assay Reactive			FDA Approved HIV-1 RNA PCR Reactive	LIAISON® XL Sensitivity 95% CI	LIAISON® XL Specificity 95% CI
Specimen Population	N	NR	IR	RR	NR	IR	RR	HIV-1	HIV-2	Untypable Cross Reactive			
High Risk	488	471	17	17	471	17	17	13	0	0	1*	(13/14) 92.9% 92.9%-98.7%	(470/474) 99.2% 97.9%-99.7%
High Risk HIV-2	459[A]	369	90	88	366	93	93	67	2	15	1[**]	(84/85) 98.8% 93.6%-99.8%	(370/374) 98.9% 97.3%-99.6%
Low Risk	1838[B]	1690	148	148	1701	139	137	92	0	0	12	(104/104) 100.00% 96.4%-100.0%	(1690/1734) 97.5% 96.6%-98.1%
TOTAL	2785	2530	255	253	2538	249	247	172	2	15	14	(201/203) 99.0% 96.5%-99.7%	(2527/2582) 97.9% 97.2%-98.4%

[A] 448 adults and 11 of unknown age
[B] 1830 adults and 8 of unknown age
*One High risk sample confirmed positive from Nigeria was negative by LIAISON® XL MUREX HIV Ab/Ag HT
[**]One High risk HIV-2 sample from Cote d'Ivoire was negative by the LIAISON® XL MUREX HIV Ab/Ag HT assay, positive for HIV-1 on the FDA Approved HIV Ag/Ab Combo Assay as well as the HIV1/2 differentiation assay but was negative on the FDA Approved HIV-1 RNA PCR.

Summary Table of Reactivity in Prospectively Collected Non-US Pediatric Subjects

		LIAISON® XL MUREX HIV Ab/Ag HT			FDA Approved HIV Combo Assay			FDA Approved HIV 1/2 Differentiation Assay **Reactive**			LIAISON® XL Sensitivity 95% CI	LIAISON® XL Specificity 95% CI
Specimen Population	N	NR	IR	RR	NR	IR	RR	HIV-1	HIV-2	Untypable Cross Reactive		
Low Risk Pediatric	412	408	4	4	410	2	2	0	0	0	NA	(408/412) 99.0% 97.5%-99.6%
High Risk Pediatric	84	84	0	0	84	0	0	0	0	0	NA	(84/84) 100.0% 95.6%-100.0%
High Risk HIV-2 Pediatric	39	27	12	12	26	13	13	11	1	0	(12/12) 100.0% 75.7%-100.0%	(27/27) 100.0% 87.5%-100.0%
TOTAL	535	519	16	16	520	15	15	11	1	0	(12/12) 100.0% *77.5%-100.0%*	(519/523) 99.2% *98.%--99.7%*

The following tables show clinical results of LIAISON® XL MUREX HIV Ab/Ag on retrospective populations:

Summary Table of Retrospective Population Presumably HIV-1 Positive US Adult

		LIAISON® XL MUREX HIV Ab/Ag HT			FDA Approved HIV Ag/Ab Combo Assay			FDA Approved HIV 1/2 Differentiation Assay **Reactive**			FDA Approved HIV-1 RNA PCR **Reactive**	LIAISON® XL Sensitivity 95% CI	LIAISON® XL Specificity 95% CI
Specimen Population	N	NR	IR	RR	NR	IR	RR	HIV-1	HIV-2	Untypable Cross Reactive			
HIV-1 Positive	985	0	985	985	0	985	985	983	0	0	1	(984/984) 100.0% *99.6%-100.0%*	(0/1) 0.0% *0.0%-79.3%*
HIV-1 Infected Pregnant	10	0	10	10	0	10	10	10	0	0	0	(10/10) 100.0% *77.2%-100.0%*	NA
HIV-1 Antigen Positive w/ Subtype Identification	5	0	5	5	0	5	5	5	0	0	0	(5/5) 100.0% *56.6%-100.0%*	NA
Total	1000	0	1000	1000	0	1000	1000	998	0	0	1	(999/999)100.0% *99.6%-100.0%*	(0/1) 0.0% *0.0%-79.3%*

Summary Table of Retrospective Population Presumably HIV-1 Positive US Pediatric

		LIAISON® XL MUREX HIV Ab/Ag HT			FDA Approved HIV Ag/Ab Combo Assay			FDA Approved HIV 1/2 Differentiation Assay **Reactive**			LIAISON® XL Sensitivity 95% CI	LIAISON® XL Specificity 95% CI
Specimen Population	N	NR	IR	RR	NR	IR	RR	HIV-1	HIV-2	Untypable Cross Reactive		
HIV-1 Positive Pediatrics	44	5	39	39	6	39	38	40	0	0	(36/36) 100.0% *90.4%-100.0%*	(5/8) 62.5% *30.6%-86.3%*
HIV-1 Infected Pregnant (≤21yrs)	3	0	3	3	0	3	3	3	0	0	(3/3) 100.0% *43.8%-100.0%*	NA
Total	47	5	42	42	6	42	41	43	0	0	(39/39) 100% *91.0%-100.0%*	(5/8) 62.5% *30.6%-86.3%*

Summary Table of Retrospective Population Presumably HIV Positive non-US Adult and subjects of unknown age

		LIAISON® XL MUREX HIV Ab/Ag HT			FDA Approved HIV Ag/Ab Combo Assay			FDA Approved HIV 1/2 Differentiation Assay **Reactive**			LIAISON® XL Sensitivity 95% CI	LIAISON® XL Specificity 95% CI
Specimen Population	N	NR	IR	RR	NR	IR	RR	HIV-1	HIV-2	Untypable Cross Reactive		
HIV-2 Positive	200[A]	0	200	200	0	200	200	3	67	127	(197/197)100.0% *98.1%-100.0%*	(0/3) 0.0% *0.0%-56.2%*
HIV-1 Infected Pregnant	25[B]	0	25	25	0	25	25	25	0	0	(25/25) 100.0% *86.7%-100.0%*	NA
HIV Group O Infected	45[C]	0	45	45	0	45	45	45	0	0	(45/45) 100.0% *92.1%-100.0%*	NA
HIV-1 Antigen Positive	90	0	90	90	0	90	90	88	0	2	(90/90) 100.0% *95.9%-100.0%*	NA
Total	360	0	360	360	0	360	360	161	67	129	(357/357)100.0% *98.9%-100.0%*	(0/3) 0.0% *0.0%-79.3%*

[A] 190 adults and 10 of unknown age
[B] 24 adults and 1 of unknown age
[C] 43 adults and 2 of unknown age

Summary Table of Retrospective Population Presumably HIV Positive Non-US Pediatric

		LIAISON® XL MUREX HIV Ab/Ag HT			FDA Approved HIV Ag/Ab Combo Assay			FDA Approved HIV 1/2 Differentiation Assay **Reactive**			LIAISON® XL Sensitivity 95% CI	LIAISON® XL Specificity 95% CI
Specimen Population	N	NR	IR	RR	NR	IR	RR	HIV-1	HIV-2	Untypable Cross Reactive		
HIV-1 Positive Pediatrics	17	2	15	15	0	17	17	14	0	0	(14/14) 100.0% *78.5%-100.0%*	(2/3) 66.7% *20.8%-93.9%*
HIV-1 Infected Pregnant ≤21 yrs	13	1	12	12	0	13	13	11	0	0	(11/11) 100.0% *74.1%-100.0%*	(1/2) 50.0% *9.5%-90.5%*
Group O Infected	2	0	2	2	0	2	2	2	0	0	(2/2) 100.0% *34.2%-100.0%*	NA
HIV Ag Positive	3	0	3	3	0	3	3	3	0	0	(3/3) 100.0% *43.8%-100.0%*	NA
Total	35	3	32	32	0	35	35	30	0	0	(30/30) 100.0% *88.6%-100.0%*	(3/5) 60.0% *23.1%-88.2%*

Summary Table of Retrospective Population Presumably HIV-2 Positive

		LIAISON® XL MUREX HIV Ab/Ag HT			FDA Approved HIV Combo Assay			FDA Approved HIV 1/2 Differentiation Assay **Reactive**			HIV-2 RNA Reactive		LIAISON® XL Sensitivity 95% CI
Specimen Population	N	NR	IR	RR	NR	IR	RR	HIV-1	HIV-2	Untypable Cross Reactive	R	NR	
HIV-2 Infected Adults	190	0	190	190	0	190	190	3*	62	122	187	3**	(187/187) 100.0% *98.0%-100.0%*
HIV-2 Infected unknown Age	10	0	10	10	0	10	10	0	5	5	10	0	(10/10) 100.0% *72.2%-100.0%*
Total	200	0	200	200	0	200	200	3	67	127	197	3	(197/200) 100.0% *98.1%-100.0%*

R = Reactive; NR = Non Reactive
*Three samples purchased as HIV-2 positive were found to be HIV-1 positive only.
**Three samples reactive on the LIAISON® XL MUREX HIV Ab/Ag HT and FDA Approved HIV Ag/Ab Combo Assay were tested on the HIV1/2 differentiation assay and were Neg (1) or indeterminate (2). All 3 were negative on the RNA PCR test.

Summary Table Results from Pregnant Women including subjects ≤ 21 years of Age

		LIAISON® XL MUREX HIV Ab/Ag HT			FDA Approved HIV Combo Assay			FDA Approved HIV 1/2 Differentiation Assay **Reactive**			LIAISON® XL Sensitivity 95% CI	LIAISON® XL Specificity 95% CI
Specimen Population	N	NR	IR	RR	NR	IR	RR	HIV-1	HIV-2	Untypable Cross Reactive		
Low Risk (Healthy) Pregnant	396	396	0	0	396	0	0	0	0	0	NA	(396/396) 100.0% *99.0%-100.0%*
High Risk Pregnant	404	391	13	13	395	9	9	4	0	0	(4/4) 100.0% *51.0%-100.0%*	(391/400) 97.8% *95.8%-98.8%*
HIV Positive Pregnant	51	1	50	50	0	51	51	49	0	0	(49/49)100.0% *92.7%-100.0%*	(1/2) 50.0% *9.5%-90.5%*
TOTAL	851	788	63	63	791	60	60	53	0	0	(53/53)100.0% *93.2%-100.0%*	(788/798) 98.7% *97.7%-99.3%*

Summary Table Results from Reactivity in Pregnant Females at High Risk for HIV Infection by Trimester

HIV Category	Trimester	HIV Infection Status				Total	LIAISON® XL Sensitivity 95% CI	LIAISON® XL Specificity 95% CI
		HIV Infected		Not Infected				
		LIAISON® XL MUREX HIV Ab/Ag HT		LIAISON® XL MUREX HIV Ab/Ag HT				
		+	-	+	-			
Pregnant Females at High Risk for HIV-1	1	1	0	0	43	44	(1/1) 100.0%	(43/43) 100.0% *91.8%-100.0%*
	2	0	0	5	139	144	NA	(139/144) 96.5% *92.1%-98.5%*
	3	3	0	4	191	198	(3/3) 100%	(191/195) 97.9% *94.8%-99.2%*
	Unknown	0	0	0	18	18	NA	(18/18) 100.0% *82.4%-100.0%*
Total		**4**	**0**	**9**	**391**	**404**	**(4/4) 100.0%** ***51.0%-100.0%***	**(391/400) 97.8%** ***95.3%-98.8%***

14.2. Group O HIV-1 detection

The ability of the LIAISON® XL MUREX HIV Ab/Ag HT assay to detect HIV-1 group O subtype was evaluated by testing forty-seven (47) retrospective specimens available with HIV1 O subtype determined by the specimen vendor. The specimens were tested with the LIAISON® XL MUREX HIV Ab/Ag HT assay and with an FDA approved HIV Combo assay, and all detected as reactive.

Reactivity in Group O HIV-1 Positive Specimens

Serotype	Number of Specimens tested	LIAISON® XL MUREX HIV Ab/Ag HT	FDA Approved HIV Combo Assay
M and O	9	(9/9)	(9/9)
O	38	(38/38)	(38/38)
Total	47	(47/47)	(47/47)

14.3. Reactivity in AIDS Specimens stratified by CDC Classification

The study was performed to evaluate the ability of the LIAISON® XL MUREX HIV Ab/Ag HT assay to detect specimens with different CDC AIDS classification. One hundred (100) specimens were available with CDC classification (the 52 category A specimens were further subcategorized as 22 A1, 27 A2, and three (3) A3; the 30 category B specimens were further subcategorized as 11 B1, 16 B2, and three (3) B3; of the category C specimens one (1) was not further subcategorized, six (6) were C1, five (5) were C2, and six (6) were C3). All specimens were from an adult population, ages 22 to 72.
The specimens were tested with the LIAISON® XL MUREX HIV Ab/Ag HT assay and with an FDA approved HIV Combo assay, and all detected as reactive.

Reactivity in AIDS Specimens stratified by CDC Classification

CDC AIDS Classification	Number of Specimens tested	LIAISON® XL MUREX HIV Ab/Ag HT	FDA Approved HIV Combo Assay
A	52	(52/52)	(52/52)
B	30	(30/30)	(30/30)
C	18	(18/18)	(18/18)
Total	100	(100/100)	(100/100)

14.4 HIV-1 M antigen positive specimens

The ability of the LIAISON® XL MUREX HIV Ab/Ag HT assay to detect HIV1 group M antigen positive specimens with various known HIV-1 group M subtypes was evaluated by using forty-nine (49) specimens available with HIV1 M subtype determined by the specimen vendor. The specimens were tested with the LIAISON® XL MUREX HIV Ab/Ag HT assay and with an FDA approved HIV Combo assay, and all detected as reactive.

Subtype	Number of Specimens tested	LIAISON® XL MUREX HIV Ab/Ag HT	FDA Approved HIV Combo Assay
A	6	(6/6)	(6/6)
B	7	(7/7)	(7/7)
C	1	(1/1)	(1/1)
D	3	(3/3)	(3/3)
F	5	(5/5)	(5/5)
G	5	(5/5)	(5/5)
H	4	(4/4)	(4/4)
K	2	(2/2)	(2/2)
CRF	16	(16/16)	(16/16)
TOTAL	49	(49/49)	(49/49)

Summary of the Cumulative Clinical Comparison versus the HIV Infection Status:

The sensitivity and specificity of the LIAISON XL HIV Ab/Ag HT are summarized in the tables below.

Clinical Comparison versus the HIV Infection for US Population (Combined Prospective & Retrospective)

LIAISON® XL HIV Ab/Ag HT	HIV Infection Status		Total
	HIV Infected	Not HIV Infected	
Reactive	1059	23	1082
Non-Reactive	0	4677	4677
Total	1059	4700	5759

Sensitivity: 1059/1059 = 100% 95% CI = 99.6–100%
Specificity: 4677/4700 = 99.5% 95% CI = 99.3–99.7%

Clinical Comparison versus the HIV Infection for Non-US Population (Combined Prospective & Retrospective)

LIAISON® XL HIV Ab/Ag HT	HIV Infection Status		Total
	HIV Infected	Not HIV Infected	
Reactive	600	61	661
Non-Reactive	2	3052	3054
Total	602	3113	3715

Sensitivity: 600/602 = 99.7% 95% CI = 98.8 – 99.9%
Specificity: 3052/3113 = 98.0% 95% CI = 97.5 – 98.5%

14.5 Pediatric samples

Pediatric samples were tested to determine if these types of samples provide equivalent results to adult human serum samples.
A total of thirty (30) negative pediatric patient samples were used for this study. The pediatric samples were spiked with HIV high positive sample to obtain low positive samples. One (1) negative Adult pool sample was used as a control. . One (1) adult sample was spiked with HIV high positive sample to obtain low positive samples. The results of the study suggest that pediatric samples react in the same manner as adult samples.

14.6 Samples from pregnant women

Samples from pregnant women were tested to determine if these types of samples provide equivalent results to non-pregnant adult human serum samples. A total of thirty (30) negative patient samples from pregnant women encompassing all three (3) trimesters of pregnancy were tested. Samples from pregnant women were spiked with HIV high positive sample to obtain low positive samples. Adult negative pool samples, from non-pregnant adults, were used as controls. One (1) adult sample was spiked with HIV high positive sample to obtain low positive samples. Pregnant women samples react in the same way as the adult samples and are acceptable for use in the LIAISON® XL MUREX HIV Ab/Ag HT assay.

14.7 Analytical sensitivity at cut-off

The analytical sensitivity of the LIAISON® XL MUREX HIV Ab/Ag HT assay was evaluated using the 1st International Standard HIV-1 p24 Antigen, NIBSC code 90/636. The standard was diluted with HIV negative serum, to obtain samples spanning the assay range. Testing was performed using three lots of reagent, in five (5) replicates, recovering an average of 1.17 IU/mL at the cut off.

14.8 Analytical Sensitivity as Seroconversion Panel Performance

Thirty-eight (38) commercially available HIV seroconversion panels were tested using LIAISON® XL MUREX HIV Ab/Ag HT assay and a commercially available FDA-approved HIV comparator assay to determine the sensitivity of the assay. The results are summarized in the following table:

Seroconversion Panel				First Confirmed Positive Bleed		Difference between LIAISON® XL MUREX HIV Ab/Ag HT and Comparator Assay
				LIAISON® XL MUREX HIV Ab/Ag HT	HIV Comparator Assay	
N	PANEL ID	Reactivity	Collection Days	(Day)	(Day)	Difference in First Positive Bleed (Bleed Number)
1	PRB969	Ag/Ab	0,29,48,53,55,61, 63,70,72,77	70	70	0
2	PRB966 (0600-0248)	Ag/Ab	0,2,20,22,30,35, 37,44,48,51	44	44	0
3	PRB968	Ag/Ab	0,3,8,10,15,17, 26,28,33,35	26	26	0
4	PRB971 (0600-0253)	Ag/Ab	0,2,7,11	7	7	0
5	PRB953 (0600-237)	Ag/Ab	0,3,7,10	7	7	0
6	PRB946 (0600-0227)	Ag	0,4,7,11	7	7	0
7	PRB950 (0600-0232)	Ag/Ab	0.18,21,28	18	18	0

Seroconversion Panel				First Confirmed Positive Bleed		Difference between LIAISON® XL MUREX HIV Ab/Ag HT and Comparator Assay
				LIAISON® XL MUREX HIV Ab/Ag HT	HIV Comparator Assay	
N	PANEL ID	Reactivity	Collection Days	(Day)	(Day)	Difference in First Positive Bleed (Bleed Number)
8	PRB949 (0600-0230)	Ab	0,6,9,18	18	18	0
9	PRB976 (0600-0261)	Ag	0,2,7,9	7	7	0
10	PRB977 (0600-0262)	Ag/Ab	0,2,13,15	13	13	0
11	PRB956	Ag	0,40,42,47,50	47	47	0
12	PRB955 (0600-0239)	Ag/Ab	0,3,7,12,14	7	3	1
13	PRB975	Ag	0,2,7,9,14	14	14	0
14	PRB962	Ag	0,2,7,9,14,17	14	14	0
15	PRB967	Ag/Ab	0,3,7,17,19,24	17	17	0
16	PRB963	Ag	0,2,7,9,14,17,21	17	17	0
17	PRB954 (0600-0238)	Ag/Ab	0,2,7,10,14,17,21	17	17	0
18	PRB961	Ag	0,5,7,12,14,19,21, 27,29	27	27	0
19	PRB960	Ag	0,4,7,11,14,18,21, 28,30	28	28	0
20	HIV9081	Ag/Ab	0,24,26,33	24	24	0
21	HIV9011	Ag/Ab	0,4,9,11,16,18,23, 25,30,38,40	38	38	0
22	HIV9012	Ag/Ab	0,2,7,9,14,16,21, 23	16	16	0
23	HIV9013	Ag	0,7,9,14,18,23,25	25	25	0
24	HIV9014	Ab	0,10,22,27,29	10	10	0
25	HIV9019	Ag/Ab	0,3,8	8	8	0
26	HIV9020	Ag/Ab	0,5,7,12,33,35,53, 55,61,63,68,70,75,77,82,84,89,92,96,99,10 3,106	99	99	0
27	HIV9021	Ag/Ab	0,3,7,11,14,18,21, 25,28,32,36,39,43,47,50,54,57	47	47	0
28	HIV9022	Ag/Ab	0,3,7,10,15,17,23, 25,31	25	25	0
29	HIV9023	Ag	0,2,7,9,14,16,28, 30,35,37,42,44,55,57,62,64,69,71,76,78,83 ,85	83	78	1
30	HIV9025	Ag/Ab	0,7,14,23,28,37,58,60,65,68,85,91	85	85	0
31	HIV9015	Ag/Ab	0,4,11,14,23,28	23	23	0
32	HIV9016	Ag	0,2,7,9,15,18,23, 27,30,34	30	30	0
33	HIV9018	Ag/Ab	0,4,7,11,14,18,21, 25,28,32,35	28	28	0
34	HIV9026	Ag/Ab	0,5,13,15,26,31,44	44	44	0
35	HIV9030	Ag/Ab	0,4,7,11,14,18,21, 25,28,33,35,40,42,47,49,54	47	47	0
36	HIV9033	Ag/Ab	0,11,14,18,21,25, 30,33,40,43,49,53,60,63,82,84	82	82	0
37	HIV10234	Ag/Ab	0,3,38	38	38	0
38	HIV12007	Ag/Ab	0,2,54,117,119, 124,126,131,133	117	117	0

14.9 HIV commercial panels

Forty-four (44) samples from three (3) commercially available HIV panels were tested using the LIAISON® XL MUREX HIV Ab/Ag HT assay and a commercially available FDA-approved HIV comparator assay to determine the sensitivity of the assay. All results were concordant between the LIAISON® XL MUREX HIV Ab/Ag HT assay and the FDA-approved HIV comparator assay.

14.10 Analytical Sensitivity as detection of antigen subtypes

Fifty (50) cell culture supernatants including different HIV-1 subtypes (group M including CRF and HIV-1 group O) and HIV-2 were tested using LIAISON® XL MUREX HIV Ab/Ag HT assay and a commercially available FDA-approved HIV comparator assay to determine the sensitivity of the assay on the detection of the different subtypes. All samples were detected on the LIAISON® XL MUREX HIV Ab/Ag HT assay as well as the comparator assay.

Cell culture supernatants subtype	Number of samples tested	Number of samples detected using LIAISON® XL MUREX HIV Ab/Ag HT	Number of samples detected using comparator assay
HIV-1 Group M, Subtype A	3	3	3
HIV-1 Group M, Subtype AE	10	10	10
HIV-1 Group M, Subtype AG	3	3	3
HIV-1 Group M, Subtype B	10	10	10
HIV-1 Group M, Subtype C	7	7	7
HIV-1 Group M, Subtype CRF06	1	1	1
HIV-1 Group M, Subtype D	3	3	3
HIV-1 Group M, Subtype F	5	5	5
HIV-1 Group M, Subtype G	2	2	2
HIV-1, Subtype O	4	4	4
HIV-2, Subtype A	1	1	1
HIV-2, Subtype B	1	1	1
TOTAL:	**50**	**50**	**50**

4.11 Within Laboratory Precision

A twenty (20) day reproducibility/precision study was performed by using a coded panel of fourteen (14) serum samples that was prepared by either spiking or diluting samples as necessary to obtain negative, low positive and mid positive samples. Kit Control sets were also included in the 20-day study. The panel samples and kit controls were tested on three (3) LIAISON® XL MUREX HIV Ab/Ag HT kit lots in two (replicates) per run, two (2) runs per day for twenty (20) operating days on one (1) LIAISON® XL Analyzer. The CLSI document EP5-A3 was consulted in the preparation of the testing protocol.

Sample ID	N	Mean S/CO	Repeatability		Between Run		Between Day		Between Lot		Total	
			SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%
Negative Control lot 1	240	0.27	0.013	4.8%	0.010	3.6%	0.014	5.1%	0.061	22.4%	0.064	23.7%
Negative Control lot 2	240	0.24	0.011	4.4%	0.009	3.8%	0.011	4.7%	0.053	22.3%	0.056	23.5%
Negative Control lot 3	240	0.25	0.010	4.1%	0.010	3.8%	0.013	5.2%	0.055	21.8%	0.059	23.1%
HIV p24 Ag Control lot 1	240	1.67	0.050	3.0%	0.023	1.4%	0.033	1.9%	0.086	5.2%	0.107	6.4%
HIV p24 Ag Control lot 2	240	1.59	0.039	2.4%	0.024	1.5%	0.045	2.8%	0.080	5.1%	0.103	6.5%
HIV p24 Ag Control lot 3	240	1.72	0.061	3.5%	0.019	1.1%	0.032	1.9%	0.089	5.2%	0.114	6.6%
HIV-1 M Ab Control lot 1	240	1.29	0.029	2.2%	0.038	3.0%	0.034	2.7%	0.038	3.0%	0.070	5.5%
HIV-1 M Ab Control lot 2	240	1.42	0.036	2.6%	0.044	3.1%	0.050	3.6%	0.035	2.5%	0.084	5.9%
HIV-1 M Ab Control lot 3	240	1.39	0.051	3.7%	0.026	1.9%	0.027	1.9%	0.051	3.7%	0.081	5.9%
HIV-1 O Ab Control lot 1	240	1.53	0.040	2.6%	0.049	3.2%	0.026	1.7%	0.269	17.6%	0.278	18.2%
HIV-1 O Ab Control lot 2	240	1.57	0.037	2.3%	0.042	2.7%	0.040	2.5%	0.330	21.1%	0.337	21.5%
HIV-1 O Ab Control lot 3	240	1.63	0.063	3.9%	0.027	1.6%	0.025	1.5%	0.315	19.4%	0.323	19.9%
HIV-2 Ab Control lot 1	240	1.19	0.027	2.3%	0.039	3.2%	0.016	1.3%	0.154	12.9%	0.162	13.6%
HIV-2 Ab Control lot 2	240	1.11	0.028	2.5%	0.027	2.5%	0.017	1.6%	0.140	12.6%	0.146	13.1%
HIV-2 Ab Control lot 3	240	1.05	0.035	3.3%	0.016	1.5%	0.013	1.3%	0.140	13.3%	0.146	13.9%
Negative-U1	240	0.23	0.009	3.7%	0.009	3.7%	0.011	4.6%	0.054	23.2%	0.056	24.2%
Negative-U2	240	0.24	0.010	4.1%	0.006	2.7%	0.010	4.3%	0.055	23.3%	0.057	24.2%
HIV-1MAbU3	240	0.48	0.013	2.8%	0.013	2.8%	0.018	3.8%	0.055	11.4%	0.061	12.6%
HIV-1MAbU4	240	1.10	0.025	2.3%	0.032	2.9%	0.039	3.5%	0.046	4.2%	0.073	6.6%
HIV-1MAbU5	240	1.96	0.052	2.6%	0.052	2.7%	0.092	4.7%	0.035	1.8%	0.123	6.3%

HIV-2AbU6	240	0.37	0.010	2.8%	0.009	2.5%	0.014	3.8%	0.068	18.2%	0.071	19.0%
HIV-2AbU7	240	0.58	0.023	4.0%	0.016	2.7%	0.024	4.1%	0.085	14.6%	0.093	15.9%
HIV-2AbU8	240	1.27	0.033	2.6%	0.043	3.4%	0.051	4.1%	0.174	13.8%	0.189	15.0%
HIV-1OAbU9	240	0.37	0.010	2.6%	0.010	2.6%	0.013	3.6%	0.037	9.9%	0.042	11.2%
HIV-1OAb10	240	1.05	0.028	2.7%	0.021	2.0%	0.031	2.9%	0.157	14.9%	0.163	15.6%
HIV-1OAb11	240	1.76	0.038	2.2%	0.047	2.7%	0.039	2.2%	0.346	19.7%	0.354	20.1%
HIVp24AgU12	240	0.48	0.013	2.7%	0.011	2.3%	0.015	3.1%	0.055	11.5%	0.059	12.4%
HIVp24AgU13	240	0.57	0.022	3.9%	0.011	2.0%	0.017	3.0%	0.051	8.9%	0.059	10.3%
HIVp24AgU14	240	2.14	0.055	2.6%	0.040	1.8%	0.071	3.3%	0.105	4.9%	0.144	6.7%

Reproducibility

A 5-day reproducibility/precision study was conducted at three (3) laboratories (2 external and 1 internal). Each site used a different lot of LIAISON® XL MUREX HIV Ab/Ag HT assay. The coded panel used in the 5-day study was the same panel used in the 20-day study. The coded panel was tested at all three (3) sites, using six (6) replicates per run in one (1) run 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.

			LIAISON® XL MUREX HIV Ab/Ag HT Ab Assay 5 Day Multi-Site / Multi-Lot									
Panel member	**N**	**Mean (S/CO)**	**Repeatability**		**Between Days / Runs**		**Within Laboratory Precision**		**Between Sites / Lots**		**Reproducibility**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
HIV p24 Ag Control	90	1.760	0.065	3.7%	0.056	3.2%	0.086	4.9%	0.156	8.9%	0.178	10.1%
HIV-1 M Ab Control	90	1.410	0.063	4.5%	0.053	3.8%	0.083	5.9%	0.127	9.0%	0.151	10.7%
HIV-1 O Ab Control	90	1.747	0.062	3.5%	0.055	3.1%	0.083	4.7%	0.360	20.6%	0.370	21.2%
HIV-2 Ab Control	90	1.165	0.045	3.9%	0.015	1.3%	0.048	4.1%	0.144	12.4%	0.152	13.1%
Negative Control	90	0.255	0.011	4.4%	0.014	5.3%	0.018	6.9%	0.030	11.7%	0.035	13.6%
Negative-U1	90	0.234	0.010	4.3%	0.020	8.7%	0.023	9.7%	0.040	17.3%	0.046	19.8%
Negative-U2	90	0.232	0.011	4.5%	0.016	6.8%	0.019	8.2%	0.041	17.6%	0.045	19.4%
HIV-1MAbU3	90	0.476	0.054	11.4%	0.030	6.2%	0.062	13.0%	0.000	0.0%	0.060	12.7%
HIV-1MAbU4	90	1.097	0.054	4.9%	0.045	4.1%	0.070	6.4%	0.071	6.4%	0.100	9.1%
HIV-1MAbU5	90	1.955	0.092	4.7%	0.158	8.1%	0.183	9.3%	0.199	10.2%	0.270	13.8%
HIV-2AbU6	90	0.402	0.017	4.2%	0.004	0.9%	0.017	4.3%	0.044	11.0%	0.048	11.9%
HIV-2AbU7	90	0.619	0.032	5.2%	0.035	5.6%	0.048	7.7%	0.064	10.4%	0.080	12.9%
HIV-2AbU8	90	1.346	0.082	6.1%	0.115	8.6%	0.142	10.5%	0.154	11.4%	0.209	15.5%
HIV-1OAbU9	90	0.395	0.059	15.0%	0.004	0.9%	0.059	15.0%	0.007	1.8%	0.060	15.2%
HIV1OAbU10	90	1.122	0.052	4.6%	0.044	4.0%	0.068	6.1%	0.167	14.9%	0.181	16.1%
HIV1OAbU11	90	1.866	0.095	5.1%	0.114	6.1%	0.149	8.0%	0.334	17.9%	0.366	19.6%
HIVp24AgU12	90	0.478	0.017	3.5%	0.016	3.3%	0.023	4.8%	0.010	2.2%	0.025	5.3%
HIVp24AgU13	90	0.572	0.023	4.0%	0.037	6.5%	0.044	7.6%	0.013	2.3%	0.046	8.0%
HIVp24AgU14	90	2.066	0.105	5.1%	0.135	6.5%	0.171	8.3%	0.173	8.4%	0.243	11.8%

14.12 Matrix Comparison

Thirty (30) paired sets of matched serum (with and without gel SST) and plasma (lithium and sodium heparin, sodium citrate and K2 EDTA) were tested to determine if these sample types provide equivalent results on the LIAISON® XL MUREX HIV Ab/Ag HT assay. Each sample was divided into three aliquots. Two sets of aliquots were spiked with an HIV positive sample to achieve two (2) levels of samples: high negative and low positive samples. The third set of aliquots was un-spiked to serve as control samples. The results of the negative and low positive samples did not change the classification of the expected result. The results obtained on the serum-plasma paired samples indicated that there is equivalent performance among serum (with and without gel SST), K2 EDTA, lithium heparin, sodium citrate and sodium heparin plasma matrices.

Summarized results for sample matrix equivalence evaluation:

X reference	Serum without Gel SST				
y exam	**Serum with Gel SST**	**K2 EDTA**	**Na Citrate**	**Li Heparin**	**Na Heparin**
Slope (Passing Bablok fit)	1.000	0.9861	1.011	1.039	0.9958
Intercept (Passing Bablok fit)	0.009	0.00898	-0.006915	-0.02276	0.005142
Intercept (95% CI)	-0.03302 to 0.04977	-0.03520 to 0.05594	-0.05083 to 0.02433	-0.07395 to 0.03007	-0.04185 to 0.05387
Correlation	0.934	0.932	0.948	0.932	0.944

14.13 Potential interfering substances- Endogenous

Controlled studies of potentially interfering substances at two (2) levels for each specific reactivity (HIV1O, HIV1M, HIV2 and Ag) around the cutoff, showed no interference at the concentration for each substance listed below in the LIAISON® XL MUREX HIV Ab/Ag HT assay. The testing was based on CLSI-EP07.

Substance	Tested concentrations
Lipids (Glyceryl trioleate)	3000 mg/dL
Lipids (Intralipid)	1000 mg/dL
Hemoglobin	2.5 g/L
Unconjugated bilirubin	40 mg/dL
Conjugated bilirubin	40 mg/dL
Albumin	6 g/dL
Cholesterol total	400 mg/dL
Immunoglobulin G	20 g/L
Biotin (Vitamin H)	3510 ng/mL
Total protein	150 g/L

14.14 Potential interfering substances – Drugs

Testing was performed to determine whether the presence of most commonly used drugs may interfere with assay results. Studies of potentially interfering drugs at two (2) levels (high negative and low positive) for each marker (HIV Ag, anti HIV-1M, HIV-1O anti HIV-2) showed no interference at the concentration for each substance listed below in the LIAISON® XL MUREX HIV Ab/Ag HT assay.

Substance	Concentrations tested (mg/dL)	Substance	Concentrations tested (mg/dL)
Acetylcysteine	41.5	Phenylbutazone	40
Ampicillin-Na	100	Doxycycline	5
Ascorbic acid	30	Acetylsalicylic acid	100
Cyclosporine	0.5	Rifampicin	6
Cefoxitin	660	Acetaminophen	20
Heparin	5000 (U/L)	Ibuprofen	50
Levodopa	2	Theophylline	10
Methyldopa+1.5	2.25	Tetracycline	5
Metronidazole	20	Ca-Dobesilate	20

14.15 Cross-reactivity

The cross-reactivity study for the LIAISON® XL MUREX HIV Ab/Ag HT assay was designed to evaluate potential interference from other organisms that may cause infectious disease (CMV, HSV, EBV, T. pallidum, HIV, HTLV) and from other conditions that may result from atypical immune system activity (i.e. rheumatoid factor, anti-nuclear antibodies, HAMA). In the study, all 263 samples were found to be non-reactive with both the LIAISON® XL MUREX HIV Ab/Ag assay and the FDA-approved HIV reference assay. Conclusion: No potential interference was demonstrated by the medical conditions presented in this comparison study.

In the second part of the cross-reactivity study for the LIAISON® XL MUREX HIV Ab/Ag HT assay, the samples used in the evaluation above were spiked with HIV positive anti-HIV-1 M, anti-HIV-1 O, anti-HIV-2, and HIV p24 Ag material to provide samples of low positive reactivity. In the study, all samples were found to be reactive with the LIAISON® XL MUREX HIV Ab/Ag assay

Conclusion: No potential interference was demonstrated by the medical conditions presented in this comparison study.

Potential Cross Reactant	Spiked samples - N of observed Reactive results with LIAISON XL MUREX HIV Ab/Ag HT				Samples Non-Reactive by Comparator and LIAISON XL HIV Ab/Ag
	HIV-1M	HIV-1 O	HIV-2	HIV p24 Ag	
Anti-nuclear antibodies (ANA)	10/10	10/10	10/10	10/10	All
E. Coli (anti-*E.Coli* positive)	9/9	4/4	4/4	4/4	All
CMV (anti-CMV positive IgG and IgM)	10/10	10/10	10/10	10/10	All
Common Cold	9/9	3/3	3/3	3/3	All
Crohn's Disease	10/10	7/7	7/7	7/7	All
C. Trachomatis	10/10	8/8	8/8	8/8	All
EBV (anti-EBV positive IgG and IgM)	10/10	10/10	10/10	10/10	All
Elevated IgG	11/11	10/10	10/10	10/10	All
Elevated IgM	10/10	9/9	9/9	9/9	All
Fungal Infections	6/6	10/10	10/10	10/10	All
Graves Disease	10/10	9/9	9/9	9/9	All
HAMA	10/10	10/10	10/10	10/10	All
Hemodialysis patient	9/9	10/10	10/10	10/10	All
Hepatitis A Virus (anti-HAV positive IgG/IgM)	8/8	10/10	10/10	10/10	All
Hepatitis B Virus (anti-HBV positive PCR)	10/10	10/10	10/10	10/10	All
Hepatitis C Virus (anti-HCV positive)	10/10	10/10	10/10	10/10	All
HSV (anti-HSV positive IgG)	9/9	10/10	10/10	10/10	All
HTLV-1/2 (anti-HTLV positive)	10/10	8/8	8/8	8/8	All
IgM monoclonal gammopathy	2/2	2/2	2/2	2/2	All
Influenza vaccine recipients	10/10	10/10	10/10	10/10	All
Multiparous pregnancies	10/10	10/10	10/10	10/10	All
Pregnancy 1st trimester	9/9	10/10	10/10	10/10	All
Pregnancy 2nd trimester	8/8	10/10	10/10	10/10	All
Pregnancy 3rd trimester	9/9	9/9	9/9	9/9	All
Rheumatoid Factor	9/9	10/10	10/10	10/10	All
Rubella Virus	10/10	10/10	10/10	10/10	All
Systemic Lupus Erythematosis	9/9	6/6	6/6	6/6	All
T. pallidum (anti-*T.pallidum* positive)	8/8	10/10	10/10	10/10	All
Varicella Zoster Virus (anti-VZV positive IgG)	8/8	10/10	10/10	10/10	All
TOTAL	**263/263**	**255/255**	**255/255**	**255/255**	All

14.16 Hook effect

No high-dose hook effect was observed for any of the 3 different antibody types (HIV-1 Group M, HIV-1 Group O and HIV-2). High dose hook was observed for 1 HIV p24 antigen sample at a dilution greater than a S/CO value of 1540.

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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 HIV Ab/Ag HT (REF 318291

1. INTENDED USE

The LIAISON® XL murex Control HIV Ab/Ag HT is intended for use as assayed quality control samples to monitor the performance of the LIAISON® XL MUREX HIV Ab/Ag HT assay. The performance characteristics of LIAISON® controls have not been established for any other assays or instrument platforms different from LIAISON® XL.
For details, refer to the Analyzer Operator's Manual.

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

2. MATERIALS PROVIDED

Negative control CONTROL- (1 x 4,5mL)	Human serum non-reactive for HIV antigens and antibodies, 0.2% ProClin® 300, preservatives.
Positive control anti-HIV-2 CONTROL+ (1 x 4,5mL)	Human serum/plasma reactive for HIV-2 antibodies, 0.2% ProClin® 300, preservatives.
Positive control anti-HIV-1O CONTROL+ (1 x 4,5mL)	Rabbit polyclonal reactive for HIV-1 O antibodies, human serum, 0.2% ProClin® 300, preservatives.
Positive control anti-HIV-1M CONTROL+ (1 x 4,5mL)	Human serum/plasma reactive for HIV-1 M antibodies, 0.2% ProClin® 300, preservatives.
Positive control HIV Ag CONTROL+ (1 x 4,5mL)	HIV p24 recombinant antigen (obtained in *E.coli*), stabilized in PBS buffer, bovine aprotinin, casein, 0.2% ProClin® 300.

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

All reagents are supplied ready to use. The range of values of each control is reported on the certificate of analysis and indicates the limits established by DiaSorin for control values that can be obtained in reliable assay runs. Each laboratory is responsible for adopting different limits to meet individual requirements.
The certificate of analysis bar codes 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

- Controls are not kit lot specific and may be safely interchanged even with different reagent integral lots.
- All human blood source material used to produce the components provided in this test kit derives from units found to be non-reactive for HBsAg, antibodies to HCV, HIV-1, HIV-2 when tested by an FDA-approved method, except for the positive controls which are reactive for antibodies to HIV-2, HIV-1 group M, or HIV-1 group O. The units positive for hepatitis B surface antigen have been inactivated by heat treatment (60°C for one hour) The units positive for HIV antibodies have been obtained from individuals infected with HIV-1 and/or HIV-2. Although these have been inactivated by heat treatment (56 °C for one hour) during the manufacturing process they should be considered as potentially infectious.
- 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.
- The controls are not calibrators and should not be used for assay calibration.
- Do not pipette by mouth. Do not eat, drink, smoke or apply cosmetics in the assay laboratory.
- 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 requirements of local and federal agencies.
- 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 and European Union EC Regulation 1272/2008 (CLP).
- Hazardous reagents are classified and labelled as follows:

REAGENTS:	CONTROL-, anti-HIV-2 CONTROL+, anti-HIV-1O CONTROL+, anti-HIV-1M CONTROL+, HIV Ag 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 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. The controls should not be used past the expiry date indicated on the vial labels.
After removing the seals, the control vial is stable for nine (9) weeks when stored upright at 2–8°C. Avoid bacterial contamination of controls.

5. 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® controls are intended to monitor for substantial reagent failure. Whenever LIAISON® controls lie outside the expected ranges, 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 HIV Ab/Ag HT kit are necessary to obtain reliable results.

6. LIMITATIONS

The LIAISON® XL MUREX Control HIV Ab/Ag HT positive controls will not ensure precision at the assay cut-off.
Control values for assays other the LIAISON® XL MUREX HIV Ab/Ag HT assay have not been established.
If users wish to use this control material with other assays, it is their responsibility to establish appropriate ranges.

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