510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT

I Background Information:

A 510(k) Number

K260770

B Applicant

DiaSorin, Inc.

C Proprietary and Established Names

LIAISON Murex HBsAg Qual; LIAISON XL; LIAISON diluteX

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
LOM	II	866.3172 Qualitative hepatitis B virus antigen assays	MI - Microbiology
JJF	I	862.2170 analyzer, chemistry, micro, for clinical use	Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

Clearance of the LIAISON diluteX as an accessory to LIAISON XL analyzer with the LIAISON Murex HBsAg Qual.

B Measurand:

Hepatitis B surface antigen (HBsAg).

C Type of Test:

In vitro chemiluminescent immunoassay (CLIA).

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

LIAISON Murex HBsAg Qual

The LIAISON Murex HBsAg Qual assay is an in vitro chemiluminescent immunoassay for the qualitative detection of hepatitis B surface antigen (HBsAg) in human adult and pediatric (2 to 21 years) serum and plasma (lithium and sodium heparin, sodium citrate and potassium EDTA) including separator tubes, on the LIAISON XL and LIAISON XS Analyzers. Assay results in conjunction with other hepatitis B virus (HBV) serological and clinical information, may be used as an aid in the diagnosis of HBV infection in patients with symptoms of hepatitis or who may be at risk for HBV infection. The assay may also be used to screen for HBV infection in pregnant women to identify neonates who are at risk for acquiring hepatitis B during the perinatal period. This assay is not approved for use in screening blood, plasma or tissue donors.
Caution: U.S. Federal Law restricts this device to sale by or on the order of a licensed practitioner.

LIAISON diluteX

The LIAISON diluteX is an accessory for the LIAISON XL analyzer.
It is designed to automatically dilute the LIAISON Wash/System Liquid with purified water and to distribute both the purified water and the diluted Wash/System Liquid (referred to as "Wash Buffer") to each connected LIAISON XL. The LIAISON diluteX utilizes purified water (referred to as "sourced water"), which must be supplied to the device. The device automatically dilutes the LIAISON Wash/System Liquid, stored on the device, with the sourced water and distributes both the diluted Wash/System Liquid and the sourced water to the LIAISON XL via separate tubes directly into the analyzer's tanks.
For professional use only.

LIAISON XL

The LIAISON XL Analyzer is an automated discrete continuous loading chemiluminescent immunoassay (CLIA) analyzer for in vitro diagnostic analysis of CLIAs on human specimens cleared for use on the analyzer.
It is only to be used with FDA cleared chemiluminescent immunoassays that are marketed by DiaSorin for the LIAISON XL Analyzer. The analyzer can be connected to a third party Laboratory Automation System (LAS) which has been previously cleared for use with FDA cleared assays.

C Special Conditions for Use Statement(s):

Rx- For Prescription Use Only.

D Special Instrument Requirements:

For use with the LIAISON XL analyzer.

IV Device/System Characteristics:

A Device Description:

LIAISON Murex HBsAg Qual

The method for qualitative determination of HBsAg is a direct sandwich chemiluminescence immunoassay (CLIA). A mixture of mouse monoclonal antibodies is used for coating magnetic particles (solid phase) and a different mixture of mouse monoclonal antibodies directed to different epitopes is linked to an isoluminol derivative (isoluminol-antibody conjugate). During the first incubation, HBsAg present in calibrators, samples or controls binds to the solid phase. During the second incubation, the antibody conjugate reacts with HBsAg already bound to the solid phase. After second 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 directly proportional to HBsAg concentration present in calibrators, samples or controls.

LIAISON diluteX

The LIAISON diluteX is an accessory for the LIAISON XL analyzer.
The LIAISON diluteX interfaces with the LIAISON XL analyzer in order to automatically fill the LIAISON XL tanks with purified water and properly pre-diluted LIAISON Wash/System Liquid (code 319100). The LIAISON diluteX enables automatic dilution of the LIAISON Wash/System Liquid in a range between 1 to 9.5/10.5 from the more concentrated bottled LIAISON Wash/System liquid. An accurate fluidic system controlled by pressure regulators, pumps, valves and tubes allows the diluted solution to go out of the system and reach the LIAISON XL analyzer. By the usage of customized caps installed on the LIAISON XL analyzer, the LIAISON diluteX is able to automatically refill the diluted solution in the Wash Buffer tank of the LIAISON XL analyzer. In the same way, the LIAISON diluteX is able to refill the deionized water tank of LIAISON XL analyzer.

B Principle of Operation:

LIAISON Murex HBsAg Qual

The method for qualitative determination of HBsAg is a direct sandwich chemiluminescence immunoassay (CLIA). A mixture of mouse monoclonal antibodies is used for coating magnetic particles (solid phase) and a different mixture of mouse monoclonal antibodies directed to different epitopes is linked to an isoluminol derivative (isoluminol-antibody conjugate). During the first incubation, HBsAg present in calibrators, samples or controls binds to the solid phase. During the second incubation, the antibody conjugate reacts with HBsAg already bound to the solid phase. After second 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 directly proportional to HBsAg concentration present in calibrators, samples or controls.

LIAISON diluteX

The diluteX connects with the LIAISON XL LXL) analyzer in order to automatically fill the LXL tanks with purified water and properly pre-diluted LIAISON Wash/System Liquid. The

diluteX enables automatic dilution of the LIAISON Wash/System Liquid in a range between 1:9.5 and 1:10.5. An accurate fluidic system controlled by pressure regulators, pumps, valves and tubes allows the diluted solution to go out of the system and reach the LXL analyzer. By means of customized caps installed on the tanks of the LXL analyzer, the diluteX is able to automatically refill the diluted solution in the Wash Buffer tank of the LXL analyzer. In the same way, the diluteX can refill the deionized water tank of LXL analyzer.
Up to two Analyzers can be fed at a time.
To achieve the device function, the following must happen:

1. The Device is connected to a purified water supply, able to deliver purified water in the pressure range 1 through 10 atmospheres.
2. The LIAISON Wash/System Liquid tank on the Device is filled with concentrate solution.
3. Through a pressure regulator and a valve, purified water enters in the diluteX.
4. By means of a valve-controlled T connection the purified water flow is divided between the line supplying the purified water to the Analyzer(s) and the line supplying purified water for the preparation of the Wash Buffer.
5. Each of the two Analyzers receives the proper amount of purified water based upon the monitoring by the sensor in the canister and the opening/closing of a valve on the specific connection.
6. By means of a valve and an intermediate 200 mL tank, the line of the purified water for the preparation of the Wash Buffer is connected to the larger head of a two-heads metering pump.
7. By means of a valve the line aspirating from the LIAISON Wash/System Liquid tank is connected to the smaller head of the same two-heads metering pump.
8. The two-heads metering pump operates simultaneously the two heads, in a volume ratio 9 (for purified water) to 1 (for LIAISON Wash/System Liquid), thus achieving the 1:10 dilution ratio required for the preparation of the wash Buffer.
9. The outpour from the two heads mixes in a crisscrossed tubing set downstream the pump and it is then collected in an intermediate 200 mL tank, thus making the Wash Buffer.
10. From the intermediate tank, the Wash Buffer is then delivered to the Analyzer(s) by the opening of a valve on the relevant tube, based upon the monitoring of the sensor in the canister.
11. As soon as the proper level of Wash Buffer is reached in the canister, the valve on the relevant tube closes and the pump stops.

The Device can automatically monitor the status of the lines and intermediate tanks and oversees their proper priming. Priming eluates are directed to waste.
Other in-process controls monitor the correct actuation of the pumps and valves and filling of the lines.
At preset intervals, the diluteX guides the user through a maintenance routine, meant to the cleansing of the lines and internal canisters and the replacement of the filters on the inlet ports of the diluteX, the connection to the purified water source, the LIAISON Wash/System Liquid tank and the cleaning tank.

C Instrument Description Information:

1. Instrument Name:
   LIAISON XL Analyzer

2. Specimen Identification:

   Specimen identification is automated and read by the barcode scanner.

3. Specimen Sampling and Handling:

   Specimen sampling and handling is automated on the analyzer.

4. Calibration:

   Components of the LIAISON XL Murex HBsAg Qual reagent contain Calibrator 1, low levels of recombinant HBsAg contained in the reagent integral allows the analyzer to set the assay cut-off.

5. Quality Control:

   The LIAISON XL Murex Control HBsAg Qual (negative and positive) is intended for use as assayed quality control samples to monitor the performance of the LIAISON XL MUREX HBsAg Qual assay.

V Substantial Equivalence Information:

A Predicate Device Name(s):
LIAISON Murex HBsAg Qual

B Predicate 510(k) Number(s):
P190017

C Comparison with Predicate(s):

Device & Predicate Device(s):	K260770	P190017
Device Trade Name	LIAISON Murex HBsAg Qual; LIAISON XL; LIAISON diluteX	LIAISON Murex HBsAg Qual; LIAISON XL analyzer
General Device Characteristic Similarities		
Intended Use/Indications For Use	**LIAISON Murex HBsAg Qual**: The LIAISON Murex HBsAg Qual assay is an in vitro chemiluminescent immunoassay for the qualitative detection of hepatitis B surface antigen (HBsAg) in human adult and pediatric (2 to 21 years) serum and plasma (lithium and sodium heparin, sodium citrate and potassium EDTA) including separator tubes, on the LIAISON XL and LIAISON XS Analyzers. Assay results in	**LIAISON Murex HBsAg Qual:** The LIAISON Murex HBsAg Qual assay is an in vitro chemiluminescent immunoassay for the qualitative detection of hepatitis B surface antigen (HBsAg) in human adult and pediatric (2 to 21 years) serum and plasma (lithium and sodium heparin, sodium citrate and potassium EDTA) including separator tubes, on the LIAISON XL and LIAISON XS Analyzers. Assay results in

	conjunction with other hepatitis B virus (HBV) serological and clinical information, may be used as an aid in the diagnosis of HBV infection in patients with symptoms of hepatitis or who may be at risk for HBV infection. The assay may also be used to screen for HBV infection in pregnant women to identify neonates who are at risk for acquiring hepatitis B during the perinatal period. This assay is not approved for use in screening blood, plasma or tissue donors. Caution: U.S. Federal Law restricts this device to sale by or on the order of a licensed practitioner. **LIAISON diluteX:** The LIAISON diluteX is an accessory for the LIAISON XL analyzer. It is designed to automatically dilute the LIAISON Wash/System Liquid with purified water and to distribute both the purified water and the diluted Wash/System Liquid (referred to as "Wash Buffer") to each connected LIAISON XL. The LIAISON diluteX utilizes purified water (referred to as "sourced water"), which must be supplied to the device. The device automatically dilutes the LIAISON Wash/System Liquid, stored on the device, with the sourced water and distributes both the diluted Wash/System Liquid and the sourced water to the LIAISON XL via separate tubes directly into the analyzer's tanks. For professional use only. **LIAISON XL:** The LIAISON XL Analyzer is an automated discrete continuous loading chemiluminescent immunoassay (CLIA) analyzer for in vitro diagnostic analysis of CLIAs on human specimens cleared for use on the analyzer. It is only to be used with FDA cleared chemiluminescent immunoassays that are marketed by DiaSorin for the LIAISON XL Analyzer. The analyzer can be connected to a third party Laboratory Automation System	conjunction with other hepatitis B virus (HBV) serological and clinical information, may be used as an aid in the diagnosis of HBV infection in patients with symptoms of hepatitis or who may be at risk for HBV infection. The assay may also be used to screen for HBV infection in pregnant women to identify neonates who are at risk for acquiring hepatitis B during the perinatal period. This assay is not approved for use in screening blood, plasma or tissue donors. Caution: U.S. Federal Law restricts this device to sale by or on the order of a licensed practitioner. **LIAISON XL:** The LIAISON XL Analyzer is an automated discrete continuous loading chemiluminescent immunoassay (CLIA) analyzer for in vitro diagnostic analysis of CLIAs on human specimens cleared for use on the analyzer. It is only to be used with FDA cleared chemiluminescent immunoassays that are marketed by DiaSorin for the LIAISON XL Analyzer. The analyzer can be connected to a third party Laboratory Automation System (LAS) which has been previously cleared for use with FDA cleared assays.

	(LAS) which has been previously cleared for use with FDA cleared assays.	
General Device Characteristic Differences		
Purified Water supply: Provision of purified water to the LXL, upon the liquid level reaching a lower threshold in the tank on board the LXL	The diluteX is connected to a purified water source by a dedicate tube; The diluteX, by means of a sensor of its own in the purified water tank of the LXL and completely independent from the LXL, detects the liquid level below a lower threshold; The diluteX then automatically opens a set of valves, allowing the purified water flowing directly from the faucet to the canister by the tube line connected to the LXL tank; The independent sensor in the canister monitors the liquid level until it reaches an upper threshold; At this point, the diluteX switches the valve set and stops the purified water flow; The whole process is possible without interruption of the LXL operation. Errors in feeding are monitored by the independent SW of the diluteX. In case these are such to limit a satisfactory provision of purified water, the LXL SW shall independently halt the progression of the routine, before any failure in the purified water provision happens. In fact, being the two devices operated by completely independent SWs, each of them retains the whole suite of in process controls typical of the specific SW.	The LXL signals by means of a display on the GUI the shortage of purified water; The user accesses the lower cabinet and disconnects the purified water tank from the intermediate tank; The user moves the tank to a purified water faucet; The user fills the tank at the purified water faucet; The user returns the tank to cabinet and reconnect it to the LXL; The LXL detects the increased liquid level; The whole process is possible without interruption of the LXL operation, provided the refilling is faster than the exhaustion of the intermediate tank internal to the LXL. Otherwise, The LXL may need more purified water than the residual in the intermediate tank. The LXL SW shall then independently halt the progression of the routine, before any failure in the purified water provision happens.
Wash Buffer: Detection of the liquid level reaching a lower threshold in the tank on board the LXL	The diluteX, by means of a sensor of its own in the tank completely independent from the LXL, detects the liquid level below a lower threshold.	The LXL signals by means of a display on the GUI the shortage of Wash Buffer.
Wash Buffer: Preparation of the Wash Buffer from the concentrate	The diluteX is connected to a purified water source by a dedicated tube; The user pours in the LIAISON Wash/System Liquid tank on the diluteX up to 5 bottles, 1 L each, of concentrate solution; The diluteX, by means of a sensor of its own in the tank completely independent from the LXL, detects the liquid level below a lower threshold;	The user accesses the lower cabinet and disconnects the Wash Buffer tank from the intermediate tank; The user manually empties the tank of the remnant of Wash Buffer; The user moves the tank to a purified water faucet; The user rinses the tank and fills the tank at the purified water faucet up to the mark (9 L);

	The diluteX automatically opens a set of valves directing the purified water to the dilution pump; The diluteX automatically opens a set of valves directing the LIAISON Wash/System Liquid to the dilution pump; The dilution pumps add both liquids in a predefined fixed mixing ratio (1 part of the LIAISON Wash/System Liquid and 9 of purified water) to a mixing line and Wash Buffer intermediate tank. Mixing line and intermediate tank are laid out in a way such that full homogenization is immediately achieved, preventing foam development at the same time. Therefore, the 6-hour waiting time is not needed any longer.	The user slowly pours the whole content of a 1 L bottle of LIAISON Wash/System Liquid in the Wash Buffer tank; The user allows a waiting time of 6 hour to homogenize and degas, with the cap loosely screwed on the tank.
Wash Buffer: Provision of the Wash Buffer to the LXL	The diluteX then automatically opens a set of valves, allowing the Wash Buffer to flow directly from the intermediate tank to the canister by the tube line connected to the LXL tank; The independent sensor in the canister monitors the liquid level until it reaches an upper threshold; At this point, the diluteX switches the valve set, stops the dilution pump and stops the Wash Buffer flow; The whole process is possible without interruption of the LXL operation. Errors in the feeding are monitored by the independent SW of the diluteX. In case these are such to limit a satisfactory provision of Wash Buffer, the LXL SW shall independently halt the progression of the routine, before any failure in the Wash Buffer provision happens. In fact, being the two devices operated by completely independent SWs, each of them retains the whole suite of in process controls typical of the specific SW.	After the 6 hour of waiting time elapsed, the user tightens the cap, returns the filled tank to cabinet and reconnects it to the LXL; The LXL detects the increased liquid level. The whole process is possible without interruption of the LXL operation, provided a second prefilled tank is already available when the former is disconnected. Otherwise, during the 6 hour waiting time, the LXL may need more Wash Buffer than the residual in the intermediate tank internal to the LXL. The LXL SW shall then independently halt the progression of the routine, before any failure in the Wash Buffer provision happens.
Use of the LIAISON Wash/System Liquid	The LIAISON Wash/System Liquid is delivered to the user in 1 L plastic bottles. The content of up to five plastic bottles, for an overall volume of 5 L, can be poured in the dedicated tank on the diluteX. The content of the tank is stable for twenty-eight (28) days and a SW driven maintenance task prompts the user to empty, rinse and fill again	The LIAISON Wash/System Liquid is delivered to the user in 1 L plastic bottles. When needed, a single bottle is opened and carefully poured in a Wash Buffer tank already filled with 9 L of purified water.

	with liquid from new bottles the tank at the expiration of the 28-day span.	

VI Standards/Guidance Documents Referenced:

CLSI EP05-A3: Clinical Laboratory Standards Institute. *Evaluation of the Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition*. CLSI Guideline EP05-A3, CLSI: Wayne, PA, 2014.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

A 5-day precision study was conducted at one internal site using three instruments to verify the precision of the LIAISON XL analyzer when connected to the LIAISON diluteX when using the previously approved LIAISON Murex HBsAg Qual assay (P190017). The study used a panel of contrived serum samples prepared internally. The samples were diluted or spiked to span three analyte levels, representing negative, near cut-off, and positive HBsAg levels.

The panel was tested using one lot of LIAISON Murex HBsAg Qual assay; each sample was tested for five days on three instruments, one run per day and six replicates per run. Calibration and quality control testing were performed in accordance with the product Instructions for Use (IFU). For each sample, the mean, standard deviation (SD), and coefficient of variation (%CV) were calculated for the following variance components: repeatability (within-run precision), between-day, within-instrument, between-instrument, and reproducibility (overall precision). The summary of the precision results is presented in Table 1.

Table 1. Summary of Precision for LIAISON Murex HBsAg Qual assay on LIAISON XL with diluteX Precision

Sample ID	N	Mean (S/CO)	Within-Run (Repeatability)		Overall (Reproducibility)[a]	
			SD	%CV	SD	%CV
01	90	0.848	0.0335	3.95%	0.0468	5.52%
02	90	0.750	0.0325	4.33%	0.0466	6.12%
03	90	1.50	0.0409	2.73%	0.0667	4.46%
04	90	1.15	0.0363	3.17%	0.0579	5.06%
05	90	2.78	0.0553	1.99%	0.1181	4.24%
06	90	4.12	0.0912	2.22%	0.2345	5.70%

[a] Overall includes Within-Run, Between-Day, and Between-Instrument Components.

In addition to within-run repeatability and overall reproducibility results, additional variance components are presented in Table 2.

Table 2. Summary of the additional variance components results of LIAISON Murex HBsAg Qual 5-days precision

Sample ID	N	Mean (S/CO)	Between-Day		Within-Instrument		Between-Instrument	
			SD	%CV	SD	%CV	SD	%CV
01	90	0.848	0.0327	3.86%	0.0468	5.52%	0.000	0.00%*
02	90	0.750	0.0334	4.45%	0.0466	6.21%	0.000	0.00%*
03	90	1.50	0.0372	2.49%	0.0553	3.69%	0.0373	2.49%
04	90	1.15	0.0411	3.59%	0.0548	4.78%	0.0188	1.64%
05	90	2.78	0.0389	1.40%	0.0677	2.43%	0.0968	3.48%
06	90	4.12	0.1049	2.55%	0.1390	3.38%	0.1889	4.59%

* Variance components were 0 for samples 01 and 02; within-run and between-day variance components were already accounted for when calculating the instrument-to-instrument variance.

The observed overall reproducibility %CV ranged from 4.24% to 6.21% across all six panel members testing the LIAISON Murex HBsAg Qual assay. The level of precision of the LIAISON Murex HBsAg Qual assay on the LIAISON XL analyzer with the LIAISON diluteX is equivalent to the precision of the predicate device.

2. Linearity:
   Not Applicable.

3. Analytical Specificity/Interference:
   See P190017.

4. Detection Limit and Assay Reportable Range:
   Not Applicable.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):
   See P190017.

6. Assay Cut-Off:
   See P190017.

7. Carry-Over:
   To evaluate within-assay sample carryover when the LIAISON XL analyzer is connected to the LIAISON diluteX, alternating high positive and negative samples were tested in multiple runs using the LIAISON Murex HBsAg Qual assay. None of the results from the negative samples obtained after testing a positive sample were positive. Results demonstrated no sample carryover.

B Comparison Studies:

1. Method Comparison with Predicate Device:

Not applicable. See Clinical Studies below.

2. Matrix Comparison:
See P190017.

C Clinical Studies:

1. Clinical Sensitivity:
Not Applicable.

2. Clinical Specificity:
Not Applicable.

3. Clinical Cut-Off
Not Applicable.

4. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

A method comparison study was conducted to compare results from samples run on the LIAISON XL analyzer in its standard configuration versus the analyzer connected to LIAISON diluteX, both using the LIAISON Murex HBsAg Qual assay. A total of 103 samples from the matrices claimed in the IFU and covering the assay range were tested, this included 60 samples from DiaSorin internal preparations and 43 from external suppliers.

Each sample was tested once on one LIAISON XL instrument in standard configuration and once on one LIAISON XL instrument connected to LIAISON diluteX. The results obtained for each sample were analyzed and used to calculate the negative percent agreement (NPA) and positive percent agreement (PPA). The following summarizes the results obtained to evaluate the performance of the LIAISON Murex HBsAg Qual assay when LIAISON XL analyzer is connected to LIAISON diluteX, compared to LIAISON XL in standard configuration (Tables 3 and 4).

Table 3. LIAISON Murex HBsAg Qual results from the LIAISON XL analyzer connected to the diluteX

		LIAISON XL with diluteX		
		Negative	**Positive**	**Total**
LIAISON XL	**Negative**	53	2	55
	Positive	1	47	48
	Total	54	49	103

Table 4. Analysis Agreement Results for LIAISON XL Analyzer connected to the diluteX

Agreement	Detected	Percentage	95% CI
Positive Percent Agreement	47/48	97.9%	89.1-99.6%
Negative Percent Agreement	53/55	96.4%	87.7-99.0%

The PPA and NPA results are acceptable to establish equivalence between the LIAISON Murex HBsAg Qual assay performed on the LIAISON XL analyzer in its standard configuration and when connected to the LIAISON diluteX.

D Expected Values/Reference Range:
See P190017.

E Other Supportive Instrument Performance Characteristics Data:

EMC:
Electrical safety and electromagnetic compatibility (EMC) testing were performed, and the system was found to be acceptable.

Software and cybersecurity:
Software and cybersecurity documentation were reviewed and found to be acceptable.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.