SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Detection of Hepatitis B surface antigen (HBsAg)

Device Trade Name: LIAISON® XL MUREX HBsAg Qual
LIAISON® XL MUREX Control HBsAg Qual
LIAISON XL MUREX HBsAg Confirmatory Test

Device Procode: LOM

Applicant's Name and Address: DiaSorin Inc.
1951 Northwestern Avenue
Stillwater, MN 55082-0285

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P190017

Date of FDA Notice of Approval: August 29, 2020

II. INDICATIONS FOR USE

LIAISON XL MUREX HBsAg Qual

The LIAISON® XL MUREX HBsAg Qual assay is an *in vitro* chemiluminescent immunoassay (CLIA) 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 Analyzer. 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.

LIAISON XL MUREX Control HBsAg Qual

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. The performance characteristics of LIAISON® controls have not been established for any other assays or instrument platforms difference from LIAISON® XL.

III. CONTRAINDICATIONS

There are no known contraindications

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the LIAISON XL MUREX HBsAg Qual labeling.

V. DEVICE DESCRIPTION

LIAISON XL MUREX HBsAg Qual is a qualitative direct sandwich chemiluminescent 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. 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 conjugate, is measured by a photomultiplier as relative light units (RLU) and is directly proportional to HBsAg concentration present in calibrators, samples or controls.

Components of the LIAISON XL MUREX HBsAg Qual assay

All reagents are supplied ready to use

The table below describes the components of the LIAISON XL MUREX HBsAg Qual kit.

Table 1: Components of the LIAISON XL MUREX HBsAg Qual

Magnetic Particles 1 vial – 2.3 mL	Magnetic particles coated with antibodies to HBsAg (mouse monoclonal), biotinylated BSA, streptavidin, BSA, PBS buffer, < 0.1% sodium azide.
Calibrator 1 1 vial – 3.0 mL	Low levels of recombinant HBsAg (obtained in mammalian cells), BSA, phosphate buffer, EDTA, 0.2% ProClin® 300, an inert yellow dye.
Buffer L 1 vial – 28 mL	Non-specific IgG (mouse polyclonal), casein, TRIS buffer, EDTA, 0.1% ProClin® 300.
Conjugate 2 vial – 23.0 mL	Mouse monoclonal antibodies to HBsAg having balanced reactivity for ad and ay subtypes, conjugated to an isoluminol derivative, human and animal sera, BSA, phosphate buffer, preservatives.
Number of tests	200

LIAISON XL MUREX Control HBsAg Qual set consists of two controls (positive and negative) that are ready to use. Each control set contains enough solution to allow for at least 20 tests. The control set is an additional material required to perform the test. The controls are used for monitoring the performance of the LIAISON XL MUREX HBsAg Qual assay.

The control set is additional material required to perform the test.

NEGATIVE CONTROL 2 vials – 4.0 mL each	Human plasma non-reactive for hepatitis B surface antigen and antibody 0.2% ProClin® 300 and preservatives.
POSITIVE CONTROL 2 vials – 4.0 mL each	Human serum containing HBsAg (obtained in E. coli by the recombinant DNA technology), 0.2% ProClin® 300, preservatives

Interpretation of the Results (HBsAg):

The interpretation of results for the LIAISON XL MUREX HBsAg Qual is as follows:

Cutoff of 1.00 index value determines whether a sample has detectable levels of HbsAg:

- **Reactive:** Samples with HBsAg levels equal to or above an index value of 1.00 are considered Reactive and presumed positive for HBsAg.
- **Non-Reactive:** Samples with HBsAg levels below an index value of 1.00 are considered Non-reactive and presumed negative for HBsAg
- Initially reactive samples must be retested in duplicate. Samples with HBsAg levels below a S/CO value of 1.00 in both replicates at the retest are considered Non-Reactive and presumed negative for HBsAg. Samples that are repeatedly equal to or above a S/CO of 1.00 (i.e. at least 2 out of 3 results) are considered repeatedly Reactive and presumed positive for HBsAg. Samples that are repeatedly Reactive for HBsAg must be evaluated with the LIAISON XL MUREX HBsAg Confirmatory Test.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the detection of HBsAg. There are currently several FDA approved in vitro diagnostic tests commercially available for serological markers of hepatitis B virus (HBV) infection which, when used in conjunctionwith a patient's medical history, clinical examination and other laboratory finding, 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 be used as an aid in determining acute infection. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The LIAISON® XL MUREX HBsAg Qual assay (318250) and LIAISON® XL MUREX Control HBsAg Qual (318251) are new kits for the United States and have not been marketed in the U.S. or any foreign country. LIAISON® XL MUREX HBsAg Confirmatory assay (318110) has not been marketed in the U.S. or any foreign country

LIAISON® XL MUREX HBsAg Confirmatory assay (318110) is essentially the same as the CE-marked LIAISON® HBsAg Confirmatory Test assay (310110) except for the replacement in the neutralizing solution composition of the Human serum/plasma

positive for Anti-HBs with the Goat plasma positive for Anti-HBs and some minor modifications to raw material manufacturing processes.

The LIAISON® HBsAg Confirmatory Test (310110) has been marketed in multiple countries and has not been withdrawn from the market in any country for reasons relating to safety and effectiveness.

Table 2: Countries Where CE-Marked Versions Have Been Marketed

Austria	Algeria
Australia	Belgium
Belarus	Bahrain
Brazil	Brunei
Croatia	Czech Republic
Denmark	Dominican Republic
Egypt	Finland
France	Germany
Hongkong	Hungary
Iran	Iraq
Ireland	Italy
Kuwait	Jordan
Lithuania	Luxembourg
Mexico	Morocco
Netherlands	Norway
Poland	Qatar
Russia	Saudi Arabia
Slovak republic	Spain
Thailand	The Philippines
Trinidad, Tobago	Tunisia
Turkey	United Kingdom
Uruguay	

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

The LIAISON XL MUREX HBsAg Qual is intended for *in vitro* diagnostic use, and as a result, there is no direct adverse effect on the patient. Standard good laboratory practices are considered sufficient to minimize risks to the end user.

Failure of the product to perform as intended or human error in the use of the test may lead to a false result. Appropriate Warnings and Precautions for identified risks are contained in the labeling and assay Instructions for Use.

The risks associated with the device, when used as intended, are those related to the risk of false test results, failure to correctly interpret the test results, and failure to correctly operate the instrument.

Risks of a false positive test include improper patient management, including further investigation of hepatitis B infection with other laboratory tests to determine if a patient is acutely or chronically infected. It is possible that a clinician would decide to treat hepatitis B infection with antiviral medications in a patient without hepatitis B infection. Antiviral medication has risks including toxicity and more rarely allergic reactions. Over time, viral resistance in patients who are co-infected but undiagnosed with other viruses using the same antiviral medication, such as HIV, can lead to viral resistance, however the chance of an undiagnosed co-infection in a patient tested for hepatitis B is exceedingly unlikely. These risks are mitigated by the fact that this test would then be part of a panel, and incongruous test results in a hepatitis panel would lead a clinician to retest the patient before starting treatment.

Risks of a false negative test include improper patient management, including missing the opportunity to treat chronic Hepatitis B infection. A clinician may falsely believe that a patient is not acutely or chronically infected, but rather is currently susceptible or immune to the infection. False negative results may lead a clinician to vaccinate an infected patient. This risk is likely mitigated by the fact that this test is usually ordered as part of a panel of hepatitis B tests, and incongruous test results in a hepatitis panel would lead a clinician to retest the patient. A false negative result may alternatively result in a clinician missing the opportunity to further investigate and initiate treatment in a patient in whom treatment is otherwise be recommended, as HBsAg is often the first test sent as part of the evaluation of hepatitis B infection.

IX. SUMMARY OF NONCLINICAL STUDIES

A. Laboratory Studies

1. Cut-Off Determination

   The cut-off was established internally at DiaSorin and verified by testing a total of 100 samples (50 known negative and 50 known positive). A receiver Operating Characteristics (ROC) analysis was performed on the results of the specimens tested. The assay's cutoff was evaluated with the observed results to demonstrate that its selection represents the best level of specificity, without compromising the sensitivity.

   The cut-off value of 1.00 is within the optimal range determined by the ROC curve to discriminate between negative and positive results.

2. Sensitivity/Seroconversion Panels

   The seroconversion sensitivity of the LIAISON XL MUREX HBsAg Qual assay has been demonstrated by testing 30 commercial seroconversion panels in comparison to a reference HBsAg immunoassay in terms of number of days from initial draw to first positive sample, as well as the difference between the last negative results and the first positive results.

   The LIAISON XL MUREX HBsAg Qual yielded a positive result sooner by one or more blood draws than the comparator assay in 1 of the 30 panels and later than the reference HBsAg assay in 2 panels.

3. Analytical Sensitivity/Dilution Study with Standard
   The sensitivity of the LIAISON XL MUREX HBsAg Qual was evaluated by preparing serial dilutions of the WHO 3rd International Standard for HBsAg, (HBV genotype B4, HBsAg subtypes ayw1/adw2) – NIBSC standard code 12/226.

   Dilutions were tested in five replicates on three reagent lots, using one lot of kit controls, across four LIAISON XL Analyzers.

   The cutoff concentration corresponds to 0.05 IU/mL.

4. Analytical Specificity (Cross-Reactivity)
   A study was conducted to evaluate the LIAISON XL MUREX HBsAg Qual for cross-reactivity with specimens from individuals with medical conditions unrelated to HBV infection. A total of 385 samples from 28 unrelated medical conditions were tested in singlicate on one kit lot of LIAISON XL MUREX HBsAg Qual and on a reference HBsAg assay.

   Of the 385 samples, 1 sample was found to be non-reactive with the reference assay and reactive with the LIAISON XL MUREX HBsAg Qual assay. The results of each potential cross reactant are shown in table below.

Table 3: Summary of Cross-Reactivity Study

Organism/Condition	**N**	**Comparator HBsAg assay**	**LIAISON® XL MUREX HBsAg Qual**	
			Nonreactive	**Reactive**
Anti-nuclear antibodies (ANA)	14	Negative	14	0
Non-viral liver diseases (i.e. Auto-immune hepatitis)	15	Negative	15	0
C. trachomatis (anti-chlamydia positive)	15	Negative	14	1
CMV (anti-CMV positive)	13	Negative	13	0
EBV (anti-EBV positive)	13	Negative	13	0
HSV (anti-HSV positive)	15	Negative	15	0
Fatty liver disease	14	Negative	10	0
HAMA	10	Negative	15	0
Hemodialysis patient	15	Negative	11	0
Hepatitis A Virus (anti-HAV positive)	11	Negative	15	0
Hepatitis C Virus (anti-HCV positive)	15	Negative	12	0
Hepatocellular carcinoma	12	Negative	2	0
HIV-1 (anti-HIV-1 positive)	2	Negative	13	0
HIV-2 (anti-HIV-2 positive)	12	Negative	12	0
HIV (anti-HIV positive)	15	Negative	15	0
HTLV-1/2 (anti-HTLV positive)	15	Negative	15	0
IgG monoclonal gammopathy	16	Negative	16	0

Organism/Condition	N	Comparator HBsAg assay	LIAISON® XL MUREX HBsAg Qual	
			Nonreactive	Reactive
IgM monoclonal gammopathy	4	Negative	4	0
Influenza vaccine recipients	15	Negative	15	0
Multiparous pregnancies	15	Negative	15	0
Multiple myeloma	14	Negative	14	0
Multiple transfusion recipients	15	Negative	15	0
N. gonorrhoeae (anti-Neisseria positive)	12	Negative	12	0
Pregnancy 1st trimester	15	Negative	15	0
Pregnancy 2nd trimester	15	Negative	15	0
Pregnancy 3rd trimester	15	Negative	15	0
Rheumatoid Factor	15	Negative	15	0
T. pallidum (anti-treponema positive)	12	Negative	12	0
T. cruzi (anti-*T. cruzi* positive)	14	Negative	14	0
Syphilis (*T. pallidum*)	10	Negative	10	0
Toxoplasmosis (Toxoplasma gondii)	10	Negative	10	0
CMV (Cytomegalovirus)	13	Negative	13	0
EBV (Epstein-Barr virus)	10	Negative	10	0
HAV (Hepatitis A virus)	10	Negative	10	0
HIV (human immunodeficiency virus)	27	Negative	26	1
HSV (herpes simplex virus)	10	Negative	10	0
HTLV (Human T-Lymphotropic virus)-1/2	7	Negative	7	0
Parvovirus B19	10	Negative	10	0
Rubella virus	10	Negative	9	1
Varicella-zoster virus	12	Negative	10	2
N. gonorrhoeae	12	Negative	12	0
T. Cruzi	10	Negative	10	0
Staphylococcus aureus	10	Negative	10	0
Pseudomonas aeruginosa	10	Negative	10	0
E. coli	10	Negative	10	0
Hepatitis C (HCV)	10	Negative	10	0
Chlamydia (*C. trachomatis*)	15	Negative	14	1

5. Endogenous Interference
   A study was conducted to evaluate the LIAISON XL MUREX HBsAg Qual for endogenous interference. Ten negative samples or negative pools were spiked with an HBsAg high positive sample in order to achieve two levels of samples: high negative and low positive. The spiked sets were divided into two aliquots. The first aliquot was spiked with high concentration of potentially interfering substance. The second set of high negative and low positive aliquots (samples without any potentially interfering substances) were used as control samples for the study. Both samples with and without potentially interfering substance were tested in the same run, in twenty-six replicates each, on one lot of kit reagents and with one lot of kit controls.

   No interference was observed at the concentration for each substance listed below.

Table 4: Interfering Substances

Substances	**Tested Concentrations**
Triglycerides	3000 mg/dL
Hemoglobin	1000 mg/dL
Unconjugated bilirubin	40 mg/dL
Conjugated bilirubin	40 mg/dL
Albumin	6000 mg/dL
Cholesterol	350 mg/dL
Vitamin H (Biotin)	3500 ng/mL

6. Sample Equivalence/Matrix Effect
   Twenty-five paired sets of matched serum (with and without gel SST) and plasma (lithium heparin, sodium heparin, sodium citrate, and potassium EDTA) samples were tested to determine if these sample types provided equivalent results on the LIAISON XL MUREX HBsAg Qual. Each sample was divided into three aliquots. Two sets of aliquots were spiked with an HBsAg high positive sample to achieve two levels of samples: high negative and low positive samples. The third aliquot served as un-spiked control. 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 indicate that there is equivalence among serum (with and without Gel SST), lithium heparin, sodium heparin, sodium citrate, and potassium EDTA.

7. Carry-Over Study
   A carry-over study was performed to evaluate the extent of carryover and the associated residual risk for signal carryover in the instrument's measuring cell as a result of a high signal-generating sample. The study included one HBsAg negative serum sample, one low positive serum sample and one high positive sample. The samples were tested in singlicate in five (5) runs in the following sequence: High Pos, Neg, High Pos, Neg, High Pos, Neg, High Pos, Neg, High Pos, Neg.

   All acceptance criteria were met demonstrating that no significance amount of analyte is carried over from one sample reaction into the subsequent sample reactions.

8. High Dose Hook Effect
   Testing was performed to assess the saturation effect that may appear when testing samples containing extremely high levels of analyte resulting in a reported result that is lower than the actual analyte concentration. Four samples with analyte level above the upper end of the assay were tested neat and after serial dilution in Specimen Diluent of the LIAISON XL MUREX HBsAg Confirmatory. A high dose hook effect (decrease in signal) was observed at HBsAg S/CO values >2990 S/CO (high positive); however, the samples were still high positive.

9. Stability Studies

   Sample Stability
   Studies were performed to determine the storage stability of patient serum and plasma samples at storage temperatures of 2-8°C, room temperature (RT), -20 °C. A multiple freeze/thaw (F/T) study was also performed.

   Serum and plasma samples tested contained HBsAg analyte levels of negative, high negative and low positive.
   - 2-8 °C study – samples were tested unstressed (T=0), and again after 1, 2, 3, 4, 5, 7 and 8 days of storage at 2-8°C for 24 hours per day.
   - room temperature study (RT) - samples were tested immediately after preparation and again after 4, 14, 24, 28, 43, 48, and 52 hours of storage at RT.
   - -20 °C study – samples were tested unstressed (T=0) and stored at -20 °C or lower for 1, 3, 4, and 5 months.
   - Freeze/Thaw (F/T) study – samples were tested unstressed (T=0) and after 1, 2, 3, 4, 5, 6, 7, 8, and 9 F/T cycles. Samples were frozen for 12-24 hours at -20°C or lower and thawed at room temperature.

Table 5: Sample Stability Claims in Serum and Plasma

	Sample Stability Claims			
Sample Matrix	**Number of Freeze and Thaw Cycles**	**Storage at 2-8°C**	**Storage at -20°C**	**Storage at Room Temperature**
Serum and plasma	7	7 days	3 months	3 days

Reagent Stability-Real-Time (Shelf-Life)
Studies were performed to establish the shelf-life for the LIAISON XL MUREX HBsAg Qual. Three lots of LIAISON XL MUREX HBsAg Qual were stored at the recommended storage temperature of 2-8ºC throughout the study. Performance was assessed against clinically relevant acceptance criteria using three lots of LIAISON XL MUREX Control HBsAg Qual (positive and negative) and an internal stability panel consisting of eleven samples. Study demonstrated that reagents are stable and continue to meet acceptance criteria for the following number of months when stored at 2-8ºC: LIAISON XL MUREX HBsAg Qual 15 months after date of manufacture, LIAISON MUREX CONTROL HBsAg 14 months after date of manufacture, and LIAISON XL MUREX HBsAg Confirmatory Test 12 months after date of manufacture.

Reagent Stability- Reagent On-Board
Stability studies were conducted to determine the length of time the LIAISON XL MUREX HBsAg Qual Reagent Integral can be stored on-board the LIAISON XL Analyzer in the refrigerated area once open. One lot of LIAISON XL MUREX HBsAg Qual and LIAISON XL MUREX Control HBsAg Qual (negative and positive) along with the internal stability panel were tested in duplicate at one week intervals up to 13 weeks. The LIAISON XL MUREX HBsAg Qual is stable on-board the LIAISON XL Analyzer for 12 weeks.

Reagent Stability- Open Use
The aim of this study was to assess the open use stability of the LIAISON XL MUREX HBsAg Qual kit reagents by stimulating normal conditions of use as specified in the instructions for use. Testing of samples was performed in duplicate, on one lot of LIAISON XL MUREX HBsAg Qual and one lot of LIAISON XL MUREX Control HBsAg Qual Results were calculated using the initial (time zero) assay calibration. The opened Reagent Integral was then removed from the XL Analyzer and stored at 2-8ºC. Kit performance using the opened Reagent Integral was evaluated weekly up to 13 weeks. The Reagent Integral is stable after opening for 12 weeks when stored at 2-8ºC.

Reagent Stability-Calibrator stability
The LIAISON XL MUREX HBsAg Qual calibrators are included on the Reagent Integral. All studies for the Reagent Integral are applicable to the calibrators provided.

Control Stability-Real Time Shelf-Life
Studies were performed to establish the shelf-life for the LIAISON XL MUREX Control HBsAg Qual. Three lots of LIAISON XL MUREX Control HBsAg Qual were stored at the recommended storage temperature of 2-8ºC throughout the study. Results demonstrate that the positive and negative controls are stable and continue to meet acceptance criteria at 14 months when stored at 2-8ºC.

Control Stability-Open Use
The aim of this study was to assess stability of opened Control vials by simulating normal conditions of use, as specified in the instructions for use. Testing was performed in duplicate on one lot of LIAISON XL MUREX Control HBsAg Qual. LIAISON XL MUREX Control HBsAg Qual was within the established range. The LIAISON XL MUREX Control HBsAg Qual is stable for 12 weeks after opening when stored at 2-8ºC between uses.

Temperature Stress/Reagent Transport Study
The transport simulation tests were performed in order to ensure that kit reagents maintain their properties during the shipment and delivery conditions to the customer. After being subjected to simulates stress conditions, testing was performed on 1 lot of kit reagents and 1 lot of kit controls. All testing performed met acceptance criteria under various simulated transport conditions.

10. Precision

Internal 20 Day
A precision/reproducibility study was carried out over a period of 20 days on the LIAISON XL MUREX HBsAg Qual using the LIAISON XL Analyzer. The CLSI document EP05-A3 was consulted in the preparation of the testing protocol. The testing was performed internally at DiaSorin S.p.A.

A coded panel of 11 serum-based samples and controls were tested in 2 replicates per run, in 2 runs per day, by multiple operators, using 3 reagent kit lots and 3 Controls lots, over a period of 20 days. The testing days were spanned 2 calibration cycles.

The results are shown in the following table.

Table 6: Summary of 20-Day Precision Study

			LIAISON® XL MUREX HBsAg Qual Assay - All 3 Lots Combined									
Sample ID	**N**	**Mean (S/CO)**	**Repeatability**		**Between Run**		**Between-Day**		**Between-Lots**		**Within Laboratory**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Kit Ctrl Neg lot 1	240	0.41	0.023	5.8%	0.023	5.6%	0.026	6.5%	0.035	8.6%	0.055	13.5%
Kit Ctrl Neg lot 2	240	0.41	0.026	6.4%	0.016	4.0%	0.029	7.2%	0.031	7.5%	0.053	12.8%
Kit Ctrl Neg lot 3	240	0.41	0.026	6.2%	0.014	3.4%	0.031	7.5%	0.035	8.4%	0.055	13.3%
Kit Ctrl Pos lot 1	240	1.96	0.070	3.6%	0.041	2.1%	0.085	4.4%	0.096	4.9%	0.152	7.8%
Kit Ctrl Pos lot 2	240	1.83	0.062	3.4%	0.036	2.0%	0.082	4.5%	0.065	3.5%	0.127	7.0%
Kit Ctrl Pos lot 3	240	1.79	0.059	3.3%	0.034	1.9%	0.081	4.5%	0.060	3.4%	0.122	6.8%
HBS1U10	240	0.39	0.030	7.9%	0.034	8.9%	0.022	5.8%	0.017	4.3%	0.054	13.9%
HBS1U11	240	0.73	0.035	4.8%	0.021	2.9%	0.039	5.3%	0.025	3.4%	0.062	8.4%
HBS1U12	240	0.72	0.030	4.1%	0.019	2.6%	0.046	6.3%	0.027	3.7%	0.064	8.8%
HBS1U13	240	0.72	0.028	3.9%	0.021	2.9%	0.039	5.5%	0.028	3.9%	0.060	8.3%
HBS1U14	240	1.12	0.037	3.3%	0.024	2.1%	0.082	7.3%	0.045	4.0%	0.103	9.2%
HBS1U15	240	1.12	0.039	3.5%	0.034	3.1%	0.082	7.3%	0.044	3.9%	0.106	9.5%
HBS1U16	240	1.13	0.039	3.4%	0.034	3.0%	0.074	6.5%	0.041	3.7%	0.099	8.8%
HBS1U17	240	3.02	0.079	2.6%	0.078	2.6%	0.114	3.8%	0.129	4.3%	0.205	6.8%
HBS1U18	240	3.06	0.057	1.8%	0.057	1.9%	0.135	4.4%	0.128	4.2%	0.202	6.6%
HBS1U19	240	3.04	0.055	1.8%	0.063	2.1%	0.122	4.0%	0.108	3.5%	0.183	6.0%
HBS1U20	240	1.06	0.035	3.3%	0.020	1.8%	0.042	4.0%	0.037	3.5%	0.069	6.5%

External Precision 5-day Study
A 5 day precision/reproducibility study was conducted at 2 external laboratories and at DiaSorin Inc. to verify the precision of the LIAISON XL MUREX HBsAg Qual. The CLSI document EP15-A3 was consulted in the preparation of the testing protocol. The coded panel comprised 11 serum-based samples was the same panel used in the 20-day precision study.

The precision panel was tested at all 3 sites on the LIAISON XL Analyzer using 6 replicates per run in 1 run per day for five days with multiple technicians performing the testing.

The following table shows the results.

Table 7: Summary of 5-Day Precision Study

Sample ID	N	LIAISON® XL MUREX HBsAg Qual Assay - 5 Day Multi-Site/Multi-Lot										
		Mean	Repeatability		Between-Day/Runs		Within Laboratory		Between Sites/Lots		Reproducibility	
		(S/CO)	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Ctrl Neg (all 3 lots)	90	0.38	0.033	8.6%	0.029	7.7%	0.044	11.5%	0.044	11.6%	0.062	16.3%
Ctrl Pos (all 3 lots)	90	1.859	0.041	2.2%	0.04	2.2%	0.058	3.1%	0.052	2.8%	0.077	4.2%
HBS1U10	90	0.342	0.022	6.5%	0.023	6.8%	0.032	9.4%	0.023	6.8%	0.04	11.6%
HBS1U11	90	0.734	0.026	3.5%	0.031	4.2%	0.04	5.4%	0.042	5.8%	0.058	7.9%
HBS1U12	90	0.726	0.029	4.0%	0.03	4.1%	0.042	5.8%	0.043	5.9%	0.06	8.2%
HBS1U13	90	0.721	0.031	4.3%	0.033	4.6%	0.045	6.3%	0.03	4.1%	0.054	7.5%
HBS1U14	90	1.138	0.033	2.9%	0.03	2.7%	0.045	3.9%	0.038	3.4%	0.059	5.2%
HBS1U15	90	1.135	0.031	2.7%	0.041	3.6%	0.051	4.5%	0.036	3.2%	0.062	5.5%
HBS1U16	90	1.146	0.035	3.0%	0.037	3.2%	0.051	4.4%	0.026	2.3%	0.057	5.0%
HBS1U17	90	3.213	0.065	2.0%	0.051	1.6%	0.083	2.6%	0.116	3.6%	0.143	4.4%
HBS1U18	90	3.196	0.057	1.8%	0.04	1.2%	0.069	2.2%	0.104	3.2%	0.125	3.9%
HBS1U19	90	3.211	0.066	2.1%	0.052	1.6%	0.084	2.6%	0.107	3.3%	0.136	4.2%
HBS1U20	90	1.099	0.034	3.1%	0.034	3.1%	0.048	4.3%	0.05	4.5%	0.069	6.3%

11. Pediatric and Adult Sample equivalency

Pediatric samples were tested to determine if these types of samples provide equivalent results to adult human serum

Thirty (30) negative pediatric patient samples were used for this study. The pediatric samples encompassed the age range of 2 months to 21 years. Ten (10) pediatric samples were spiked with an HBsAg high positive sample to obtain high negative samples. Ten (10) pediatric samples were spiked with an HBsAg high positive sample to obtain low positive samples. Ten (10) pediatric samples were spiked with an HBsAg high positive sample to obtain moderate positive samples. Adult negative pool samples were used as controls and were spiked with an HBsAg high positive sample to achieve the same 3 levels of samples: high negative, low positive and moderate positive samples.

The samples were tested in duplicate, with the LIAISON XL MUREX HBsAg Qual. Percent (%) recovery of the analyte from the pediatric and adult blood was calculated for each sample.

All acceptance criteria were met demonstrating acceptable performance of pediatric samples. It can be concluded that pediatric samples react in the same way as the adult samples and are acceptable for use in the LIAISON XL MUREX HBsAg Qual.

12. HBsAg Genotypes Detection
    Thirty (30) specimens from commercially available HBsAg performance panels containing the most common hepatitis B surface antigen genotypes (A through H) were tested to assess the performance of the assay. All 30 specimens were HBsAg reactive with both the LIAISON XL MUREX HBsAg Qual and an FDA-approved reference assay.

13. HBsAg mutant detection
    A panel of 10 recombinant mutants were tested with the LIAISON XL MUREX HBsAg Qual and an FDA-approved reference assay to determine correct antigenic detection of the HBsAg structure. The mutants contained important epitope clusters within amino acids 100-160 that include the "a determinant region" (amino acids 124-147), the most important target for serological diagnosis. The recombinant mutants were diluted in HBsAg negative human serum to yield a low positive sample. All 10 recombinant mutants were recognized with LIAISON XL MUREX HBsAg Qual and are shown in the following table.

Table 8: HBsAg Recombinant Mutants Tested

Sample ID	Mutation	Comparator HBsAg assay	LIAISON® XL MUREX HBsAg Qual assay
Mutant-01	T123N	Reactive	Reactive
Mutant-02	T123N-T124S	Reactive	Reactive
Mutant-03	P142L-F/Y143H-D144E-G145-R	Reactive	Reactive
Mutant-04	I110R-SS117I-G119R-T123N	Reactive	Reactive
Mutant-05	122+DT	Reactive	Reactive
Mutant-06	122+DT-G145R	Reactive	Reactive
Mutant-07	G145R	Reactive	Reactive
Mutant-08	D114A	Reactive	Reactive
Mutant-09	P142L-G145R	Reactive	Reactive
Mutant-10	P142S-G145R	Reactive	Reactive

B. Animal Studies
Not Applicable

C. Additional Studies
Not Applicable

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness for the detection of hepatitis-B e antigen with the LIAISON XL MUREX HBsAg Qual using samples that would routinely be tested for hepatitis in the US. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

A multi-site clinical agreement study was conducted to evaluate the clinical performance of the LIAISON XL MUREX HBsAg Qual on samples that would routinely be tested for hepatitis and samples that were selected from individuals that were diagnosed with acute or chronic Hepatitis B infection.

The clinical agreement study involved the testing of 3082 samples on six (6) FDA approved reference assays, each detecting a unique serological marker (HBsAg, HBeAg, Anti-HBs, Anti-HBc, Anti-HBc IgM, and Anti-HBe) in order determine the HBV classification for each of the samples tested.

The samples were collected from 6 different countries: Russia, Colombia, Cameroon, Ghana, Nigeria, and the United States. The U.S. samples were from multiple locations including Ohio, Pennsylvania, Indiana, Florida, California, Texas, New Jersey, Tennessee, Massachusetts, and Puerto Rico.

Prospective (unselected) subjects were as follows:

- Pediatric and adult male (38.2%), female (61.6%) and unknown gender (0.2%) subjects at risk for hepatitis due to medical conditions (dialysis, transplantation), occupation, lifestyle, behavior or a known exposure event.
- Subjects showing signs or symptoms and individuals living in an area with a higher probability of HBV infection.
- The demographic breakdown of the prospective population was as follows: American Indian/Alaskan Native (0.1%), Asian (0.8%), Black/African American (31.2%), Caucasian (62.5%), Other (5.2%), and Unknown (0.2%) with an age range of 2 - 98 years of age.

The retrospective (selected/archived) samples were from male (69.5%), female (21.9%), and unknown gender (8.6%) subjects diagnosed with acute and/or chronic Hepatitis having an age range of 17 - 67 years of age from the following ethnicities: Asian (1.6%), Black/African American (23.8%), Caucasian (73%), other (1.2%) and 0.4% Unknown.

A total of 800 pregnant women were all from the United States including Puerto Rico. Of the 800 total, 797 (99.6%) were between the ages of 15 and 47, with 3 (0.4%) of unknown age. Of the 800 pregnant women, 383 (48%) were in their 1st trimester of pregnancy, 193 (24%) in the 2nd trimester, 190 (24%) in the 3rd trimester, and 35 (4%) trimester was unknown. The pregnant women included the following ethnicities: Asian (4.6%), Black/African American (12.4%), Native Hawaiian/Pacific Islander (0.1%), White (81.4%), Other (1.3%), and Unknown (0.3%).

The distribution of LIAISON XL MUREX HBsAg Qual reactive and non-reactive results by age and gender of the overall prospective population are presented below.

Table 9: Demographic Summary of Prospective Population

Age Range	Gender	LIAISON® XL MUREX HBsAg Qual				Total
		+		-		
		n	%	n	%	
0-9	F	0	0.0%	5	100.0%	5
	M	0	0.0%	10	100.0%	10
10-19	F	0	0.0%	40	100.0%	40
	M	0	0.0%	15	100.0%	15
20-29	F	13	3.3%	376	96.7%	389
	M	15	6.4%	218	93.6%	233
30-39	F	9	1.9%	465	98.1%	474
	M	16	7.1%	208	92.9%	224
40-49	F	4	1.4%	286	98.6%	290
	M	8	4.0%	193	96.0%	201
50-59	F	4	1.7%	228	98.3%	232
	M	3	1.6%	182	98.4%	185
60-69	F	2	1.3%	156	98.7%	158
	M	0	0.0%	108	100.0%	108
70-79	F	0	0.0%	46	100.0%	46
	M	0	0.0%	39	100.0%	39
80-89	F	0	0.0%	14	100.0%	14
	M	0	0.0%	7	100.0%	7
90-98	F	0	0.0%	4	100.0%	4
	M	0	NA	0	NA	0
Unk	F	0	0.0%	1	100.0%	1
	M	0	0.0%	1	100.0%	1
Total		74	2.8%	2602	97.2%	2676

Table 10: Pregnant Women Results Stratified by Age

Age Range	LIAISON® XL MUREX HBsAg Qual				Total
	+		-		
	n	%	n	%	
10-19	0	0.0%	62	100.0%	62
20-29	0	0.0%	464	100.0%	464
30-39	3	1.2%	246	98.8%	249
40-49	1	4.5%	21	95.5%	22
50-59	0	NA	0	NA	0
Unk	0	0.0%	3	100.0%	3
Total	4	0.5%	796	99.5%	800

Hepatitis B Status Classification

Hepatitis B status classification was based on testing all samples with FDA approved HBV assays for HBsAg, HBeAg, Anti-HBc, Anti-HBc IgM, Anti-HBe and Anti-HBs. HBV classification for the prospective and retrospective specimens is presented below.

Table 11: Hepatitis B Infection Status Classification

HBV Classification	HBsAg	HBeAg	Anti-HBc	Anti-HBc IgM	Anti-HBe	Anti-HBs	Prospective (n)	Retrospective (n)
Acute	R	NR	NR	NR	NR	NR	12	97
Acute	R	R	NR	NR	NR	NR		
Acute	R	R	R	R	NR	NR		
Acute	R	R	R	R	R	NR		
Acute	R	R	R	R	EQV	NR		
Acute	R	NR	R	EQV	R	NR		
Acute	R	NR	R	R	EQV	NR		
Acute	R	EQV	R	R	R	NR		
Acute	R	NR	R	R	NR	NR		
Acute	R	R	R	EQV	NR	NR		
Acute	R	R	R	R	NR	R		
Acute	R	R	R	R	EQV	R		
Acute	R	R	R	R	R	EQV		
Late Acute	R	NR	R	R	R	NR	2	32
Late Acute	R	NR	R	R	R	R		
Chronic	R	NR	NR	NR	R	NR	76	68
Chronic	R	NR	R	NR	NR	R		
Chronic	R	R	R	NR	NR	R		
Chronic	R	R	R	NR	NR	NR		
Chronic	R	EQV	R	NR	NR	NR		
Chronic	R	NR	R	NR	R	NR		
Chronic	R	NR	R	NR	NR	NR		
Chronic	R	NR	R	NR	R	R		
Chronic	R	EQV	R	NR	NR	NR		
Early Recovery	NR	NR	R	R	R	NR	48	9
Early Recovery	NR	NR	R	EQV	R	R		
Early Recovery	NR	NR	R	R	NR	NR		
Early Recovery	NR	NR	R	NR	R	NR		
Early Recovery	NR	NR	R	NR	NR	NR		
Early Recovery	NR	NR	R	R	NR	R		
Early Recovery	NR	NR	R	R	R	R		
Recovery	NR	NR	R	NR	R	R	131	36
Recovery	NR	NR	NR	NR	R	R		
Recovery	NR	NR	R	NR	EQV	R		
Immune Due to Natural Infection	NR	NR	R	NR	NR	R	104	3
Immune Due toNatural Infection	NR	NR	R	NR	NR	EQV		

HBV Classification	HBsAg	HBeAg	Anti-HBc	Anti-HBc IgM	Anti-HBe	Anti-HBs	Prospective (n)	Retrospective (n)
HBV Vaccine Response	NR	NR	NR	NR	NR	R	1144	8
HBV Vaccine Response	NR	NR	NR	NR	NR	EQV		
Not Previously Infected	NR	NR	NR	NR	NR	NR	1302	1
Not Interpretable	NR	NR	NR	R	NR	NR	7	2
Not Interpretable	NR	R	NR	NR	NR	NR		
Not Interpretable	NR	R	NR	NR	NR	R		
Not Interpretable	NR	R	R	R	NR	EQV		
Not Interpretable	NR	R	R	R	NR	R		
Not Interpretable	R	NR	NR	NR	NR	R		
Not Interpretable	R	NR	NR	NR	NR	R		
Total							2826	256

Clinical Agreement Study Analysis

Comparison results of the LIAISON XL MUREX HBsAg Qual to the reference HBsAg assay are presented with negative and positive percent agreement (NPA and PPA, respectively) with the 95% confidence intervals for combined prospective and retrospective specimens for each of the HBV classification categories. Additional performance tables for the pregnancy and pediatric cohorts are presented.

Table 12: Cumulative Adult and Pediatric Clinical Agreement (Combined Prospective and Retrospective) HBV Classification

	Reference HBsAg assay				Total
	Reactive		Nonreactive		
	LIAISON® XL MUREX HBsAg Qual		LIAISON® XL MUREX HBsAg Qual		
	Reactive	Non reactive	Reactive	Non reactive	
Acute	106	3	0	0	109
Late Acute	33	1	0	0	34
Chronic	144	0	0	0	144
Early Recovery	0	0	0	57	57
Recovery	0	0	4	163	167
Immune Due to Natural Infection	0	0	0	107	107
HBV Vaccine Response	0	0	0	1152	1152
Not Previously Infected	0	0	2	1301	1303
Not Interpretable	0	1	0	8	9
Total	283	5	6	2788	3082

Table 13: Cumulative Adult and Pediatric Clinical Agreement
(Combined Prospective and Retrospective)

HBV Classification	Positive Percent Agreement (PPA)	Negative Percent Agreement (NPA)
Acute	106/109 (97.2%) 95% CI: 92.2% to 99.1%	N/A
Late Acute	33/34 (97.1%) 95% CI: 85.1% to 99.5%	N/A
Chronic	144/144 (100.0%) 95% CI: 97.4% to 100.0%	N/A
Early Recovery	N/A	57/57 (100.0%) 95% CI: 93.7% to 100.0%
Recovery	N/A	163/167 (97.6%) 95% CI: 94.0% to 99.1%
Immune Due to Natural Infection	N/A	107/107 (100.0%) 95% CI: 96.5% to 100.0%
HBV Vaccine Response	N/A	1152/1152 (100.0%) 95% CI: 99.7% to 100.0%
Not Previously Infected	N/A	1301/1303 (99.8%) 95% CI: 99.4% to 100.0%
Not Interpretable	0/1 (0.0%) 95% CI: 0.0% to 79.3%	8/8 (100.0%) 95% CI: 67.6% to 100.0%
Total	283/288 (98.3%) 95% CI: 96.0% to 99.3%	2788/2794 (99.8%) 95% CI: 99.5% to 99.9%

Table 14: Prospective Pregnancy Cohort Clinical Agreement by Trimester

Pregnancy (Trimester)	Reference HBsAg assay				Total
	Reactive		Nonreactive		
	LIAISON® XL MUREX HBsAg Qual		LIAISON® XL MUREX HBsAg Qual		
	Reactive	Non reactive	Reactive	Non reactive	
First	2	0	0	380	382
Second	0	0	0	193	193
Third	1	0	0	189	190
Unknown	1	0	0	34	35
Total	4	0	0	796	800

Table 15: Prospective Pregnancy Cohort Clinical Agreement by Trimester

Pregnancy (Trimester)	Positive Percent Agreement (PPA)	Negative Percent Agreement (NPA)
First	2/2 (100.0%) 95% CI: 34.2% to 100.0%	380/380 (100.0%) 95% CI: 99.0% to 100.0%
Second	N/A	193/193 (100.0%) 95% CI: 98.0% to 100.0%
Third	1/1 (100.0%) 95% CI: 20.7% to 100.0%	189/189 (100.0%) 95% CI: 98.0% to 100.0%
Unknown	1/1 (100.0%) 95% CI: 20.7% to 100.0%	34/34 (100.0%) 95% CI: 89.8% to 100.0%
Total	4/4 (100.0%) 95% CI: 51.0% to 100.0%	796/796 (100.0%) 95% CI: 99.5% to 100.0%

Table 16: Cumulative Pediatric Agreement Summary
(Combined Prospective and Retrospective)

HBV Classification	Positive Percent Agreement (PPA)	Negative Percent Agreement (NPA)
Acute	20/20 (100.0%) 95% CI: 83.9% to 100.0%	N/A
Late Acute	7/7 (100.0%) 95% CI: 64.6% to 100.0%	N/A
Chronic	7/7 (100.0%) 95% CI: 64.6% to 100.0%	N/A
Early Recovery	N/A	1/1 (100.0%) 95% CI: 20.7% to 100.0%
Recovery	N/A	5/5 (100.0%) 95% CI: 56.6% to 100.0%
Immune Due to Natural Infection	N/A	3/3 (100.0%) 95% CI: 43.9% to 100.0%N/A
HBV Vaccine Response	N/A	63/63 (100.0%) 95% CI: 94.3% to 100.0%
Not Previously Infected	N/A	84/84 (100.0%) 95% CI: 95.6% to 100.0%
Not Interpretable	N/A	2/2 (100.0%) 95% CI: 34.2% to 100.0%
Total	34/34 (100%) 95% CI:89.5% to 100.0%	158/158 (100%) 95% CI: 97.6% to 100.0%

Clinical Endpoints

As an in vitro diagnostic test, the LIAISON XL MUREX HBsAg Qual test involves taking a sample of plasma or serum from a patient. The test, therefore, presents no more safety hazard to an individual being tested than other tests where blood samples are drawn. Safety issues regarding false positive and negative test results are discussed in section VIII.

With regards to effectiveness, the clinical performance of the LIAISON XL MUREX HBsAg Qual was evaluated versus an FDA approved HBsAg test for patients at risk of infection with hepatitis B and for patients with signs and symptoms of hepatitis.

With regard to success/failure criteria, the assay performed well with a positive percent agreement (PPA) of 98.3% and a negative percent agreement (NPA) of 99.8% among subjects in various states of HBV infection.

B. Accountability of PMA Cohort

The clinical agreement study involved the testing of 3082 on six (6) FDA approved reference assays, each detecting a unique serological marker (HBsAg, HBeAg, Anti-HBs, Anti-HBc, Anti-HBc IgM, and Anti-HBe in order determine the HBV classification for each of the samples tested.

The samples were collected from 6 different countries: Russia, Colombia, Cameroon, Ghana, Nigeria, and the United States. The U.S. samples were from multiple locations including Ohio, Pennsylvania, Indiana, Florida, California, Texas, New Jersey, Tennessee, Massachusetts, and Puerto Rico.

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for an HBsAg detection study performed in the US.

The prospective (unselected) subjects were defined as follows:

- Pediatric and adult male (38.2%), female (61.6%), and unknown gender (0.2%) subjects at risk for hepatitis due to medical conditions (dialysis, transplantation), occupation, lifestyle, behavior or a known exposure event.
- Subjects showing signs or symptoms and individuals living in an area with a higher probability of HBV infection.

The tables below shows the demographic distribution of the cohort.

Table 17: Prospective and Retrospective Demographic Summary by Gender

	Adult				Pediatric (2-21)				Unknown Age			
	Prospective		Retrospective		Prospective		Retrospective		Prospective		Retrospective	
Gender	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Female	1643	61.7%	54	26.2%	98	60.9%	2	6.5%	1	50.0%	0	0.0%
Male	1017	38.2%	151	73.3%	61	37.9%	29	93.5%	1	50.0%	0	0.0%
Unknown	3	0.1%	1	0.5%	2	1.2%	0	0.0%	0	0.0%	21	100.%
Total	2663	100.%	206	100.%	161	100.%	31	100.%	2	100.%	21	100.%

Table 18: Prospective and Retrospective Demographic Summary by Race

	Adult				Pediatric (2-21)				Unknown Age			
	Prospective		Retrospective		Prospective		Retrospective		Prospective		Retrospective	
Race	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
American Indian/ Alaskan Native	2	0.1%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Asian	21	0.8%	4	1.9%	3	1.9%	0	0.0%	0	0.0%	0	0.0%
Black/African American	832	31.2%	57	27.7%	64	39.8%	4	12.9%	0	0.0%	0	0.0%
Native Hawaiian or Other Pacific	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
White	1664	62.5%	141	68.4%	89	55.3%	27	87.1%	2	100.0%	21	100.0%
Unknown	6	0.2%	1	0.5%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Other	138	5.2%	3	1.5%	5	3.1%	0	0.0%	0	0.0%	0	0.0%
Total	2663	100.0%	206	100.0%	161	100.0%	31	100.0%	2	100.0%	21	100.0%

The following table shows the combined prospective pregnancy cohort clinical agreement.

D. Safety and Effectiveness Results

1. Safety Results
   With regard to safety, as an in vitro diagnostic test, the LIAISON XL MUREX HBsAg Qual test involves taking a sample of plasma or serum for a patient. The test, therefore, presents no more safety hazard to an individual being tested than other tests where blood samples are drawn.

   There were no adverse effects that occurred in the PMA clinical study.

2. Effectiveness Results
   The analysis of effectiveness was based on the 3082 evaluable patients. Key effectiveness outcomes are presented in Section X above.

3. Subgroup Analyses
   The study design enabled an assessment of assay performance by subgroup as depicted in table above which show subjects stratified by state of HBV infection.

4. Pediatric Extrapolation
   In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 3 investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Microbiology Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The effectiveness of the LIAISON XL MUREX HBsAg Qual test for the qualitative detection of hepatitis-B s antigen in human serum and plasma, lithium heparin, sodium citrate, and dipotassium EDTA) samples including separator tubes, on the LIAISON XL Analyzer has been demonstrated in the following patient populations: adults and pediatric patients (2-21 years). The results of this test may be used as an aid in the diagnosis of hepatitis B virus (HBV) infection in patients with symptoms of hepatitis. The PPA of the assay is 98.3% with a two-sided 95% confidence interval (CI) of 96.0%-99.3% and the NPA of 99.8% with a two-sided 95% CI of 99.5%-99.9%.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory studies as well as data collected in a clinical study conducted to support PMA approval as described above. Based on the results of these studies the LIAISON XL MUREX HBsAg Qual when used according to the manufacturer's instructions can aid the physician in the diagnosis of HBV infection. The PPA of the assay is 98.3% with a two-sided 95% confidence interval (CI) of 96.0%-99.3% and the NPA of 99.8% with a two-sided 95% CI of 99.5%-99.9%.

C. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. The benefits of the assay are as part of a hepatitis B panel, the appropriate diagnosis and treatment of hepatitis B infection. Treatment for appropriate patients can mitigate the sequelae of hepatitis B infection and may result in improved morbidity and mortality in these patients. Known sequelae of hepatitis B infection include continued symptoms, increases in all-cause mortality, liver disease-related complications and death, hepato-cellular carcinoma rates, and need for liver transplantation. Additionally, diagnosis and

appropriate treatment for hepatitis B infection can potentially decrease transmission and disease burden in the general population and particularly in populations at high risk for hepatitis B infection. While the performance of the device in the clinical study suggests that patients will benefit from the assay, low prevalence of certain HBV classifications is a source of potential uncertainty when analyzing the samples. The wide confidence intervals for those subgroups is expected due to the biology of hepatitis B infection and is acceptable.

The risks associated with the device, when used as intended, are those related to the risk of false test results, failure to correctly interpret the test results, and failure to correctly operate the instrument.

Risks of a false positive test include improper patient management, including further investigation of hepatitis B infection with other laboratory tests to determine if a patient is acutely or chronically infected. It is possible that a clinician would decide to treat hepatitis B infection with antiviral medications in a patient without hepatitis B infection. Antiviral medication has risks including toxicity and more rarely allergic reactions. Over time, viral resistance in patients who are co-infected but undiagnosed with other viruses using the same antiviral medication, such as HIV, can lead to viral resistance, however the chance of an undiagnosed co-infection in a patient tested for hepatitis B is exceedingly unlikely. These risks are mitigated by the fact that this test would then be part of a panel, and incongruous test results in a hepatitis panel would lead a clinician to retest the patient before starting treatment.

Risks of a false negative test include improper patient management, including missing the opportunity to treat chronic Hepatitis B infection. A clinician may falsely believe that a patient is not acutely or chronically infected, but rather is currently susceptible or immune to the infection. False negative results may lead a clinician to vaccinate an infected patient. This risk is likely mitigated by the fact that this test is usually ordered as part of a panel of hepatitis B tests, and incongruous test results in a hepatitis panel would lead a clinician to retest the patient. A false negative result may alternatively result in a clinician missing the opportunity to further investigate and initiate treatment in a patient in whom treatment is otherwise be recommended, as HBsAg is often the first test sent as part of the evaluation of hepatitis B infection.

1. Patient Perspective
   This submission either did not include specific information on patient perspectives or the information did not serve as part of the basis of the decision to approve or deny the PMA for this device.

In conclusion, given the available information above, the data support the claimed intended use and that the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The

probable clinical benefits outweigh the potential risks for the proposed assay considering the performance of the device in the clinical study and the low risk and associated risk mitigations in clinical practice. The proposed assay labeling will facilitate accurate assay implementation and interpretation of results. The clinical performance observed in the prospective and retrospective clinical trial suggests that errors will be uncommon and that the assay may provide substantial benefits to patients as an accurate and sensitive aid in the diagnosis of HBV infection when used in conjunction with other laboratory results and clinical information.

XIII. CDRH DECISION

CDRH issued an approval order on August 29, 2020.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.