SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Total Antibody to Hepatitis B Core Antigen (Anti-HBc Total assay)

Device Trade Name: LIAISON® XL MUREX Anti-HBc
LIAISON® XL MUREX Control Anti-HBc

Device Procode: LOM

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

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P180038

Date of FDA Notice of Approval: January 2, 2020

II. INDICATIONS FOR USE

The **LIAISON XL MUREX Anti-HBc** assay is an *in vitro* chemiluminescent immunoassay (CLIA) for the qualitative detection of IgG and IgM (total) antibodies to hepatitis B core antigen (anti-HBc) in human adult and pediatric (2 – 21 years) serum and plasma (lithium and sodium heparin, sodium citrate and K_2 EDTA), including separator tubes, on the LIAISON XL Analyzer. Assay results in conjunction with other laboratory results and clinical information may be used as an aid in the diagnosis of hepatitis B virus (HBV) infection in patients with symptoms of hepatitis or who may be at risk for HBV infection.

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

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

III. CONTRAINDICATIONS

There are no known contraindications.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the LIAISON XL MUREX Anti-HBc labeling.

V. DEVICE DESCRIPTION

Kit Components

Reagents: The LIAISON XL MUREX Anti-HBc is an *in vitro* diagnostic device consisting of five (5) reagents provided in individual compartments within a plastic container called the Reagent Integral. The assay configuration allows performance of 100 tests.

The assay is comprised of the following components:

- 1 vial of Magnetic particles coated with HBcAg obtained in *E. coli* by the recombinant DNA technology, Bovine Serum Albumin (BSA), phosphate buffer, < 0.1% sodium azide.
- 1 vial Calibrator 1 containing Calf serum with high anti-HBc antibody levels and 0.2% ProClin 300, preservatives.
- 1 vial Calibrator 2 containing human serum without anti-HBc antibodies, 0.2% ProClin 300, preservatives, and an inert blue dye.
- 1 vial Buffer F containing Acetate buffer.
- 1 vial Conjugate containing Antibody to HBcAg (mouse monoclonal) conjugated to an isoluminol derivative, human serum, newborn calf serum, phosphate buffer, EDTA, 0.2% ProClin 300, preservatives, and an inert blue dye.

Controls: LIAISON XL MUREX Control Anti-HBc set consists of two (2) levels (positive and negative) ready to use controls. Each control solution allows at least twenty (20) tests to be performed. The control set is an additional material required to perform the test.
The controls are comprised of the following components:

- 2 vials Negative control containing Human serum without anti-HBc antibodies with 0.2% ProClin 300 and preservatives.
- 2 vials Positive control containing Human serum with anti-HBc antibodies (human), 0.2% ProClin 300 and preservatives.

In addition, the following Analyzer and accessories are required for performing the LIAISON XL MUREX Anti-HBc and LIAISON XL MUREX Control Anti-HBc:

- LIAISON XL Analyzer - an automated chemiluminescent analyzer that performs the complete sample processing steps of the chemiluminescent assay and interprets the results.
- LIAISON Wash/System Liquid (10x) - phosphate buffer solution, < 0.1% sodium azide.
- LIAISON XL Starter Kit – catalyst in 4% sodium hydroxide solution and 0.12% hydrogen peroxide solution.

Assay Principle

The qualitative determination of anti-HBc is a two-step competitive chemiluminescent immunoassay (CLIA). Anti-HBc present in samples, calibrators, or controls binds to a limited amount of antigen on the coated magnetic particles. The isoluminol-antibody conjugate links the unbound solid phase epitopes. After each incubation, the unbound material is removed with a wash cycle. Subsequently, the starter reagents are added, and a flash chemiluminescent reaction is thus induced. The light signal, and hence the amount of isoluminol-antibody conjugate, is measured by a photomultiplier as relative light units (RLU) and is inversely indicative of anti-HBc concentration present in the sample.

Table 1: Interpretation of Results:

Initial Result (s/co)	Repeat Result (s/co)	Interpretation
≥ 1.1	N/A	Non-reactive
<1.1 >0.9	2 or 3 are <0.9	Reactive
	2 or 3 are ≥1.0	Non-reactive
≤ 0.9	N/A	Reactive

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the detection of antibodies to hepatitis B core antigen (Anti-HBc). 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 conjunction with a patient's medical history, clinical examination and other laboratory findings, 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. 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 Anti-HBc assay (318130) and LIAISON XL MUREX Control Anti-HBc (318131) are essentially the same as the CE-marked LIAISON Anti-HBc assay (310130) and LIAISON Control Anti-HBc (310131) with some minor modifications to raw material manufacturing processes.

The LIAISON XL MUREX Anti-HBc assay (318130) and LIAISON XL MUREX Control Anti-HBc (318131) have not been marketed in the U.S. or any foreign country.

The CE marked LIAISON Anti-HBc and the LIAISON Control Anti-HBc have been marketed in multiple countries. These devices have not been withdrawn from the market in any country for reasons relating to safety and effectiveness.

The table below includes a list all countries where the CE-marked versions have been marketed:

Table 2

Australia	Switzerland	Jordan
Austria	United Kingdom	Bahrain
Belgium	Colombia	Qatar
Brazil	Peru	Kuwait
China	Dominican Republic	Iraq
Czech	Guatemala	Greece
France	Panama	Russia
Germany	Paraguay	Cipro
Israel	Chile	Hungary
Italy	Argentina	Bulgaria
Mexico	Indonesia	Croatia
Netherlands	Pakistan	Lithuanian Republic
Nordic	Thailand	Romania
Poland	Morocco	South Africa Republic
Portugal	Tunisia	Turkey
Spain	Saudi Arabia	

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device. The LIAISON XL MUREX Anti-HBc 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.

Risks of false positive tests includes improper patient management, including treatment for hepatitis B with antiviral medication. Antiviral medical 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. Additionally and likely more importantly, because hepatitis B core antibody is ordered as part of a panel in clinical practice, this risk will likely be mitigated as incongruous test results would lead a clinician to either retest the patient or further investigate the etiology of hepatitis. As the performance of the assay in the clinical trial suggests that false positive results will be uncommon, the true risk of a false negative is likely minimal.

Risks of false negative tests include potentially missing and undertreating a patient who has hepatitis B infection and whose clinical picture warrants antiviral treatment. Again, because hepatitis B core antibody is ordered as part of a panel in clinical practice, the risk of missing and undertreating a patient who has hepatitis B infection will likely be mitigated as incongruous test results would lead a clinician to either retest the patient or further investigate the etiology of hepatitis. As the performance of the assay in the clinical trial suggests that false negative results will be uncommon, the true risk of a false negative is likely minimal.

For the specific adverse events that occurred in the clinical study, please see Section X below.

IX. SUMMARY OF NONCLINICAL STUDIES

A. Laboratory Studies

1. Cut-off Determination

   The cut-off was established internally at DiaSorin by testing at total of 111 samples (60 known negative and 51 known positive). A Receiver Operating Characteristics (ROC) analysis was performed on the results of the specimens tested. The assay's cut-off 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 at an Index of 1.00 is within the optimal range determined by the ROC curve to discriminate between negative and positive results.

   The established cut-off Index is 1.00 with an equivocal range of ± 10% (0.9 - 1.1).

2. Sensitivity / Seroconversion Panels

   The seroconversion sensitivity of the LIAISON XL MUREX Anti-HBc assay has been demonstrated by testing 9 commercial seroconversion panels in comparison to a reference anti-HBc immunoassay in terms of number of days from initial draw to first positive sample, as well as the difference between the last non-reactive results and the first reactive results.

   The LIAISON XL MUREX Anti-HBc assay yielded a reactive result sooner by one blood draw or more than the comparator assay in 5 panels, a reactive result in the same blood draw as the comparator assay in 3 panels and yielded a reactive result one blood draw later than the comparator method in one panel.

3. Analytical Sensitivity / Dilution Study with Standard

   The sensitivity of the LIAISON XL MUREX Anti-HBc assay was evaluated by preparing serial dilutions of the HBc Reference Material 82 (IgG anti-HBc, Paul-

Ehrlich-Institute Germany) in serum and EDTA plasma negative for Anti-HBc. Dilutions were tested in triplicate on 3 different kit lots and on four (4) LIAISON XL Analyzers. The maximum dose (PEI U/mL) for all 3 kit lots were 0.571, 0.563 and 0.574.

4. Endogenous Interference

   Potential interference of high levels of endogenous substances including Triglycerides (3000 mg/dL), Hemoglobin (1000 mg/dL), Bilirubin (conjugated and unconjugated 20 mg/dL), Albumin (6000 mg/dL) and Cholesterol (350 mg/dL) were evaluated. Ten (10) negative samples or negative pools were spiked with an IgG anti-HBc positive sample to achieve high negative and low positive samples. Samples were tested in 26 replicates each on one (1) kit lot. No interference was observed at the levels tested.

5. Analytical Specificity (Cross-Reactivity)

   A study was conducted to evaluate the LIAISON XL MUREX Anti-HBc assay for cross-reactivity with specimens from individuals with medical conditions unrelated to HBV infection. A total of 304 samples from 28 unrelated medical conditions were tested in singlicate on one (1) kit lot of LIAISON XL MUREX Anti-HBc and on a reference Anti-HBc assay.

   Of the 304 samples, no evidence of cross-reactivity was observed. The results of each potential cross-reactant are shown in in table below.

Table 3: Summary of Cross-Reactivity Testing

		N° of observed negative results	
Potential cross reactant (nature of samples to be clarified)	**N° of expected negative samples**	**LIAISON XL MUREX Anti HBc**	**Reference Method**
Anti-nuclear antibodies (ANA)	10	10	10
Auto-immune hepatitis	10	10	10
C. trachomatis	11	11	11
CMV (IgG / IgM)	11	11	11
EBV (IgM)	11	11	11
Fatty liver disease	11	11	11
HAMA	11	11	11
Hemodialysis patient	11	11	11
Hepatitis A Virus (anti-HAV IgM)	11	11	11
Hepatitis C Virus (anti-HCV)	11	11	11
Hepatocellular carcinoma	11	11	11
HIV-1 (anti-HIV-1)	11	11	11
HIV-2 (anti-HIV-2)	11	11	11
HSV (IgG / IgM)	11	11	11
HTLV-1/2 (anti-HTLV)	11	11	11
IgG monoclonal gammopathy	11	11	11

		N° of observed negative results	
Potential cross reactant (nature of samples to be clarified)	**N° of expected negative samples**	**LIAISON XL MUREX Anti HBc**	**Reference Method**
IgM monoclonal gammopathy	10	10	10
Influenza vaccine recipients	11	11	11
Multiparous pregnancies	11	11	11
Multiple myeloma	11	11	11
Multiple transfusion recipients	11	11	11
N. gonorrhoea	11	11	11
Pregnancy 1st trimester	11	11	11
Pregnancy 2nd trimester	10	10	10
Pregnancy 3rd trimester	11	11	11
Rheumatoid Factor	11	11	11
T. pallidum	11	11	11
***T.cruzi* (anti-*T. cruzi*)**	11	11	11

6. Sample Equivalence/Matrix Effect

   Twenty-five (25) paired sets of matched serum (with and without gel SST) and plasma (lithium and sodium heparin, sodium citrate and K_2EDTA) were tested to determine if these sample types provide equivalent results on the LIAISON XL MUREX Anti-HBc assay. Each sample was divided into three aliquots. Two sets of aliquots were spiked with an anti-HBc high 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 indicate that there is equivalence among serum (with and without Gel SST), K_2-EDTA, Lithium Heparin and Sodium Heparin plasma. However, the data show that plasma samples collected in Sodium Citrate can lead to lower Index values (approximately 10%) in comparison to normal serum. The LIAISON XL MUREX Anti-HBc assay package insert notes:

   > Specimens collected in sodium citrate may yield lower Index values (about 10%) in comparison to normal serum which may cause an increased likelihood of false negative results.

7. Carry-Over Study

   The LIAISON XL Analyzer uses disposable tips for sample pipetting. 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 the result of a high signal-generating sample.

   Two samples were used for this evaluation: one (1) anti-HBc negative human serum sample and one (1) human positive sample/pool with a high level of anti-HBc analyte.

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 significant amount of analyte is carried over from one sample reaction into the subsequent sample reactions.

8. 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 Anti-HBc 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 1, 2, 3, 4, and 5 days of storage at RT for 24 hours each day.
- -20 °C study – samples were tested unstressed (T=0) and stored at -20 °C or lower for 1, 3, and 4 months.
- Freeze/Thaw (F/T) study – samples were tested unstressed (T=0) and after 1, 2, 3, 4, 5, 6, and 7 F/T cycles. Samples were frozen for 12-24 hours at -20°C or lower and thawed at room temperature.

The results of the studies indicate serum and plasma samples are stable for:

- 4 days at 2-8°C
- 4 days at room temperature
- 3 months at -20°C
- 3 Freeze/Thaw cycles.

Reagent Stability

Real-Time (Shelf-Life)

Studies were performed to establish the shelf-life for the LIAISON XL MUREX Anti-HBc assay. Three (3) lots of LIAISON XL MUREX Anti-HBc were stored at the recommended storage temperature of 2-8°C throughout the study. Performance was assessed against clinically relevant acceptance criteria using three (3) lots LIAISON XL MUREX Control Anti-HBc (positive and negative) and an internal stability panel consisting of eight (8) samples. Study results demonstrate that reagents are stable and continue to meet acceptance criteria eighteen (18) months after the date of manufacture for the LIAISON XL MUREX Anti-HBc.

Reagent On-Board

Stability studies were conducted to determine the length of time the LIAISON XL MUREX Anti-HBc Reagent Integral can be stored on-board the LIAISON XL Analyzer in the refrigerated area once opened.

One (1) lot of the LIAISON XL MUREX Anti-HBc assay was stored on-board the LIAISON XL Analyzer throughout the 13 weeks of the study. The LIAISON XL MUREX Control Anti-HBc (negative and positive) along with the internal stability panel were tested in duplicate at one (1) week intervals up to the 13 weeks.

The LIAISON XL MUREX Anti-HBc assay is stable on-board the LIAISON XL Analyzer for 12 weeks.

Reagent Open Use

The aim of this study was to assess the open use stability of the LIAISON XL MUREX Anti-HBc kit reagents by simulating normal conditions of use as specified in the instruction for use.

Testing of samples was performed in duplicate, on one (1) lot of LIAISON XL MUREX Anti-HBc and one (1) lot of LIAISON XL MUREX Control Anti-HBc. Results were calculated using the initial (time zero) assay calibration.

The opened Reagent Integral was then removed from the XL Analyzer and stored at 2-8 °C. 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 2-8 °C.

Temperature Stress/Reagent Transport Study

The transport simulation tests were performed in order to verify that kit reagents maintain their properties during the shipment and delivery conditions to the customer. After being subjected to simulated stress conditions, testing was performed on 1 lot of LIAISON XL MUREX Anti-HBc at midlife and will be tested at expiration.

All testing performed meets acceptance criteria under various simulated transport conditions.

Calibrator Stability

The LIAISON XL MUREX Anti-HBc calibrators are included on the Reagent Integral. All studies for the Reagent Integral are applicable to the 2 levels of calibrators provided.

Calibration Interval Stability

The aim of this study was to assess stability of the product calibration by simulating normal condition of use as specified in the instruction for use.

A calibration was performed at time 0 and the Reagent Integral was stored on board the analyzer for the duration of the study. Kit performance was evaluated weekly up to nine (9) weeks by testing the stability panel and LIAISON XL MUREX Control Anti-HBc on one (1) lot of LIAISON XL MUREX Anti-HBc reagents. Results were generated using the initial (time zero) assay calibration and performance was assessed against clinically relevant acceptance criteria.

Results demonstrate that the LIAISON XL MUREX Anti-HBc calibration is stable for eight (8) weeks.

Control stability

Real-time (Shelf-Life)

Studies were performed to establish the shelf-life for the LIAISON XL MUREX Control Anti-HBc. Three lots of LIAISON XL MUREX Control Anti-HBc were stored at the recommended storage temperature of 2-8°C throughout the study.
Current results demonstrate that the positive and negative controls are stable and continue to meet acceptance criteria at eighteen (18) months.

Open use

The aim of this study was to assess stability of the opened Control vials by simulating normal conditions of use, as specified in the instruction for use. Testing was performed in duplicate, on one lot of LIAISON XL MUREX Control Anti-HBc.

LIAISON XL MUREX Control Anti-HBc (negative and positive) were within their established ranges and were assessed against clinically relevant acceptance criteria.

The LIAISON XL MUREX Control Anti-HBc (negative and positive) are stable for 12 weeks after opening when stored at 2-8 °C between uses.

Temperature Stress/Reagent Transport Study

The transport simulation tests were performed in order to ensure that kit Controls maintain their properties during the shipment and delivery conditions to the customer. After being subjected to simulated stress conditions testing was performed on 1 lot of LIAISON XL MUREX Control Anti-HBc.

All testing performed meets acceptance criteria under various simulated transport conditions.

9. Precision

Internal 20 Days

A precision/reproducibility study was carried out over a period of twenty (20) days on the LIAISON XL MUREX Anti-HBc assay 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 ten (10) serum samples consisting of 1 Negative, 3 High Negative, 3 Low Positive, and 3 Moderate Positive and 3 lots of the LIAISON XL MUREX Control Anti-HBc (neg and pos) were tested in 2 replicates per run, 2 runs per day for 20 days using 3 different LIAISON XL MUREX Anti-HBc assay reagents and spanning at least 2 calibration cycles.

The Repeatability of the combined 3 lots of LIAISON XL MUREX Anti-HBc ranged from 1.4% to 2.3%. The with-in Laboratory %CV of the combined 3 lots of LIAISON XL MUREX Anti-HBc ranged from 4.2% to 12.9%. The results are shown below.

Table 4: Summary of Precision Study

Sample ID	N	Mean	Repeatability (within-run)		Between Run		Between Day		Between Lot		Within Laboratory	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Ctrl Neg #RS-672	240	*156933	2455	1.6%	4303	2.7%	3288	2.1%	4868	3.1%	7684	4.9%
Ctrl Neg #RS-673	240	*155995	2351	1.5%	4801	3.1%	886	0.6%	4729	3.0%	7192	4.6%
Ctrl Neg #RS-674	240	*155885	2161	1.4%	4524	2.9%	2073	1.3%	4378	2.8%	6972	4.5%
Ctrl Pos #RS-675	240	0.368	0.007	1.9%	0.014	3.8%	0.012	3.2%	0.029	7.8%	0.035	9.5%
Ctrl Pos #RS-676	240	0.369	0.006	1.6%	0.016	4.3%	0.011	3.0%	0.029	7.8%	0.035	9.5%
Ctrl Pos #RS-677	240	0.389	0.007	1.8%	0.018	4.7%	0.015	3.8%	0.036	9.3%	0.044	11.2%
AHBC-1-U1	240	2.31	0.032	1.4%	0.062	2.7%	0.053	2.3%	0.04	1.7%	0.097	4.2%
AHBC-1-U2	240	1.50	0.031	2.1%	0.075	5.0%	0.042	2.8%	0.08	5.3%	0.122	8.1%
AHBC-1-U3	240	1.58	0.036	2.3%	0.076	4.8%	0.047	3.0%	0.079	5.0%	0.125	7.9%
AHBC-1-U4	240	1.46	0.033	2.2%	0.073	5.0%	0.047	3.2%	0.084	5.8%	0.125	8.6%
AHBC-1-U5	240	0.754	0.016	2.1%	0.033	4.3%	0.024	3.2%	0.054	7.2%	0.07	9.2%
AHBC-1-U6	240	0.773	0.017	2.2%	0.037	4.8%	0.029	3.8%	0.063	8.2%	0.081	10.4%
AHBC-1-U7	240	0.586	0.013	2.2%	0.031	5.3%	0.018	3.1%	0.044	7.5%	0.058	10.0%
AHBC-1-U8	240	0.174	0.003	1.9%	0.008	4.6%	0.005	2.9%	0.02	11.5%	0.022	12.9%
AHBC-1-U9	240	0.237	0.004	1.5%	0.007	2.9%	0.005	2.3%	0.015	6.3%	0.018	7.4%
AHBC-1-U10	240	0.262	0.005	1.8%	0.007	2.8%	0.005	1.8%	0.017	6.5%	0.02	7.5%

External Precision 5-day Study

A five (5) day precision/reproducibility study was conducted at two (2) external laboratories and at DiaSorin Inc. to verify the precision of the LIAISON® XL MUREX Anti-HBc assay. The CLSI document EP15-A3 was consulted in the preparation of the testing protocol. The coded panel, comprised of ten (10) frozen serum samples was the same panel used in the 20-day precision study.

The precision panel was tested at all three (3) sites on the LIAISON® XL Analyzer using six (6) replicates per run in one (1) run per day for five (5) operating days with multiple technicians performing the testing.

Table 5: Summary of Reproducibility Study

Sample ID	N	Mean	Repeatability (within-run)		Between Days/Runs		Within Laboratory		Between Sites/Lots		Reproducibility	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Ctrl Neg (all 3 lots)	90	*131264	3373	2.6%	4696	3.6%	5782	4.4%	3421	2.6%	6718	5.1%
Ctrl Pos (all 3 lots)	90	0.378	0.008	2.1%	0.016	4.3%	0.018	4.8%	0.013	3.4%	0.022	5.9%
AHBC-1-U1	90	2.336	0.045	1.9%	0.092	3.9%	0.103	4.4%	0.092	4.0%	0.138	5.9%
AHBC-1-U2	90	1.547	0.063	4.0%	0.133	8.6%	0.147	9.5%	0.144	9.3%	0.206	13.3%
AHBC-1-U3	90	1.624	0.061	3.8%	0.092	5.7%	0.111	6.8%	0.097	5.9%	0.147	9.0%
AHBC-1-U4	90	1.464	0.060	4.1%	0.084	5.8%	0.104	7.1%	0.126	8.6%	0.163	11.2%
AHBC-1-U5	90	0.769	0.031	4.0%	0.049	6.4%	0.058	7.6%	0.044	5.7%	0.073	9.5%
AHBC-1-U6	90	0.807	0.036	4.4%	0.063	7.8%	0.072	8.9%	0.025	3.1%	0.076	9.5%
AHBC-1-U7	84	0.595	0.023	3.8%	0.04	6.7%	0.046	7.7%	0.022	3.7%	0.051	8.6%
AHBC-1-U8	90	0.184	0.007	3.8%	0.018	9.8%	0.019	10.5%	0.016	8.9%	0.025	13.8%
AHBC-1-U9	90	0.241	0.005	2.1%	0.009	3.6%	0.010	4.2%	0.016	6.7%	0.019	7.9%
AHBC-1-U10	90	0.260	0.007	2.7%	0.004	1.6%	0.008	3.1%	0.011	4.1%	0.013	5.2%

10. Pediatric and Adult Sample Equivalency

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

A total of thirty (30) negative pediatric patient samples were used for this study. The pediatric samples encompassed the age range of two (2) months to twenty-one (21) years. Ten (10) pediatric samples were spiked with IgG anti-HBc high positive sample to obtain high negative samples. Ten (10) pediatric samples were spiked with IgG anti-HBc high positive sample to obtain low positive samples. Ten (10) pediatric samples were spiked with IgG anti-HBc high positive sample to obtain moderate positive samples. Adult negative pool samples were used as controls and were spiked with IgG anti-HBc high positive sample to achieve the same three (3) levels of samples: high negative, low positive and moderate positive samples.

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

One (1) high negative pediatric sample out of the total 30 pediatric samples tested was outside the ± 10% range. 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 Anti-HBc assay.

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 antibodies to hepatitis-B core antigen with the LIAISON XL MUREX Anti-HBc 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 Anti-HBc assay 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 3,082 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 states including Ohio, Pennsylvania, Indiana, Florida, California, Texas, New Jersey, Tennessee, Massachusetts, and Puerto Rico.

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 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.

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

Table 6: Demographic Summary of the Prospective Population

Age Range	Gender	LIAISON XL MUREX				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	18	4.6%	371	95.4%	389
	M	18	7.7%	215	92.3%	233
30-39	F	28	5.9%	446	94.1%	474
	M	29	12.9%	195	87.1%	224
40-49	F	28	9.7%	262	90.3%	290
	M	34	16.9%	167	83.1%	201
50-59	F	36	15.5%	196	84.5%	232
	M	32	17.3%	153	82.7%	185
60-69	F	27	17.1%	131	82.9%	158
	M	21	19.4%	87	80.6%	108
70-79	F	7	15.2%	39	84.8%	46
	M	4	10.3%	35	89.7%	39
80-89	F	4	28.6%	10	71.4%	14
	M	0	0.0%	7	100.0%	7
90-98	F	0	0.0%	4	100.0%	4
	M	0	N/A	0	N/A	0
Unk	F	0	0.0%	1	100.0%	1
	M	0	0.0%	1	100.0%	1

Age Range	Gender	LIAISON XL MUREX				
		+		-		Total
		n	%	n	%	
Total		286	10.7%	2390	89.3%	2676

Hepatitis B Status Classification

Hepatitis B Status Classification was based on testing all the 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 7: Hepatitis B Status Classification

HBV Classification	HBsAg	HBeAg	Total 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		

HBV Classification	HBsAg	HBeAg	Total Anti-HBc	Anti-HBc IgM	Anti-HBe	Anti-HBs	Prospective (n)	Retrospective (n)
Early Recovery	NR	NR	R	R	NR	R		
Early Recovery	NR	NR	R	R	R	R		
Recovery	NR	NR	R	NR	R	R	131	36
Recovery	NR	NR	NR	NR	R	R		
Recovery	NR	NR	R	NR	EQV	R		
Immune Due to Natural Infection	NR	NR	R	NR	NR	R	104	3
Immune Due to Natural Infection	NR	NR	R	NR	NR	EQV		
HBV Vaccine Response	NR	NR	NR	NR	NR	R	1144	8
HBV Vaccine Response	NR	NR	NR	NR	NR	EQV		
Not Previously Infected	NR	NR	NR	NR	NR	NR	1302	1
Not Interpretable	NR	NR	NR	NR	R	NR	7	2
Not Interpretable	NR	NR	NR	R	NR	NR		
Not Interpretable	NR	R	NR	NR	NR	NR		
Not Interpretable	NR	R	NR	NR	NR	R		
Not Interpretable	NR	R	R	R	NR	EQV		
Not Interpretable	NR	R	R	R	NR	R		
Not Interpretable	R	NR	NR	NR	NR	R		
Total							**2826**	**256**

Clinical Agreement Study Analysis

Comparison results of the LIAISON XL MUREX Anti-HBc to the reference anti-HBc assay are presented with Negative and Positive percent (%) agreement and 95% confidence intervals for combined prospective and retrospective specimens for each of the HBV Classification categories. In addition, Pediatric Cumulative (prospective and retrospective) Clinical Agreement results are presented below.

Table 8: Cumulative Clinical Agreement (Combined Prospective & Retrospective)

HBV Classification	Reference Anti-HBc assay				Total
	Reactive		Non-reactive		
	LIAISON® XL MUREX Anti-HBc		LIAISON® XL MUREX Anti-HBc		
	Reactive	Non-reactive	Reactive	Non-reactive	
Acute	100	0	2	7	109
Late Acute	34	0	0	0	34
Chronic	142	2	0	0	144
Early Recovery	52	5	0	0	57
Recovery	162	1	1	3	167
Immune Due to Natural Infection	99	8	0	0	107

HBV Vaccine Response	1	0	30	1121	1152
Not Previously Infected	0	0	6	1297	1303
Not Interpretable	2	0	0	7	9
Total	**592**	**16**	**39**	**2435**	**3082**

Table 9: Cumulative Clinical Agreement (Combined Prospective & Retrospective)

HBV Classification	Positive Percent Agreement (PPA)	Negative Percent Agreement (NPA)
Acute	100/100 (100.0%) 95% CI: 96.3% to 100.0%	7/9 (77.8%) 95% CI: 45.3% to 93.7%
Late Acute	34/34 (100.0%) 95% CI: 89.8% to 100.0%	N/A
Chronic	142/144 (98.6%) 95% CI: 95.1% to 99.6%	N/A
Early Recovery	52/57 (91.2%) 95% CI: 81.1% to 96.2%	N/A
Recovery	162/163 (99.4%) 95% CI: 96.6% to 99.9%	3/4 (75.0%) 95% CI: 300.1% to 95.4%
Immune Due to Natural Infection	99/107 (92.5%) 95% CI: 85.9% to 96.2%	N/A
HBV Vaccine Response	1/1 (100.0%) 95% CI: 20.7% to 100.0%	1121/1151 (97.4%) 95% CI: 96.3% to 98.2%
Not Previously Infected	N/A	1297/1303 (99.5%) 95% CI: 99.0% to 99.8%
Not Interpretable	2/2 (100.0%) 95% CI: 34.2% to 100.0%	7/7 (100.0%) 95% CI: 64.6% to 100.0%

Clinical Endpoints

With regard to safety, as an *in vitro* diagnostic test, the LIAISON XL MUREX Anti-HBc 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 regard to effectiveness, the clinical performance of the LIAISON XL MUREX Anti-HBc was evaluated versus a FDA approved anti-HBc test for patients at risk for 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 of 97.4% among subjects in various stages of HBV infection, a negative percent agreement (NPA) of 97.4% in HBV-vaccinated subjects, and an NPA of 99.8% among subjects not previously infected with HBV.

B. Accountability of PMA Cohort

The clinical agreement study involved the testing of 3,082 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 states 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 anti-HBc 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 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. The table below shows the demographic distribution of the cohort.

Table 10: Retrospective Demographic Summary

	Adult				Pediatric (0-21)				Unknown Age			
	Prospective		Retrospective		Prospective		Retrospective		Prospective		Retrospective	
Race	n	%	n	%	n	%	n	%	n	%	n	%
American Indian/ Alaskan Native	2	0.1%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Asian	21	0.8%	4	1.9%	3	1.9%	0	0.0%	0	0.0%	0	0.0%
Black/African American	832	31.2%	57	27.7%	64	39.8%	4	13.8%	0	0.0%	0	0.0%
Native Hawaiian or Other Pacific Islander	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
White	1664	62.5%	141	68.4%	89	55.3%	25	86.2%	2	100.0%	21	100.0%

	Adult				Pediatric (0-21)				Unknown Age			
	Prospective		Retrospective		Prospective		Retrospective		Prospective		Retrospective	
Race	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Unknown	6	0.2%	1	0.5%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Other	138	5.2%	3	1.5%	5	3.1%	0	0.0%	0	0.0%	0	0.0%
Total	**2663**	**100.0%**	**206**	**100.0%**	**161**	**100.0%**	**29**	**100.0%**	**2**	**100.0%**	**21**	**100.0%**

D. Safety and Effectiveness Results

1. Safety Results

With regard to safety, as an *in vitro* diagnostic test, the LIAISON XL MUREX Anti-HBc 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.

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

2. Effectiveness Results

The analysis of effectiveness was based on the 3,082 evaluable patients. Key effectiveness outcomes are presented in the tables below.

Table 11: Clinical Comparison for Prospectively Collected Samples

HBV Classification	Positive Percent Agreement (PPA)	Negative Percent Agreement (NPA)
Acute	8/8 (100.0%) 95% CI: 67.6% to 100.0%	4/4 (100.0%) 95% CI: 51.0% to 100.0%
Late Acute	2/2 (100.0%) 95% CI: 34.2% to 100.0%	N/A
Chronic	74/76 (97.4%) 95% CI: 90.9% to 99.3%	N/A
Early Recovery	43/48 (89.6%) 95% CI: 77.8% to 95.5%	N/A
Recovery	127/128 (99.2%) 95% CI: 95.7% to 99.9%	2/3 (66.7%) 95% CI: 20.8% to 93.9%
Immune Due to Natural Infection	96/104 (92.3%) 95% CI: 85.6% to 96.1%	N/A
HBV Vaccine Response	1/1 (100%) 95% CI: 20.7% to 100.0%	1113/1143 (97.4%) 95% CI: 96.3% to 98.2%
Not Previously Infected	N/A	1296/1302 (99.5%) 95% CI: 99.0% to 99.8%
Not Interpretable	1/1 (100%) 95% CI: 20.7% to 100.0%	6/6 (100.0%) 95% CI: 61.0% to 100.0%
Total	**352/368 (95.7%) 95% CI: 93.1% to 97.3%**	**2421/2458 (98.5%) 95% CI: 97.9% to 98.9%**

Table 12: Percent Agreement for Prospectively Collected Samples

HBV Classification	Positive Percent Agreement (PPA)	Negative Percent Agreement (NPA)
Acute	8/8 (100.0%) 95% CI: 67.6% to 100.0%	4/4 (100.0%) 95% CI: 51.0% to 100.0%
Late Acute	2/2 (100.0%) 95% CI: 34.2% to 100.0%	N/A
Chronic	74/76 (97.4%) 95% CI: 90.9% to 99.3%	N/A
Early Recovery	43/48 (89.6%) 95% CI: 77.8% to 95.5%	N/A
Recovery	127/128 (99.2%) 95% CI: 95.7% to 99.9%	2/3 (66.7%) 95% CI: 20.8% to 93.9%
Immune Due to Natural Infection	96/104 (92.3%) 95% CI: 85.6% to 96.1%	N/A
HBV Vaccine Response	1/1 (100%) 95% CI: 20.7% to 100.0%	1113/1143 (97.4%) 95% CI: 96.3% to 98.2%
Not Previously Infected	N/A	1296/1302 (99.5%) 95% CI: 99.0% to 99.8%
Not Interpretable	1/1 (100%) 95% CI: 20.7% to 100.0%	6/6 (100.0%) 95% CI: 61.0% to 100.0%
Total	**352/368 (95.7%) 95% CI: 93.1% to 97.3%**	**2421/2458 (98.5%) 95% CI: 97.9% to 98.9%**

Table 13: Clinical Comparison for Retrospectively Collected Samples

HBV Classification	Reference Anti-HBc				Total
	+		-		
	LIAISON® XL MUREX Anti-HBc		LIAISON® XL MUREX Anti-HBc		
	+	-	+	-	
Acute	92	0	2	3	97
Late Acute	32	0	0	0	32
Chronic	68	0	0	0	68
Early Recovery	9	0	0	0	9
Recovery	35	0	0	1	36
Immune Due to Natural Infection	3	0	0	0	3
HBV Vaccine Response	0	0	0	8	8
Not Previously Infected	0	0	0	1	1
Not Interpretable	1	0	0	1	2
Total	**240**	**0**	**2**	**14**	**256**

Table 14: Percent Agreement for Retrospectively Collected Samples

HBV Classification	Positive Percent Agreement (PPA)	Negative Percent Agreement (NPA)
Acute	92/92 (100.0%) 95% CI: 96.0% to 100.0%	3/5 (60.0%) 95% CI: 23.1% to 88.2%
Late Acute	32/32 (100.0%) 95% CI: 89.3% to 100.0%	N/A
Chronic	68/68 (100.0%) 95% CI: 94.7% to 100.0%	N/A
Early Recovery	9/9 (100.0%) 95% CI: 70.1% to 100.0%	N/A
Recovery	35/35 (100.0%) 95% CI: 90.1% to 100.0%	1/1 (100.0%) 95% CI: 20.7% to 100.0%
Immune Due to Natural Infection	3/3 (100.0%) 95% CI: 43.9% to 100.0%	N/A
HBV Vaccine Response	N/A	8/8 (100.0%) 95% CI: 67.6% to 100.0%
Not Previously Infected	N/A	1/1 (100.0%) 95% CI: 20.7% to 100.0%
Not Interpretable	1/1 (100.0%) 95% CI: 20.7% to 100.0%	1/1 (100.0%) 95% CI: 20.7% to 100.0%
Total	**240/240 (100.0%) 95% CI: 98.4% to 100.0%**	**14/16 (87.5%) 95% CI: 64.0% to 96.5%**

Table 15: Pediatric Cumulative (prospective and retrospective) agreement results

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	1/1 (100.0%) 95% CI: 20.7% to 100.0%	N/A
Recovery	5/5 (100.0%) 95% CI: 56.6% to 100.0%	N/A
Immune Due to Natural Infection	3/3 (100.0%) 95% CI: 43.9% to 100.0%	N/A
HBV Vaccine Response	N/A	62/63 (98.4%) 95% CI: 91.5% to 99.7%
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%

3. Subgroup Analyses

The study design enabled an assessment of assay performance by subgroup as depicted in tables above which show subjects stratified by stage of HBV infection and HBV vaccine response.

4. Pediatric Extrapolation

In this premarket application, existing clinical data from adult subjects was not leveraged to support approval of a pediatric patient population.
Samples from pediatric patients were tested in the clinical study in order to support a pediatric claim.

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 Anti-HBc test for detecting antibodies to hepatitis-B core antigen in human serum and plasma (lithium and sodium heparin, sodium citrate and potassium 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 or who may be at risk for hepatitis B infection. The positive agreement of the assay is 97.4% with a two-sided 95% confidence interval (CI) of 95.8% - 98.5% and the negative percent agreement is 98.4% with a two-sided 95% CI of 97.9 - 98.9%.

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 Anti-HBc assay when used according to the manufacturer's instructions can aid the physician in the diagnosis of HBV infection. The positive agreement of the assay is 97.4% with a two-sided 95% confidence interval (CI) of 95.8% - 98.5% and the negative percent agreement is 98.4% with a two-sided 95% CI of 97.9 - 98.9%.

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 the determination, as part of a hepatitis B panel, the appropriate diagnosis and treatment of current or prior 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. Additionally, diagnosis and appropriate treatment can potentially decrease transmission and disease burden in the general population as well as in populations at high risk for hepatitis B infection.

The probable risks of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. Risks of false positive tests includes improper patient management, including treatment for hepatitis B with antiviral medication. Antiviral medical has risks including toxicity and more rarely allergic reactions. Risks of false negative tests include potentially missing and undertreating a patient who has hepatitis B infection and whose clinical picture warrants antiviral treatment.

1. Patient Perspectives
   This submission did not include specific information on patient perspectives for this device.

In conclusion, given the available information above, the data support the claimed intended use, 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 trial and the low risk and associated risk mitigations in clinical practice. The proposed assay labelling 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 hepatitis B infection.

XIII. CDRH DECISION

CDRH issued an approval order on January 2, 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.