SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: IgM antibody to Hepatitis B core antigen (Anti-HBc IgM)

Device Trade Name: LIAISON® XL MUREX HBc IgM
LIAISON® XL MUREX Control HBc IgM
Device Procode: LOM

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

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P180045

Date of FDA Notice of Approval: August 29, 2020

II. INDICATIONS FOR USE

LIAISON® XL MUREX Anti-HBc IgM
The LIAISON® XL MUREX HBc IgM assay is an *in vitro* chemiluminescent immunoassay (CLIA) for the qualitative detection of IgM anti-bodies to hepatitis B virus core antigen (HBc IgM) in human adult and pediatric (2 to 21 years) serum and plasma (lithium and sodium heparin, sodium citrate and K2 EDTA), including separator tubes, on the LIAISON® XL Analyzer. Assay results, in conjunction with other hepatitis B virus (HBV) serological markers 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 presence of anti-HBc IgM is indicative of acute or recent HBV infection.

This assay is not approved for use in screening blood, plasma or tissue donors.

LIAISON® XL MUREX Control Anti-HBc IgM
The LIAISON® XL MUREX Control HBc IgM (negative and positive) is intended for use as assayed quality control samples to monitor the performance of the LIAISON® XL MUREX HBc IgM assay. The performance characteristics of LIAISON® XL MUREX Control HBc IgM 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 HBc IgM labeling.

V. DEVICE DESCRIPTION

LIAISON® XL MUREX HBc IgM is a qualitative chemiluminescent immunoassay (CLIA). IgG to human IgM (mouse monoclonal) is used for coating magnetic particles (solid phase) and recombinant HBcAg is linked to an isoluminol derivative (isoluminol-HBcAg conjugate). During the first incubation, IgM antibodies present in calibrators, samples, or controls bind to the solid phase. During the second incubation, the HBcAg conjugate reacts with IgM anti-HBc already bound to the solid phase. After each incubation, the unbound material is removed with a wash cycle. Subsequently, the starter reagents are added and a flash chemiluminescence reaction is thus induced. The light signal, and hence the amount of isoluminol-HBcAg conjugate, is measured by a photomultiplier as relative light units (RLU) and is indicative of the general IgM anti-HBc concentration present in calibrators, samples, or controls.

Components of the LIAISON XL MUREX HBc IgM assay

All reagents are supplied ready to use.

The table below describes the components of the LIAISON XL MUREX HBc IgM kit.

Table 1: Components of the LIAISON XL MUREX HBc

Magnetic Particles 1 vial – 1.3 mL	Magnetic particles coated with IgG to human IgM (mouse monoclonal), BSA, phosphate buffer, < 0.1% sodium azide.
Calibrator 1 1 vial – 3.6 mL	Low levels of chimeric IgM anti-HBc antibodies (human and mouse monoclonal), animal proteins, buffer, 0.2% ProClin® 300, preservatives, an inert red dye.
Calibrator 2 1 vial – 3.6 mL	High levels of chimeric IgM anti-HBc antibodies (human and mouse monoclonal), animal proteins, buffer, 0.2% ProClin® 300, preservatives, an inert blue dye.
Conjugate 1 vial – 1.3 mL	HBcAg (obtained in *E. coli* by the recombinant DNA technology) conjugated to an isoluminol derivative, BSA, phosphate buffer, 0.2% ProClin® 300, and preservatives.
Specimen diluent 1 vial - 15.5 mL	Non-specific human IgG (polyclonal), BSA, phosphate buffer, EDTA, 0.2% ProClin® 300, preservatives, an inert blue dye.
Buffer E 1 vial - 12 mL	Human serum/plasma, BSA, phosphate buffer, 0.2% ProClin® 300, preservatives.

LIAISON® XL MUREX Control HBc IgM set consists of two (2) 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 HBc IgM assay.

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

NEGATIVE CONTROL 2 vials - 0.9 mL each	Human serum without anti-HBc antibodies with 0.2% ProClin® 300 and preservatives.
POSITIVE CONTROL 2 vials - 0.9mL each	Chimeric IgM anti-HBc antibodies (human and mouse monoclonal), 0.2% ProClin® 300, preservatives and an inert yellow dye.

Interpretation of the Results (anti-HBc IgM):

The interpretation of results for the LIAISON XL MUREX HBc IgM is as follow:

Table 2: Results Interpretation

Initial Result (mIU/ml)	Repeat Result (mIU/ml)	Interpretation
$x \geq 9.00$	N/A	Reactive
$7.00 \leq x < 9.00$ (Equivocal)	2 out of 3 are ≥8.00	Reactive
	2 out of 3 are <8.00	Non-reactive
$x < 7.00$	N/A	Non-Reactive

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the detection of IgM antibodies to hepatitis B core antigen (Anti-HBc IgM). 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 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

LIAISON® XL MUREX HBc IgM (318140) is essentially the same as the CE-marked LIAISON® HBc IgM (310140) with improvements to some of the raw material manufacturing processes. LIAISON® XL MUREX Control HBc IgM (Catalog Number 318141) is a different composition (serum based) compared to the CE marked LIAISON® Control HBc IgM (Catalog Number 310141).

The LIAISON® XL MUREX HBc IgM assay (318140) and LIAISON® XL MUREX Control HBc IgM (318141) have not been marketed in the U.S. or any foreign country.

The LIAISON® HBc IgM (310140) and the LIAISON® Control HBc IgM (310141) 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 following table includes a list all countries where the CE-marked versions have been marketed in the past year.

Table 3: Countries Where CE-Marked Versions Have Been Marketed

Austria	Argentina	Australia
Bangladesh	Belgium	Bulgaria
Brunei	Brazil	Bahamas
Switzerland	Chile	Colombia
Cyprus	Czech Republic	Germany
Denmark	Dominican Republic	Ecuador
Egypt	Spain	Finland
France	United Kingdom	Greece
Croatia	Hungary	Israel
Iraq	Iran	Italy
Lebanon	Luxembourg	Morocco
Mexico	Netherlands	Norway
Peru	Poland	Portugal
Paraguay	Qatar	Romania
Serbia	Saudi Arabia	Slovenia
Sweden	Thailand	Tunisia
Turkey	Venezuela	Vietnam
South Africa	China	

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 HBc IgM is intended for *in vitro* diagnostic use, and as a result, there is no direct adverse effect on the patient. A blood draw is unlikely to cause adverse effects on the patient. In performing the test, standard good laboratory practices are considered sufficient to minimize risks to the end user of obtaining an incorrect result.

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.

A false positive result in a diagnostic setting 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.

Because hepatitis B core IgM antibody is ordered as part of a panel in clinical practice, the risk of a false positive result will likely be mitigated as incongruous test results would lead a clinician to either retest the patient or further investigate the etiology of hepatitis. Hepatitis B core antigen IgM is only used as the sole diagnostic for acute hepatitis B in a patient with clinical findings suspicious for acute hepatitis who is in the "window period" between HBsAg seroconversion to HBsAg antibodies; however, the number of patients that will be tested who are in this specific category is extremely small, mitigating the risk of a false positive.

A false negative result includes missing the opportunity to treat a patient who has hepatitis B infection and whose clinical picture warrants antiviral treatment. Again, because hepatitis B core IgM 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 and further investigate the etiology of clinical hepatitis.

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 105 samples (55 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 0.8 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 HBc IgM assay has been demonstrated by testing eight (8) commercial seroconversion panels in comparison to a reference HBc IgM 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 HBc IgM yielded a positive result sooner by one or more blood draws or more than the comparator assay in six (6) of the eight (8) panels.

3. Analytical Sensitivity/Dilution Study with Standard
   The sensitivity of the LIAISON® XL MUREX HBc IgM was evaluated by preparing serial dilutions of the HBc Reference material IgM 84 (IgM anti-HBc, Paul-Ehrlich-Institute Germany).

   Dilutions were tested in triplicate on three (3) reagent lots, using one lot of kit controls, across four (4) LIAISON XL Analyzers.

   The cutoff concentration corresponds to 15.9 PEI U/mL.

4. Analytical Specificity (Cross-Reactivity)
   A study was conducted to evaluate the LIAISON XL MUREX HBc IgM for cross-reactivity with specimens from individuals with medical conditions unrelated to HBV infection. A total of 301 samples from 28 unrelated medical conditions were tested in singlicate on one kit lot of LIAISON XL MUREX HBc IgM and on a reference HBC IgM assay.

   Of the 301 samples, no evidence of cross-reactivity was observed. The results of each potential cross reactant are shown in table below.

Table 4: Summary of Cross-Reactivity Study

		No. of observed negative results	
Potential cross reactant	**No. of expected negative samples**	**LIAISON® XL MUREX HBc IgM**	**ETI-CORE-IgMK PLUS**
Anti-nuclear antibodies (ANA)	10	10	10
Auto-immune hepatitis	10	10	10
C. trachomatis	11	11	11
CMV (anti-CMV IgG and/or IgM positive)	11	11	11
EBV (anti-VCA IgG and/or IgM positive)	11	11	11
Fatty liver disease	11	11	11
HAMA	11	11	11
Hemodialysis patient	11	11	11
Hepatitis A Virus (anti-HAV IgG and/or IgM positive)	11	11	11
Hepatitis C Virus (anti-HCV IgG and/or IgM positive)	11	11	11
Hepatocellular carcinoma	11	11	11
HIV-1 (anti-HIV-1 positive)	11	11	11
HIV-2 (anti-HIV-2 positive)	11	11	11
HSV (anti-HSV IgG and/or IgM positive)	11	11	11
HTLV-1/2 (anti-HTLV positive)	11	11	11

		No. of observed negative results	
Potential cross reactant	**No. of expected negative samples**	**LIAISON® XL MUREX HBc IgM**	**ETI-CORE-IgMK PLUS**
IgG monoclonal gammopathy	11	11	11
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. gonorrhoeae	11	11	11
Pregnancy 1st trimester	11	11	11
Pregnancy 2nd trimester	11	11	11
Pregnancy 3rd trimester	11	11	11
Rheumatoid Factor	11	11	11
***T. pallidum* (anti-*T. pallidum* IgG and/or IgM positive)**	11	11	11
***T. cruzi* (anti-*T. cruzi* positive)**	11	11	11

5. Endogenous Interference

   A study was conducted to evaluate the LIAISON® XL MUREX HBc IgM for endogenous interference. Ten (10) negative samples or negative pools were spiked with an HBc IgM high positive sample in order to achieve two (2) levels of samples: high negative and low positive. The spiked sets were divided into two (2) 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 26 replicates each, on one lot of kit reagents and with one lot of kit controls. Biotin was not evaluated in this study because the assay does not employ biotin-streptavidin technology.

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

Table 5: Interfering Substances

Substances	Tested Concentrations
Triglycerides	3000 mg/dL
Hemoglobin	1000 mg/dL
Unconjugated bilirubin	20 mg/dL
Conjugated bilirubin	20 mg/dL
Albumin	6000 mg/dL
Cholesterol	350 mg/dL

6. Antibody Class Specificity
   Antibody class specificity for IgM has been demonstrated by testing 10 specific IgM positive samples (including samples around the cut-off value) treated with dithiotreitol (DTT) in order to denature IgM and very the assay specificity in the detection of specific antibodies bellowing to IgM class. The results show that the assay specifically detects HBc IgM.

7. Sample Equivalence/Matrix Effect
   Twenty-five (25) paired sets of matched serum (with and without gel SST) and plasma (lithium heparin, sodium heparin, sodium citrate, and dipotassium EDTA) were tested to determine if these sample types provide equivalent results on the LIAISON XL MUREX HBc IgM. Each sample was divided into three (3) aliquots. Two (2) sets of aliquots were spiked with an HBc IgM high positive sample to achieve two (2) 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), plasma (lithium heparin, sodium heparin, sodium citrate, and dipotassium EDTA).

8. 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 on HBc IgM 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.

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 HBc IgM 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.

Table 6: 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	6	7 days	3 months	4 days

Reagent Stability-Real-Time (Shelf-Life)

Studies were performed to establish the shelf-life for the LIAISON® XL MUREX HBc IgM. Three lots of LIAISON® XL MUREX HBc IgM were stored at the recommended storage temperature of 2-8°C throughout the study. Performance was assessed against clinically relevant acceptance criteria using three lots of LIAISON XL MUREX Control HBc IgM (positive and negative) and an internal stability panel consisting of eleven samples. Study demonstrated that reagents are stable and continue to meet acceptance criteria 9 months after date of manufacture.

Reagent Stability- Reagent On-Board

Stability studies were conducted to determine the length of time the LIAISON® XL MUREX HBc IgM Reagent Integral can be stored on-board the LIAISON® XL Analyzer in the refrigerated area once open. One lot of LIAISON® XL MUREX HBc IgM and LIAISON® XL MUREX Control HBc IgM (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 HBc IgM 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 HBc IgM 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 HBc IgM and one lot of LIAISON® XL MUREX Control HBc IgM. 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.

Reagent Stability-Calibrator stability

The LIAISON® XL MUREX HBc IgM 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 HBc IgM. Three (3) lots of LIAISON® XL MUREX Control HBc IgM were stored at the recommended storage temperature of 2-8°C throughout the study. Results demonstrate that the positive and negative controls are stable and continue to meet acceptance criteria at 19 months when stored at 2-8°C.

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 HBc IgM. LIAISON® XL MUREX Control HBc was within the established range. The LIAISON® XL MUREX Control HBc IgM is 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 reagents maintain their properties during the shipment and delivery conditions to the customer. After being subjected to simulates stress conditions, testing was performed on three (3) lots of kit reagents and three (3) lots of kit controls, with a fresh calibration at each test time point. All testing performed met acceptance criteria under various simulated transport conditions.

10. Precision

Internal 20 Days

A precision/reproducibility study was carried out over a period of 20 days on the LIAISON® XL MUREX HBc IgM 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 10 serum-based samples and controls were tested in two (2) replicates per run, in two (2) runs per day, by multiple operators, using three (3) reagent kit lots and three (3) Controls lots, over a period of 20 days. The testing days were within one calibration cycle.

The results are shown in the following table.

Table 7: Summary of 20-Day Precision Study

	LIAISON® XL MUREX HBc IgM Assay All 3 Lots Combined											
Sample ID	**N**	**Mean**	**Repeatability**		**Between Run**		**Between Day**		**Between Lot**		**Within Laboratory**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Ctrl Neg #RS-707	240	570.03*	24.423	4.3%	17.557	3.1%	15.698	2.8%	29.190	5.1%	44.757	7.9%
Ctrl Neg	240	571.97*	22.276	3.9%	16.431	2.9%	17.512	3.1%	29.218	5.1%	43.892	7.7%

	LIAISON® XL MUREX HBc IgM Assay All 3 Lots Combined											
Sample ID	N	Mean	Repeatability		Between Run		Between Day		Between Lot		Within Laboratory	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
#RS-708												
Ctrl Neg #RS-709	240	572.29*	24.086	4.2%	18.344	3.2%	15.987	2.8%	28.939	5.1%	44.830	7.8%
Ctrl Pos #RS-710	240	2.27	0.037	1.6%	0.038	1.7%	0.068	3.0%	0.085	3.8%	0.121	5.3%
Ctrl Pos #RS-711	240	2.95	0.052	1.8%	0.083	2.8%	0.077	2.6%	0.092	3.1%	0.155	5.2%
Ctrl Pos #RS-712	240	2.60	0.045	1.7%	0.067	2.6%	0.060	2.3%	0.090	3.5%	0.134	5.2%
HBCM-1-U1	240	0.43	0.008	1.8%	0.009	2.0%	0.016	3.7%	0.032	7.5%	0.038	8.8%
HBCM-1-U2	240	0.60	0.011	1.8%	0.010	1.7%	0.025	4.1%	0.032	5.3%	0.043	7.2%
HBCM-1-U3	240	0.63	0.011	1.7%	0.013	2.0%	0.023	3.7%	0.036	5.7%	0.046	7.3%
HBCM-1-U4	240	0.63	0.011	1.7%	0.011	1.7%	0.026	4.1%	0.017	2.7%	0.034	5.5%
HBCM-2-U5	240	3.76	0.048	1.3%	0.078	2.1%	0.107	2.9%	0.083	2.2%	0.164	4.4%
HBCM-2-U6	240	1.75	0.022	1.2%	0.023	1.3%	0.038	2.2%	0.056	3.2%	0.075	4.3%
HBCM-2-U7	240	4.43	0.062	1.4%	0.083	1.9%	0.126	2.8%	0.080	1.8%	0.181	4.1%
HBCM-2-U8	240	1.74	0.018	1.0%	0.026	1.5%	0.050	2.9%	0.086	5.0%	0.105	6.0%
HBCM-1-U9	240	2.00	0.027	1.3%	0.030	1.5%	0.052	2.6%	0.057	2.8%	0.087	4.3%
HBCM-1-U10	240	3.22	0.045	1.4%	0.058	1.8%	0.090	2.8%	0.089	2.7%	0.146	4.5%

*Samples below the reading range of the assay, precision calculations are based on signal (RLU)

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 HBc IgM. The CLSI document EP15-A3 was consulted in the preparation of the testing protocol. The coded panel comprised 10 serum-based 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 1 run per day for five (5) days with multiple technicians performing the testing.

The following table shows the results.

Table 8: Summary of 5-Day Precision Study

Sample ID	N	Mean	Repeatability		Between-Day/Run		Within Laboratory Precision		Between-Site/Lots		Total Reproducibility	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Ctrl Neg (all 3 lots)	90	*482.28	19.71	4.1%	15.44	3.2%	25.04	5.2%	24.33	5.0%	34.03	7.1%
Ctrl Pos (all 3 lots)	90	2.386	0.046	1.9%	0.118	5.0%	0.127	5.3%	0.492	20.6%	0.505	21.2%
HBCM-1-U1	90	0.469	0.011	2.4%	0.028	5.9%	0.030	6.3%	0.052	11.1%	0.059	12.5%
HBCM-1-U2	90	0.662	0.015	2.3%	0.033	4.9%	0.036	5.4%	0.093	14.0%	0.098	14.9%
HBCM-1-U3	90	0.679	0.015	2.2%	0.031	4.6%	0.035	5.1%	0.100	14.8%	0.105	15.5%
HBCM-1-U4	90	0.682	0.015	2.1%	0.028	4.1%	0.032	4.6%	0.082	12.1%	0.087	12.8%
HBCM-2-U5	90	3.845	0.075	1.9%	0.167	4.3%	0.183	4.7%	0.281	7.3%	0.326	8.5%
HBCM-2-U6	90	1.779	0.024	1.4%	0.078	4.4%	0.082	4.6%	0.106	6.0%	0.129	7.3%
HBCM-2-U7	90	4.482	0.078	1.7%	0.182	4.1%	0.198	4.4%	0.241	5.4%	0.301	6.7%
HBCM-2-U8	90	1.795	0.027	1.5%	0.058	3.2%	0.063	3.5%	0.175	9.7%	0.184	10.3%
HBCM-1-U9	90	2.056	0.032	1.6%	0.089	4.3%	0.095	4.6%	0.120	5.8%	0.147	7.2%
HBCM-1-U10	90	3.297	0.057	1.7%	0.138	4.2%	0.149	4.5%	0.203	6.2%	0.244	7.4%

*Precision calculations are based on signal (RLU) for the negative cohort

11. 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 30 negative pediatric patient samples were used for this study. The pediatric samples encompassed the age range of two (2) months to 21 years. Ten (10) pediatric samples were spiked with an HBc IgM high positive sample to obtain high negative samples. Ten (10) pediatric samples were spiked with an HBc IgM high positive sample to obtain low positive samples. Ten (10) pediatric samples were spiked with an HBc IgM high positive sample to obtain moderate positive samples. Adult negative pool samples were used as controls and were spiked with an HBc IgM 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 HBc IgM. 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 HBc IgM.

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 HBc IgM using samples that would routinely be tested for hepatitis in the United States. 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 HBc IgM 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 six (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.

The prospective (unselected) subjects were defined as follows:

- Pediatric and adult male (38.2%), female (61.8%), and unknown gender (0.1%) 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 distribution of LIAISON® XL MUREX HBc IgM 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				
		+		-		Total
		n	%	n	%	
0-9	F	5	100.0%	0	0.0%	5
	M	3	30.0%	7	70.0%	10
10-19	F	21	52.5%	19	47.5%	40
	M	8	53.3%	7	46.7%	15
20-29	F	251	64.5%	138	35.5%	389
	M	130	55.8%	103	44.2%	233
30-39	F	253	53.4%	221	46.6%	474
	M	111	49.6%	113	50.4%	224
40-49	F	121	41.7%	169	58.3%	290
	M	68	33.8%	133	66.2%	201
50-59	F	106	45.7%	126	54.3%	232
	M	70	37.8%	115	62.2%	185
60-69	F	62	39.2%	96	60.8%	158
	M	50	46.3%	58	53.7%	108
70-79	F	15	32.6%	31	67.4%	46
	M	16	41.0%	23	59.0%	39
80-89	F	8	57.1%	6	42.9%	14
	M	2	28.6%	5	71.4%	7
90-98	F	4	100.0%	0	0%	4
	M	0	0%	0	0%	0
Unk	F	1	100.0%	0	0%	1
	M	1	100.0%	0	0%	1
Total		**1306**	**48.8%**	**1370**	**51.2%**	**2676**

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 10: Serological Classification by FDA-approved HBV Panel

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		
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		

HBV Classification	HBsAg	HBeAg	Total Anti-HBc	Anti-HBc IgM	Anti-HBe	Anti-HBs	Prospective (n)	Retrospective (n)
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 HBc IgM to the reference HBc IgM 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. In addition, Pediatric Cumulative (prospective and retrospective) Clinical Agreement results are presented below.

Table 11: Cumulative Clinical Agreement Adult and Pediatric (Combined Prospective and Retrospective) LIAISON® XL MUREX HBc IgM vs Reference Assay by Characterization

HBV Classification	Reference HBc IgM Assay						Total
	Reactive		Equivocal		Positive		
	LIAISON MUREX HBc IgM		LIAISON MUREX HBc IgM		LIAISON MUREX HBc IgM		
	Positive	Negative	Positive	Negative	Positive	Negative	
Acute	97	1	2	0	0	9	109
Late Acute	32	2	0	0	0	0	34
Chronic	0	0	0	0	21	123	144
Early Recovery	10	0	0	1	1	45	57
Recovery	0	0	0	0	7	160	167
Immune Due to Natural Infection	0	0	0	0	0	107	107
HBV Vaccine Response	0	0	0	0	2	1150	1152
Not Previously Infected	0	0	0	0	1	1302	1303
Not Interpretable	2	1	0	0	0	6	9
Total	**141**	**4**	**2**	**1**	**32**	**2902**	**3082**

Table 12: Cumulative Clinical Agreement Adult and Pediatric (Combined Prospective and Retrospective) LIAISON® XL MUREX HBc IgM vs Reference Assay by Characterization

HBV Classification	Positive Percent Agreement (PPA)	Negative Percent Agreement (NPA)
Acute	97/98 (99.0%) 95% CI: 99.4% to 99.8%	9/11 (81.4%) 95% CI: 52.3% to 94.9%
Late Acute	32/34 (94.1%) 95% CI: 80.9% to 98.4%	N/A
Chronic	N/A	123/144 (85.4%) 95% CI: 78.7% to 90.3%
Early Recovery	10/11 (90.9%) 95% CI: 62.3% to 98.4%	45/46 (97.8%) 95% CI: 88.7% to 99.6%
Recovery	N/A	160/167 (95.8%) 95% CI: 91.6% to 98.0%
Immune Due to Natural Infection	N/A	107/107 (100.0%) 95% CI: 96.5% to 100.0.0%
HBV Vaccine Response	N/A	1150/1152 (99.8%) 95% CI: 99.4% to 100.0%

HBV Classification	Positive Percent Agreement (PPA)	Negative Percent Agreement (NPA)
Not Previously Infected	N/A	1302/1303 (99.9%) 95% CI: 99.6% to 100.0%
Not Interpretable	2/3 (66.7%) 95% CI: 20.8% to 93.9%	6/6 (100%) 95% CI: 61.0% to 100.0%
Total	**141/146 (96.6%) 95% CI: 92.2% to 98.5%**	**2902/2936 (98.8%) 95% CI: 98.4% to 99.2%**

Clinical Endpoints

With regard to safety, as an in vitro diagnostic test, the LIAISON® XL MUREX HBc IgM test involves taking a sample of plasma or serum from a patient. The test, therefore, presents no additional safety hazard to an individual being tested relative to 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 HBc IgM was evaluated versus an FDA approved HBc IgM 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 96.6% and a negative percent agreement (NPA) of 98.2% among subjects in various states of HBV infection.

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 six (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 HBc IgM detection study performed in the U.S.

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 tables below shows the demographic distribution of the cohort.

Table 13: 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	100.0%
Total	2663	100.0%	206	100.0%	161	100.0%	31	100.0%	2	100.0%	21	100.0%

Table 14: 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	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%	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 and retrospective pediatric clinical agreement.

Table 15: Cumulative Pediatric Clinical Agreement (Combined Prospective and Retrospective) LIAISON® XL MUREX HBc IgM vs Reference Assay by Characterization

HBV Classification	Positive Percent Agreement (PPA)	Negative Percent Agreement (NPA)
Acute	20/20 (100%) 95% CI: 83.9% to 100.0%	N/A
Late Acute	7/7 (100%) 95% CI: 64.6% to 100.0%	N/A
Chronic	N/A	6/7 (85.7%) 95% CI: 48.7% to 97.4%
Early Recovery	1/1 (100%) 95% CI: 20.7% to 100.0%	N/A
Recovery	N/A	5/5 (100%) 95% CI: 56.6% to 100.0%
Immune Due to Natural Infection	N/A	3/3 (100%) 95% CI: 43.9% to 100.0%
HBV Vaccine Response	N/A	63/63 (100%) 95% CI: 94.3% to 100.0%
Not Previously Infected	N/A	84/84 (100%) 95% CI: 95.6% to 100.0%
Not Interpretable	0/1 (0.0%) 95% CI: 0.0% to 79.4%	1/1 (100%) 95% CI: 20.7% to 100.0%
Total	28/29 (96.6%) 95% CI: 82.8% to 99.4%	162/163 (99.4%) 95% CI: 96.6% to 99.9%

D. **Safety and Effectiveness Results**

1. Safety Results

   With regard to safety, as an in vitro diagnostic test, the LIAISON® XL MUREX HBc IgM 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 Tables below.

Table 16: Cumulative Clinical Agreement (Combined Prospective and Retrospective)

HBV Classification	Reference HBc IgM Assay						Total
	Reactive		Equivocal		Positive		
	LIAISON MUREX HBc IgM		LIAISON MUREX HBc IgM		LIAISON MUREX HBc IgM		
	Positive	Negative	Positive	Negative	Positive	Negative	
Acute	97	1	2	0	0	9	109
Late Acute	32	2	0	0	0	0	34
Chronic	0	0	0	0	21	123	144
Early Recovery	10	0	0	1	1	45	57
Recovery	0	0	0	0	7	160	167
Immune Due to Natural Infection	0	0	0	0	0	107	107
HBV Vaccine Response	0	0	0	0	2	1150	1152
Not Previously Infected	0	0	0	0	1	1302	1303
Not Interpretable	2	1	0	0	0	6	9
Total	**141**	**4**	**2**	**1**	**32**	**2902**	**3082**

Table 17: Cumulative Clinical Agreement (Combined Prospective and Retrospective)

HBV Classification	Positive Percent Agreement (PPA)	Negative Percent Agreement (NPA)
Acute	97/98 (99.0%) 95% CI: 99.4% to 99.8%	9/11 (81.4%) 95% CI: 52.3% to 94.9%
Late Acute	32/34 (94.1%) 95% CI: 80.9% to 98.4%	N/A
Chronic	N/A	123/144 (85.4%) 95% CI: 78.7% to 90.3%
Early Recovery	10/11 (90.9%) 95% CI: 62.3% to 98.4%	45/46 (97.8%) 95% CI: 88.7% to 99.6%
Recovery	N/A	160/167 (95.8%) 95% CI: 91.6% to 98.0%
ıne Due to Natural Infection	N/A	107/107 (100.0%) 95% CI: 96.5% to 100.0.0%
HBV Vaccine Response	N/A	1150/1152 (99.8%) 95% CI: 99.4% to 100.0%
Not Previously Infected	N/A	1302/1303 (99.9%) 95% CI: 99.6% to 100.0%
Not Interpretable	2/3 (66.7%) 95% CI: 20.8% to 93.9%	6/6 (100%) 95% CI: 61.0% to 100.0%
Total	**141/146 (96.6%)** **95% CI: 92.2% to 98.5%**	**2902/2936 (98.8%)** **95% CI: 98.4% to 99.2%**

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 three (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 HBc IgM test for the qualitative detection of IgM antibodies to hepatitis-B core antigen in human serum and plasma (lithium heparin, sodium heparin, sodium citrate, and K_2EDTA) 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 96.6% with a two-sided 95% confidence interval (CI) of 92.2%-98.5%, and the NPA of 98.8% with a two-sided 95% CI of 98.4%-99.2%.

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 HBc IgM when used according to the manufacturer's instructions can aid the physician in the diagnosis of HBV infection. The PPA of the assay is 96.6% with a two-sided 95% confidence interval (CI) of 92.2%-98.5%, and the NPA of 98.8% with a two-sided 95% CI of 98.4%-99.2%.

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 acute or chronic hepatitis B infection including initiation of appropriate monitoring, antiviral medications, and improved patient knowledge regarding the condition. 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 can potentially decrease transmission and disease burden in the general population as well as in populations at high risk for hepatitis B infection. While the clinical performance of the LIAISON® XL MUREX HBc IgM suggests

that patients will benefit from the assay, low prevalence of certain HBV classifications (namely acute infection, chronic infection, and early recovery) is a source of expected and acceptable uncertainty when analyzing the prospective and retrospective samples, contributing to wide confidence intervals for those subgroups.

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

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 IgM 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. Hepatitis B c IgM is only used as the sole diagnostic for acute hepatitis B in a patient with clinical findings suspicious for acute hepatitis who is in the "window period" between disappearance of HBsAg and appearance if HBsAb; however, the number of patients that will be tested who are in this specific category is extremely small, mitigating the risk of a false positive.

Risks of false negative tests include missing the opportunity to treat a patient who has hepatitis B infection and whose clinical picture warrants antiviral treatment. As noted previously, because hepatitis B core IgM 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.

The clinical benefits outweigh the risks for the proposed assay, considering the mitigations of the risks provided in the premarket approval as well as general controls. The required premarket approval helps to ensure that errors will be uncommon and will facilitate accurate assay implementation and interpretation of results. The device's performance observed in the clinical study suggests that errors will be uncommon and that the assay will provide substantial benefits to patients as an aid in the diagnosis of HBV infection when used in conjunction with other laboratory results and clinical information.

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 probable 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 implement 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.