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

I Background Information:

A 510(k) Number

K254059

B Applicant

Beckman Coulter, Inc.

C Proprietary and Established Names

Access anti-HBc IgM

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
SEI	Class II	21 CFR 866.3173 Hepatitis B Virus (HBV) Antibody Assay	Microbiology

II Submission/Device Overview:

A Purpose for Submission:

To obtain clearance for a new device, Access anti-HBc IgM.

B Measurand:

Hepatitis B virus core antigen IgM antibody (anti-HBc IgM)

C Type of Test:

The Access anti-HBc IgM assay is a chemiluminescent 2-step enzyme immunoassay (CLIA).

III Intended Use/Indications for Use:

A Intended Use(s):
See Indications for Use below.

B Indication(s) for Use:

Access anti-HBc IgM assay:

The Access anti-HBc IgM assay is a paramagnetic particle, chemiluminescent immunoassay for the in vitro qualitative detection of IgM antibodies to hepatitis B virus core antigen (anti-HBc IgM) in human pediatric (3 through 21 years) and adult serum and serum separator tubes or plasma [lithium heparin, lithium heparin separator tubes, dipotassium (K2) EDTA, tripotassium (K3) EDTA, sodium citrate, acid citrate dextrose (ACD), and citrate phosphate dextrose (CPD)] using the DxI 9000 Access Immunoassay Analyzer.

The Access anti-HBc IgM assay results may be used as an aid in the laboratory diagnosis of acute or recent hepatitis B virus (HBV) infection in individuals with signs and symptoms of hepatitis, when used in conjunction with other serological and clinical information.

The Access anti-HBc IgM assay is for use on the DxI 9000 Access Immunoassay Analyzer only.

This assay is not intended for the screening of blood, plasma, and cell or tissue donors.

C Special Conditions for Use Statement(s):
Rx - For Prescription Use Only

D Special Instrument Requirements:

DxI 9000 Access Immunoassay Analyzer

IV Device/System Characteristics:

A Device Description:

Access anti-HBc IgM
The Access anti-HBc IgM assay is a two-step enzyme immunoassay for qualitative detection of IgM antibodies to hepatitis B virus core antigen (anti-HBc IgM) in serum or plasma samples using Dxl 9000 Access Immunoassay Analyzer.
The Access anti-HBc IgM assay requires Access anti-HBc IgM reagent pack, Access anti-HBc IgM Calibrator (C1) and Access anti-HBc IgM Quality Controls (QC1-QC2).

B Principle of Operation:

Paramagnetic particles coated with anti-human IgM monoclonal antibody and prediluted sample are added to a reaction vessel. After incubation, material bound to the solid phase are held in a magnetic field while unbound materials are washed away. HBc antigen complexed to anti-HBc monoclonal antibody alkaline phosphatase conjugate is added and the conjugate binds to the IgM antibodies captured on magnetic particles. A second separation and wash step remove unbound conjugate.
A chemiluminescent substrate is then added to the vessel and light generated by the reaction is measured with a luminometer. The light production is compared to the cutoff value defined

during calibration of the instrument. The qualitative assessment is automatically determined from a stored calibration.

Interpretation of Results:

Test results are determined automatically by the system software. Results (Signal/Cutoff (S/CO)) are reported as reactive or nonreactive as follows

Result (S/CO)	Interpretation	Reporting Instructions
< 1.00	Nonreactive	Report results as nonreactive for anti-HBc IgM antibodies
≥ 1.00	Reactive	Report results as reactive for anti-HBc IgM antibodies

C Instrument Description Information:

1. Instrument Name:

   DxI 9000 Access Immunoassay Analyzer

2. Specimen Identification:
   Specimen identification can be done by a bar code or by manual entry. Bar code labels are read by the analyzer or when ordered by the LIS or middleware. Orders that are entered manually include the rack ID and position, so bar code labels are not necessary for sample identification.

3. Specimen Sampling and Handling:
   No specific requirements for specimen handling for the analyzer are needed. Each specific reagent package insert contains sample handling instructions.

4. Calibration:
   The Access anti-HBc IgM Calibrator, provided at one level, is used to establish calibration for the Access anti-HBc IgM assay on the DxI 9000 Access Immunoassay Analyzer. An active calibration is required for all tests. For the Access anti-HBc IgM assay, calibration is required every 56 days.

5. Quality Control:
   The Access anti-HBc IgM QC kit contains QC1 (negative for anti-HBc IgM) and QC2 (positive for anti-HBc IgM).

V Substantial Equivalence Information:

A Predicate Device Name(s):
ARCHITECT CORE-M

B Predicate 510(k) Number(s):
P060035

C Comparison with Predicate(s):

Device & Predicate Device(s):	Candidate Device K254059	Predicate Device P060035
Device Trade Name	Access anti-HBc IgM	ARCHITECT CORE-M
General Device Characteristic Similarities		
Intended Use/Indications For Use	The Access anti-HBc IgM assay is a paramagnetic particle, chemiluminescent immunoassay for the *in vitro* qualitative detection of IgM antibodies to hepatitis B virus core antigen (anti-HBc IgM) in human pediatric (2 through 21 years) and adult serum and serum separator tubes or plasma [lithium heparin, lithium heparin separator tubes, dipotassium (K_2) EDTA, tripotassium (K_3) EDTA, sodium citrate, acid citrate dextrose (ACD), and citrate phosphate dextrose (CPD)] using the DxI 9000 Access Immunoassay Analyzer. The Access anti-HBc IgM assay results may be used as an aid in the laboratory diagnosis of acute or recent hepatitis B virus (HBV) infection in individuals with signs and symptoms of hepatitis, when used in conjunction with other serological and clinical information. The Access anti-HBc IgM assay is for use on the DxI 9000 Access Immunoassay Analyzer only. This assay is not intended for the screening of blood, plasma, and cell or tissue donors.	The ARCHITECT CORE-M assay is a chemiluminescent microparticle immunoassay (CMIA) used for the qualitative detection of IgM antibody to hepatitis B core antigen (IgM anti-HBc) in human adult and pediatric serum or plasma (dipotassium EDTA, lithium heparin, and sodium heparin) and neonatal serum on the ARCHITECT i System. The ARCHITECT CORE-M assay is to be used as an aid in the diagnosis of acute or recent hepatitis B virus (HBV) infection in conjunction with other laboratory results and clinical information.
Calibrator Intended Use	The Access anti-HBc IgM Calibrator is intended to calibrate the Access anti-HBc IgM assay for the *in vitro* qualitative detection of IgM antibodies to hepatitis B virus core antigen (anti-HBc IgM) in human serum and plasma using the DxI 9000 Access Immunoassay Analyzer.	The ARCHITECT CORE-M Calibrators are used for the calibration of the ARCHITECT i System when the system is used for the qualitative detection of IgM antibody to hepatitis B core antigen (IgM anti-HBc) using the ARCHITECT CORE-M Reagent Kit. The performance of the ARCHITECT CORE-M Calibrators has not been established with any other IgM anti-HBc assays.

QC Intended Use	The Access anti-HBc IgM QC is intended for monitoring system performance of the Access anti-HBc IgM assay. The Access anti-HBc IgM QC is for use on the DxI 9000 Access Immunoassay Analyzer.	The ARCHITECT CORE-M Controls are used for monitoring the performance of the ARCHITECT i System when used for the qualitative detection of lgM antibody to hepatitis B core antigen (IgM anti-HBc) in human adult serum and plasma when using the ARCHITECT CORE-M Reagent Kit. The performance of the ARCHITECT CORE-M Controls has not been established with any other IgM anti-HBc assays.
Analyte Measured	Same	Anti-HBc IgM antibodies
Assay Type	Same	Qualitative
Detection Method	Automated, Chemiluminescence immunoassay	Automated, Chemiluminescent microparticle immunoassay (CMIA)
Reagent, Calibrator and QC format	Same	Liquid, ready-to-use
Control(s)	Same	2 levels Negative Positive
Sample Type	Same	Serum and Plasma
General Device Characteristic Differences		
Compatible Anticoagulants	Serum, Serum separator tube, Plasma [Lithium Heparin, Lithium Heparin separator tube, Dipotassium (K_2) EDTA, Tripotassium (K_3) EDTA Sodium Citrate, Acid Citrate Dextrose (ACD),Citrate Phosphate Dextrose (CPD)]	Human serum, plasma (dipotassium EDTA, Lithium Heparin, Sodium Heparin)
Sample Volume	10 µL+ dead volume	64 µL + dead volume
Instrument	DxI 9000 Access Immunoassay Analyzer	ARCHITECT i Systems
Traceability/ Standardization	Calibrator is traceable to the manufacturer's working calibrator.	Calibrator 2 is traceable to the Reference Standard of the Paul Ehrlich Institute, HBc Reference serum IgM 84 (IgM anti-HBc).
Time to Result	~ 29 minutes	~ 30 minutes
Calibration Frequency	56 days	30 days

Purpose	Aid in the laboratory diagnosis of acute or recent hepatitis B virus (HBV) infection in *individuals with signs and symptoms of hepatitis*, when used in conjunction with other serological and clinical information	Aid in the diagnosis of acute or recent hepatitis B virus (HBV) infection in conjunction with other laboratory results and clinical information

VI Standards/Guidance Documents Referenced:

1. EP05-A03: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline - Third Edition
2. EP07-3rd: Interference Testing in Clinical Chemistry - Third Edition
3. EP09c: Measurement Procedure Comparison and Bias Estimation Using Patient Samples - Third Edition
4. EP21-A2: Assessment of the Diagnostic Accuracy of Laboratory Tests Using Receiver Operating Characteristic Curves; Approved Guideline - Second Edition
5. EP25: Evaluation of Stability of In vitro Medical Laboratory Test Reagents – Second Edition
6. EP37: Supplemental Tables for Interference Testing in Clinical Chemistry – First Edition
7. GP44-A4: Procedures for the Handling and Processing of Blood Specimens for Common Laboratory Tests; Approved Guideline-Fourth Edition
8. EP12-A02: User protocol evaluation of qualitative test performance
9. ISO 14971: Medical devices – Application of risk management of medical devices – Third Edition; 2019.
10. ISO 15223-1: Medical devices - Symbols to be used with information to be supplied by the manufacturer - Part 1: General requirements – Fourth Edition; 2021.
11. ISO 17511: *In vitro* diagnostic medical devices - Requirements for establishing metrological traceability of values assigned to calibrators trueness control materials and human samples – second edition; 2020.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

A. Within-Laboratory precision:

Within- laboratory precision was evaluated for twenty days on three different DxI 9000 Access Immunoassay Analyzer at one internal site. An eight-member panel containing four serum samples (S1-S4) and four plasma samples (P1-P4) were run at two runs per day with three replicates per sample using three reagent lots of Access anti-HBc IgM and two lots of Access anti-HBc IgM calibrators. Calibration was conducted at the beginning of the study. Table 1 presents the results for within-laboratory precision study.

Table 1. Within-Laboratory precision results of the Access anti-HBc IgM

Sample	N	Mean (S/CO)	Repeatability (Within-Run)		Between-Run		Between-Day		Between-Reagent Lot		Between-Instrument		Within Laboratory	
			SD (S/CO)	%CV	SD (S/CO)	%CV	SD (S/CO)	%CV	SD (S/CO)	%CV	SD (S/CO)	%CV	SD (S/CO)	%CV
QC1	2,160	0.01	0.000	N/A	0.001	N/A	0.001	N/A	0.001	N/A	0.000	N/A	0.002	N/A
QC2	2,160	2.84	0.062	2.2	0.052	1.8	0.039	1.4	0.047	1.7	0.022	0.8	0.104	3.7
S1	2,160	0.01	0.000	N/A	0.000	N/A	0.000	N/A	0.001	N/A	0.000	N/A	0.001	N/A
S2	2,160	0.73	0.018	2.5	0.018	2.5	0.008	1.1	0.018	2.5	0.006	0.9	0.033	4.5
S3	2,160	1.13	0.028	2.5	0.033	2.9	0.015	1.3	0.036	3.1	0.01	0.9	0.059	5.2
S4	2,160	4.45	0.102	2.3	0.097	2.2	0.063	1.4	0.092	2.1	0.034	0.8	0.183	4.1
P1	2,160	0.01	0.001	N/A	0.000	N/A	0.000	N/A	0.001	N/A	0.000	N/A	0.001	N/A
P2	2,160	0.71	0.019	2.7	0.015	2.1	0.014	2	0.018	2.5	0.004	0.5	0.034	4.7
P3	2,160	1.08	0.03	2.8	0.018	1.7	0.031	2.9	0.038	3.6	0.008	0.8	0.061	5.7
P4	2,160	3.84	0.099	2.6	0.054	1.4	0.085	2.2	0.11	2.9	0.047	1.2	0.185	4.8

Note: %CV are not meaningful when S/CO approaches zero. Results are noted as N/A.P= Plasma, S= Serum, N/A= Not applicable, N=number of replicates, QC= Quality control

Within-laboratory precision of the Access anti-HB IgM assay on the Automation Line DxA 5000 total laboratory automation system coupled to the DxI 9000 Access Immunoassay Analyzer was evaluated at one internal site on one Dxl 9000 Analyzer. The same panel of samples, used in the within-laboratory precision study, were tested in 3 replicates per run, 2 runs per day, for 20 days, using 1 reagent lot and 1 calibrator lot. The study results are summarized in Table 2.

Table 2. Within-Laboratory precision results with Automation of the Access anti-HBc IgM

Sample	N	Mean (S/CO)	Repeatability (Within-run)		Between- Run		Between- Day		Within-Laboratory (total)	
			SD (S/CO)	CV (%)	SD (S/CO)	CV (%)	SD (S/CO)	CV (%)	SD (S/CO)	CV (%)
QC1	120	0.00	0.000	NA	0.000	NA	0.000	NA	0.000	NA
QC2	120	2.83	0.073	2.6%	0.046	1.6%	0.067	2.4%	0.109	3.9%
S1	120	0.01	0.004	N/A	0.002	N/A	0.003	N/A	0.005	N/A
S2	120	0.72	0.023	3.3%	0.013	1.8%	0.023	3.1%	0.035	4.9%
S3	120	1.14	0.039	3.4%	0.029	2.5%	0.037	3.3%	0.062	5.4%
S4	120	4.46	0.134	3.0%	0.085	1.9%	0.114	2.6%	0.195	4.4%
P1	120	0.01	0.000	0.0%	0.000	0.0%	0.000	0.0%	0.000	0.0%
P2	120	0.70	0.022	3.2%	0.017	2.4%	0.023	3.3%	0.036	5.2%
P3	120	1.06	0.029	2.8%	0.032	3.0%	0.021	2.0%	0.048	4.5%
P4	120	3.81	0.189	4.9%	0.000	0.0%	0.122	3.2%	0.225	5.9%

Note: %CV are not meaningful when S/CO approaches zero. Results are noted as N/A.
P= Plasma, S= Serum, N/A= Not applicable, N=number of replicates, QC= Quality control

B. Reproducibility:

Reproducibility of the Access anti-HBc IgM on the DxI 9000 Access Immunoassay analyzer was evaluated by running a five-day multi-site reproducibility study. A panel of samples, serum (S1-S6) and plasma (P1-P6), was assayed at three clinical sites, on three instruments

(one per site). Each panel member was assayed in replicates of three at two separate times (runs) per day. The results are summarized in table 3.

Table 3. Reproducibility study results of the Access anti-HBc IgM

Sample	N	Mean (S/CO)	Between-Site		Between-Day		Between-Run		Repeatability (Within-Run)		Reproducibility	
			SD (S/CO)	%CV	SD (S/CO)	%CV	SD (S/CO)	%CV	SD (S/CO)	%CV	SD (S/CO)	%CV
S1	90	0.01	0.000	N/A	0.000	N/A	0.000	N/A	0.000	N/A	0.000	N/A
S2	90	0.32	0.011	3.6	0.000	0.000	0.003	1	0.009	2.7	0.015	4.5
S3	90	0.55	0.017	3	0.000	0.000	0.015	2.8	0.015	2.7	0.027	4.9
S4	90	0.76	0.024	3.2	0.003	0.4	0.009	1.2	0.018	2.4	0.032	4.2
S5	90	1.19	0.032	2.6	0.000	0.000	0.027	2.2	0.03	2.5	0.051	4.3
S6	90	4.52	0.087	1.9	0.049	1.1	0.068	1.5	0.108	2.4	0.162	3.6
P1	90	0.01	0.000	N/A	0.000	N/A	0.000	N/A	0.000	N/A	0.000	N/A
P2	90	0.33	0.009	2.7	0.004	1.1	0.007	2	0.008	2.5	0.014	4.3
P3	90	0.53	0.017	3.2	0.000	0.000	0.012	2.2	0.013	2.6	0.025	4.7
P4	90	0.74	0.021	2.8	0.000	0.000	0.013	1.8	0.019	2.6	0.031	4.2
P5	90	1.12	0.035	3.1	0.000	0.000	0.029	2.6	0.024	2.1	0.052	4.6
P6	90	3.95	0.073	1.8	0.042	1.1	0.081	2.1	0.097	2.5	0.152	3.8

Note: %CV are not meaningful when S/CO approaches zero. Results are noted as N/A.
P= Plasma, S= Serum, N/A= Not applicable, N=number of replicates

2. Linearity:

Not applicable as this is a qualitative assay

3. Analytical Specificity/Interference:

A. Interference study:

Interference study was conducted to evaluate the susceptibility of the Access anti-HBc IgM assay to potentially interfering substances using negative, low positive and moderately positive samples. Potential endogenous, and exogenous interferents were tested. No interference was observed for any of the interferents tested at concentrations indicated in Table 4.

Table 4. Interference study results of the Access anti-HBc IgM

	Potential Interferents	**Highest Concentration tested**
Endogenous Interferents	Hemoglobin	1,000 mg/dL
	Total Protein	15 g/dL
	Bilirubin Conjugated	40 mg/dL
	Bilirubin Unconjugated	40 mg/dL
	Biotin	3,510 ng/mL
	Cholesterol	400 mg/dL
	Triglycerides (Intralipid)	37 mmol/L (3,854 mg/dL)

Exogenous Interferents	Aspirin (acetylsalicylic acid)	167 µmol/L
	Salicylic acid	207 µmol/L
	Acetaminophen (paracetamol)	1,030 µmol/L
	Ibuprofen	1,060 µmol/L
	Atorvastatin	1.34 µmol/L
	Lisinopril	0.607 µmol/L
	Levothyroxine	0.552 µmol/L
	Metformin	92.9 µmol/L
	Amlodipine	0.183 µmol/L
	Omeprazole	24.3 µmol/L
	Sertraline	3.03 µmol/L

B. Cross reactivity:

Potential cross-reactivity with the Access anti-HBc IgM assay was determined by testing specimens with antibodies to other microorganisms or with medical conditions unrelated to HBV infections. No cross reactivity was observed. The cross-reactants tested and study results are summarized in Table 5.

Table 5. Cross reactivity study results for the Access anti-HBc IgM

Cross reactants	**Number of Samples Tested**	**Number of Reactive Samples**	**Number of Non-Reactive Samples**
Pathogenic Agents and Related Diseases			
Epstein-Barr Virus (EBV)	10	0	10
Cytomegalovirus (CMV)	10	0	10
Herpes Simplex Virus (HSV1/2)	10	0	10
Toxoplasmosis	10	0	10
Human Immunodeficiency Virus (HIV)	10	0	10
Hepatitis A Virus (HAV)	10	0	10
Hepatitis C Virus (HCV)	10	0	10
Hepatitis E Virus (HEV)	10	0	10
Flavivirus (Dengue)	10	0	10
Flavivirus (West Nile)	10	0	10
Flavivirus (Zika)	10	0	10
Measles (Rubeola)	10	0	10
Mumps	10	0	10
Rubella	10	0	10
Varicella Zoster	10	0	10
Syphilis	10	0	10
Other Related Diseases			
Alcohol Liver Disease	10	0	10
Primary Biliary Cirrhosis	10	0	10

Vaccination Potential Interference			
Influenza Post Vaccination	10	0	10
Auto-Immune Diseases (Heterophile)			
HAMA	10	0	10
Anti-Nuclear Antibody (ANA)	10	0	10
Rheumatoid Factor	10	0	10
Systemic Lupus Erythematosus (SLE)	10	0	10
Multiple Myeloma	10	0	10
Cross-Reactivity Related to Design			
Anti-*E. coli* or *E. coli* Infection	10	0	10
Pregnant Women			
Pregnancy Multipara	10	0	10
Pregnancy First Trimester	10	0	10
Pregnancy Second Trimester	10	0	10
Pregnancy Third Trimester	10	0	10
Other			
Transplant Recipient	10	0	10
Dialysis Patients	10	0	10
Hemophilia / ClDTTing Factor Deficiency	10	0	10

C. IgM class specificity study:

A study was performed to demonstrate that the Access anti-HBc IgM assay specifically detects IgM not IgG and does not generate false results in the presence of IgG in patients' samples. The IgM class specificity of the Access anti-HBc IgM assay was evaluated by depleting IgM molecules present in the samples by treating with dithiothreitol (DTT). Ten anti-HBc IgM known positive samples were tested. All HBc IgM reactive samples treated with DTT showed decreased signal while untreated samples remained unaffected, indicating the Access HBc IgM assay is specifically detects HBc IgM. Results are presented in table 6.

Table 6. IgM class specificity study results of the Access anti-HBc IgM.

Sample	Condition	Reference anti-HBc Total		Access anti-HBc IgM		Reference anti-HBc IgM	
		Signal S/CO	Results	Signal S/CO	Status	Signal S/CO	Results
Positive Control	NEAT	1.38	R	8.62	R	9.72	R
	Untreated -PBS)	1.42	R	8.85	R	9.30	R
	DTT treated	0.07	NR	0.01	NR	0.54	NR
Negative Control	NEAT	7.50	R	0.18	NR	0.12	NR
	Untreated (PBS)	7.32	R	0.16	NR	0.11	NR

	DTT treated	8.11	R	0.12	NR	0.30	NR
Sample 1	NEAT	5.41	R	12.69	R	7.20	R
	Untreated (PBS)	5.38	R	12.25	R	7.38	R
	DTT treated	5.62	R	0.09	NR	0.12	NR
Sample 2	NEAT	5.44	R	10.07	R	4.14	R
	Untreated (PBS)	5.52	R	10.06	R	4.26	R
	(treated	5.85	R	0.06	NR	0.11	NR
Sample 3	NEAT	6.01	R	9.34	R	5.46	R
	Untreated (PBS)	5.94	R	8.99	R	3.77	R
	DTT treated	6.03	R	0.13	NR	0.38	NR
Sample 4	NEAT	3.82	R	12.39	R	5.70	R
	Untreated (PBS)	3.83	R	12.42	R	6.02	R
	DTT treated	3.73	R	0.16	NR	0.16	NR
Sample 5	NEAT	2.72	R	6.80	R	4.95	R
	Untreated (PBS)	2.67	R	6.50	R	4.95	R
	DTT treated	0.71	NR	0.07	NR	0.11	NR
Sample 6	NEAT	6.10	R	16.15	R	15.49	R
	Untreated <PBS)	6.14	R	15.64	R	14.06	R
	DTT treated	6.21	R	2.62	R	3.27	R
Sample 7	NEAT	4.06	R	3.34	R	2.40	R
	Untreated <PBS)	4.17	R	3.25	R	2.13	R
	DTT treated	4.31	R	0.03	NR	0.07	NR
Sample 8	NEAT	1.35	R	5.69	R	2.43	R
	Untreated (PBS)	1.45	R	6.23	R	2.49	R
	DTT treated	2.75	R	0.01	NR	0.05	NR
Sample 9	NEAT	5.72	R	6.57	R	4.93	R
	Untreated (PBS)	5.83	R	6.40	R	4.79	R
	DTT treated	6.29	R	0.06	NR	0.20	NR
Sample 10	NEAT	6.09	R	6.98	R	4.76	R
	Untreated (PBS)	6.02	R	8.07	R	5.68	R
	DTT treated	5.91	R	0.08	NR	0.36	NR

D. Hook effect:

A study was conducted to characterize the performance of the Access anti-HBc IgM assay with specimens containing high levels of anti-HBc IgM that have the potential to cause a high dose hook effect. The data demonstrated that the Access anti-HBc IgM assay is not susceptible to interference from specimens with high levels HBc IgM.

4. Detection Limit and Assay Reportable Range:

A. Seroconversion:

The ability of the Access anti-HBc IgM assay to detect anti-HBc IgM was evaluated by testing six anti-HBc IgM seroconversion panels. For each seroconversion panel, the difference in the

days from the initial draw to the first reactive result was calculated for all panels between the Access anti-HBc IgM assay and the reference assay. Equivalent detection with no difference in bleed number was observed in three of the six panels, and earlier detection by the Access anti-HBc IgM assay was observed in three panels. The results are summarized in table 7.

Table 7. Seroconversion study results of the Access HBc IgM.

Panel ID	First anti-HBc IgM Positive Result from Initial Draw Date		Access anti-HBc IgM assay vs Reference assay
	Access anti-HBc IgM assay (days)	Reference assay (days)	Difference in bleed number for the first reactive bleed*
HBV-6281	43	43	0
HBV-9092	85	92	-1
HBV-9093	49	49	0
HBV-001	36	43	-1
HBV-002	59	59	0
HBV-004	71	76	-1

*The difference in bleed number is compared to the reference assay. For example, -1 indicates that the reference assay required 1 additional bleed before reactivity was determined compared to the Access anti-HBc IgM assay.

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

A. Reagent pack, calibrators and control stability:

Four serum samples (2 samples each for HBc IgM negatives and positives) were evaluated at different storage conditions at different timepoints using three reagent lots for stability claims. Each time point signal values were compared to the baseline signal values (time 0) to assess degradation status of the reagents, controls and calibrators. The timepoint before the last tested timepoint at which all three lots of reagents meet the acceptance criteria (within +/- 0.100 S/CO from baseline for negative samples, within +/- 10.0% relative signal change from baseline for positive samples) was considered for the stability claims. Table 8 shows the stability results and claims of the Access anti-HBc IgM reagents.

Table 8. Reagent pack, calibrator and quality control stability results of the Access anti-HBc IgM

Reagent	Storage	Stability	Claimed stability
Access anti-HBc IgM Calibration curve	on the instrument	56 days	56 days
Access anti-HBc IgM Calibrator open vial	(2-10ºC)	181 days	14 days
Access anti-HBc IgM Calibrator shelf life	(2-10ºC)	365 days	As stated in the package insert
Access anti-HBc IgM Quality control open vial	(2-10ºC)	90 days	90 days
Access anti-HBc IgM Quality control shelf life	(2-10ºC)	540 Days	As stated in the package insert
Access anti-HBc IgM Reagent pack	(2-10ºC)	366 days	As stated in the package insert
Access anti-HBc IgM Open reagent	(2-10ºC)	56 days	56 days

B. Specimen stability:

A study was conducted to evaluate the specimen storage temperatures and number of freeze/thaw cycles for each blood collection tube type acceptable for use with the Access anti-HBc IgM assay. This study evaluated sample stability at room temperature (20 – 25°C), refrigerated (2 - 8°C), and frozen (≤ -18°C). Sample stability after multiple freeze/thaw cycles was also evaluated. Low negative, high negative, low positive and moderate positive samples were tested. Table 9 shows the summary of the results and specimen stability claims.

Table 9. Sample stability results of the Access anti-HBc IgM.

Specimen Stability					
Specimen	**Type**	**20 to 25°C (hours)**	**2 to 8°C (days)**	**-20°C or colder (days)**	**Number of freeze thaw**
Serum	Serum and Serum separator tube	72	7	30	Maximum 5 freeze thaws
Plasma	Lithium Heparin Lithium Heparin Separator Tube Dipotassium (K_2) EDTA Tripotassium (K_3) EDTA Sodium Citrate Acid Citrate Dextrose (ACD) Citrate Phosphate Dextrose (CPD)				

C. Fresh versus frozen samples study:

This study evaluated equivalency between fresh (never frozen) serum samples and samples frozen at ≤ -18°C using the Access Anti-HBc IgM assay on the DxI 9000 Access Immunoassay Analyzer. Total of fifty samples including different levels of anti-HBc IgM (ten low negatives, twenty-seven low positives, and thirteen moderate positives) were tested. The regression analysis demonstrated a slope of 1.00 indicating the fresh sample is equivalent to frozen samples in detection of anti-HBc IgM analyte.

6. Assay Cut-Off:

Beckman evaluated the Access HBc IgM assay cut-off by testing one hundred HBc IgM negatives and fifty HBc IgM positives from intended use population. The results of this study established cut-off of the Access HBc IgM as 1.00 S/CO.

B Comparison Studies:

1. Method Comparison with Predicate Device:

See Section C. Clinical Studies.

2. Matrix Comparison:

To determine whether the claimed matrices have equivalent performance on the Access anti-HBc IgM assay on the DxI 9000 Access Immunoassay Analyzer, matched donor sets

consisting of nine specimen types (serum with or without Gel, and plasma [lithium heparin with Gel, lithium heparin without Gel, dipotassium (K2) EDTA, tripotassium (K3) EDTA, sodium citrate, acid citrate dextrose (ACD) and citrate phosphate dextrose (CPD)] were evaluated. Serum (without gel) served as the reference tube type. Regression analysis showed equivalency between reference matrix and intended matrices. Table 10 presents the results of matrix comparison study results.

Table 10. Matrix comparison study results of the Access anti-HBc IgM

Sample Type	Slope (Bootstrap 95% CI)	Correlation Coefficient (r)
Serum with Gel	1.01 (1.00 – 1.02)	1.00
Plasma Lithium Heparin without Gel	1.02 (1.02 – 1.03)	1.00
Plasma Lithium Heparin with Gel	1.01 (0.99 – 1.02)	1.00
Plasma K2 EDTA	1.01 (1.00 – 1.02)	1.00
Plasma K3 EDTA	1.03 (1.01 – 1.03)	1.00
Plasma Sodium Citrate	1.10 (1.08 – 1.10)	1.00
Plasma Acid Citrate Dextrose	1.12 (1.08 – 1.16)	1.00
Plasma CPD	1.12 (1.10 – 1.14)	1.00

C Clinical Studies:

A multi-center study was conducted using the Access anti-HBc IgM assay with the DxI 9000 Access Immunoassay Analyzer at three clinical testing sites in the United States. A total of 2,537 specimens including prospective and retrospective specimens from intended use population were tested with the Access anti-HBc IgM assay and FDA approved reference HBc IgM assays using composite comparators method.

The HBV classification was determined by serological assessment for all prospective and retrospective specimens based on the reactivity patterns of six (6) HBV serological markers (HBsAg, HBeAg, anti-HBc IgM, total anti-HBc, anti-HBe and anti-HBS).

Comparison results of prospective and retrospective population:

The positive percent agreement (PPA) and negative percent agreement (NPA) and results with 95% confidence intervals (CI) for the prospective and retrospective populations are presented in tables 11-12.

Table 11. Access anti-HBc IgM assay PPA and NPA for prospective population by HBV Classification

HBV Classification	Total	PPA		NPA	
		% (n/N)	95% CI	% (n/N)	95% CI
Acute	4	100.0 (2/2)	34.2-100.0	100.0 (2/2)	34.2-100.0
Chronic	20	N/A (0/0)	N/A	95.00 (19/20)	76.4-99.1

Early Recovery	70	25.0 (1/4)*	4.6-69.9	100.0 (66/66)	94.5-100.0
HBV Vaccine Response	769	N/A (0/0)	N/A	100.0 (769/769)	99.5-100.0
Not Previously Infected	1,098	N/A (0/0)	N/A	100.0 (1,098/1,098)	99.7-100.0
Possible HBV Vaccination Response	73	N/A (0/0)	N/A	100.0 (73/73)	95.0-100.0
Recovered or Immune due to Natural Infection	121**	N/A (0/0)	N/A	100.0 (121/121)	96.9-100.0
Recovery	121	N/A (0/0)	N/A	100.0 (121/121)	96.9-100.0
Susceptible	1**	N/A (0/0)	N/A	100.0 (1/1)	20.7-100.0
Not Interpretable	4	N/A (0/0)	N/A	100.0 (4/4)	51.0-100.0
Total	2,281	**50.0 (3/6)**	**18.8-81.2**	**99.96 (2,274/2,275)**	**99.8-100.0**

* All 4 early recovery samples had result values close to cutoff of candidate and comparator devices; 2 of the discordant samples produced results in concordance with the Access anti-HBc IgM upon re-testing (re-test results not used in performance calculations).
** One subject classified using four-marker classification table.

Table 12. Access anti-HBc IgM retrospective population PPA by HBV Classification

HBV Classification	**PPA**	
	% (n/N)	**95% CI**
Acute	98.08 (51/52)	89.9-99.7
Acute (Late)	100.0 (85/85)	95.7-100.0
Chronic	100.0 (5/5)	56.6-100.0
Early Recovery	90.38 (47/52)*	79.4-95.8
HBV Vaccine Response	N/A (0/0)	N/A
Not Previously Infected	N/A (0/0)	N/A
Recovered or Immune due to Natural Infection	N/A (0/0)	N/A
Recovery	N/A (0/0)	N/A
Uninterpretable	42.86 (3/7)	15.8-75.0

Total	**95.02 (191/201)**	**91.1-97.3**

*All early recovery samples discordant with the Access anti-HBc IgM had result value close to cutoff values of candidate and comparator devices.

Comparison of Results for Pregnant Women

One hundred and seventy-one serum samples were prospectively collected from an increased risk and/or signs and symptoms U.S. pregnant population. This population included 21 pregnant subjects of pediatric age (range 18 - 21 years). There were 71 subjects in the first trimester, 67 subjects in the second trimester and 33 subjects in the third trimester in this study. The results of the Access anti-HBc IgM testing at all sites combined are presented in table 13.

Table 13. Percent Agreement between Access anti-HBc IgM and Comparator Final interpretation by HBV Classification: Pregnant Population.

HBV Classification	**PPA**		**NPA**	
	% (n/N)	**95% CI**	**% (n/N)**	**95% CI**
Chronic	0 (0/0)	NA	100.0 (1/1)	20.65-100.0
HBV Vaccine Response	0 (0/0)	NA	100.0 (77/77)	95.25-100.0
Not Previously Infected	0 (0/0)	NA	100.0 (82/82)	95.52-100.0
Possible HBV Vaccination Response	0 (0/0)	NA	100.0 (9/9)	70.09-100.0
Recovery	0 (0/0)	NA	100.0 (2/2)	34.24-100.0
Total	**0**	**NA**	**100.0 (171/171)**	**97.80-100.0**

Because no HBc IgM positive samples were identified in pregnant cohort, a spiking study was conducted to evaluate the Access Anti-HBC IgM performance with HBc IgM spiked pregnant samples. A total of thirty-one pregnant and control adult serum samples were spiked with unique native anti-HBc IgM positive sample. The results revealed that there were no significant differences in spiked pregnant samples versus control samples.

Comparison of Results for pediatric population

Prospectively collected one hundred and fifty-five pediatric subjects were tested by the candidate and comparator devices. Results are presented in table 14.

Table 14. Percent Agreement between Access anti-HBc IgM and Comparator Final Interpretation by HBV Classification: Pediatric Population.

HBV Classification	**Total**	**PPA**		**NPA**	
		% (n/N)	**95% CI**	**% (n/N)**	**95% CI**
Early Recovery	1	0.00 (0/1)	(0.0-79.3)	N/A	N/A
HBV Vaccine Response	53	N/A	N/A	100.0 (53/53)	(93.2-100.0)
Not Previously Infected	95	N/A	N/A	100.0 (95/95)	(96.1-100.0)

Possible HBV Vaccination Response	3	N/A	N/A	100.0 (3/3)	(43.9-100.0)
Recovered or Immune due to Natural Infection	2	N/A	N/A	100.0 (2/2)	(34.2-100.0)
Not Interpretable	1	N/A	N/A	100.0 (1/1)	(20.7-100.0)
Total	155	**0.00 (0/1)**	**(0.0-79.3)**	**100.0 (154/154)**	**(97.6-100.0)**

Supplemental retrospective pediatric study: Additional Anti-HBc IgM known positive samples from pediatric population were obtained from vendors. Table 15 shows results for retrospective samples by HBV classification.

Table 15. Access anti-HBc IgM retrospective samples: pediatric cohort PPA and NPA by HBV Classification

HBV Classification	Total	PPA	
		% (n/N)	95% CI
Acute	2	100.0 (2/2)	34.2-100.0
Acute (Late)	2	100.0 (2/2)	34.2-100.0
Early Recovery	4	100.00 (4/4)	51.0-100.0
HBV Vaccine Response	0	N/A (0/0)	N/A
Not Previously Infected	0	N/A (0/0)	N/A
Possible HBV Vaccination Response	0	N/A (0/0)	N/A
Recovered or Immune Due to Natural Infection	0	N/A (0/0)	N/A
Total	8	**100 (8/8)**	**67.6-100.0**

Because insufficient HBc IgM positive samples were identified in pediatric cohorts, a spiking study was conducted to evaluate the results when HBc IgM spiked pediatric samples tested with the Access anti-HBc IgM assay. A total of thirty-one pediatric (3-21 years) and control adult serum samples were spiked with unique native anti- HBc IgM positive sample. The results revealed that there were no significant differences in results of spiked pediatric samples versus control samples.

D Expected Values/Reference Range:

The Access anti-HBc IgM results for the prospective population for all clinical trial sites combined by age group and gender are summarized in table 16.

Table 16. Expected Results of Access HBc IgM by Age and Gender.

Age Range (years)	Sex	Access anti-HBc IgM				Total
		Nonreactive		Reactive		
		N	%	N	%	
9-12	Female	6	0.26	0	0.00	6
	Male	11	0.48	0	0.00	11
13-18	Female	34	1.49	0	0.00	34
	Male	24	1.05	0	0.00	24

19-21	Female	73	3.20	0	0.00	73
	Male	28	1.23	0	0.00	28
22-29	Female	301	13.20	0	0.00	301
	Male	108	4.73	0	0.00	108
30-39	Female	276	12.10	0	0.00	276
	Male	129	5.66	0	0.00	129
40-49	Female	190	8.33	0	0.00	190
	Male	150	6.58	1	0.04	151
50-59	Female	253	11.09	0	0.00	253
	Male	225	9.86	1	0.04	226
60-69	Female	153	6.71	0	0.00	153
	Male	178	7.80	2	0.09	180
70-79	Female	52	2.28	0	0.00	52
	Male	55	2.41	0	0.00	55
80-89	Female	9	0.39	0	0.00	9
	Male	16	0.70	0	0.00	16
90+	Female	1	0.04	0	0.00	1
	Male	5	0.22	0	0.00	5

E Other Supportive Instrument Performance Characteristics Data:

Carryover study: A Carryover study was performed to determine the Access anti-HBc IgM carryover effect by running negative and high positive samples at varying sequences. This study evaluated 1. reagent carryover and, 2. sample carryover. Results demonstrated no carryover with both studies.

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

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

VIII Proposed Labeling:

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

IX Conclusion:

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