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

I Background Information:

A 510(k) Number

K253687

B Applicant

Beckman Coulter Inc.

C Proprietary and Established Names

Access Anti-HBc Total

D Regulatory Information

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

II Submission/Device Overview:

A Purpose for Submission:

To obtain clearance for marketing the Access anti-Hepatitis B core (anti-HBc) Total Assay, Access Anti-HBc Total Calibrator, and Access Anti-HBc Total Quality Control (QC).

B Measurand:

Total (IgG and IgM) antibodies to Hepatitis B core.

C Type of Test:

Chemiluminescent 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 Total assay.

The Access anti-HBc Total assay is a paramagnetic particle, chemiluminescent immunoassay for the *in vitro* qualitative detection of total antibodies to hepatitis B virus core antigen (anti-HBc) in human pediatric (2 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 Total assay may be used as an aid in the laboratory diagnosis of acute, chronic or resolved hepatitis B virus (HBV) infection of individuals with signs and symptoms of hepatitis or at risk for hepatitis B virus infection, including pregnant women, when used in conjunction with other laboratory results and clinical information.

The Access anti-HBc Total 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.

Access anti-HBc Total Calibrator.

The Access anti-HBc Total Calibrator is intended to calibrate the Access anti-HBc Total assay for the *in vitro* qualitative detection of hepatitis B virus core total antibodies (anti-HBc) in human serum and plasma using the DxI 9000 Access Immunoassay Analyzer.

Access anti-HBc Total QC.

The Access anti-HBc Total QC is intended for monitoring system performance of the Access anti-HBc Total assay. The Access anti-HBc Total QC is for use on the DxI 9000 Access Immunoassay Analyzer.

C Special Conditions for Use Statement(s):

Rx – For Prescription Use Only

D Special Instrument Requirements:

For Use with the DxI 9000 Analyzer from Beckman Coulter, Inc.

IV Device/System Characteristics:

A Device Description:

The Access anti-HBc Total assay is a two-step competitive immunoassay for the qualitative detection of total antibodies (anti-HBc IgG and IgM) to hepatitis B core antigen of hepatitis B virus (HBV) using the DxI 9000 Analyzer. The Access anti-HBc Total assay requires Access anti-HBc Total (reagent packs), Access anti-HBc Total Calibrator (C1), and Access anti-HBc Total QC (QC1-QC2).

B Principle of Operation:

Paramagnetic particles coated with HBc antigen and sample are added to a reaction vessel. Anti-HBc antibodies present in the patient sample bind to the antigen-coated particles during the incubation, after which the material bound to the solid phase are held in a magnetic field while unbound materials are washed away. Alkaline phosphatase coupled to HBc monoclonal antibodies is added and this conjugate competes with the patient antibodies bound to the HBc antigens coated on the particles.

After incubation, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. 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.

Results interpretation:
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	Reactive	Report result as reactive for anti-HBc Total antibodies
≥ 1.00	Nonreactive	Report result as nonreactive for anti-HBc Total antibodies

C Instrument Description Information:

1. Instrument Name:

   DxI 9000 Immunoassay Analyzer

2. Specimen Identification:

   Total (IgG and IgM) antibodies to Hepatitis B core antigen in human serum and plasma

3. Specimen Sampling and Handling:

   Collection tubes include 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)].

4. Calibration:

   Access anti-HBc Total Calibrator consists of 1 level (positive) (C1) provided as liquid ready-to-use.

5. Quality Control:

Access anti-HBc Total QC consist of a negative (QC1) and a positive (QC2) control provided as liquid ready-to-use.

V Substantial Equivalence Information:

A Predicate Device Name(s):
Architect CORE

B Predicate 510(k) Number(s):
P080023

C Comparison with Predicate(s):

Device & Predicate Device(s):	P080023 Predicate	K253687 Candidate
Device Trade Name	ARCHITECT CORE	ACCESS Anti-HBc Total
General Device Characteristic Similarities		
Intended Use/Indications For Use	The ARCHITECT CORE assay is a chemiluminescent microparticle immunoassay (CMIA) for the qualitative detection of IgG and IgM antibodies to hepatitis B core antigen (anti-HBc) in human adult and pediatric serum and plasma (dipotassium EDTA, lithium heparin, sodium heparin) and neonatal serum. It is intended as an aid in the diagnosis of acute, chronic, or resolved hepatitis B virus (HBV) infection in conjunction with other laboratory results and clinical information.	The Access anti-HBc Total assay is a paramagnetic particle, chemiluminescent immunoassay for the *in vitro* qualitative detection of total antibodies to hepatitis B virus core antigen (anti-HBc) in human pediatric (2 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 Total assay may be used as an aid in the laboratory diagnosis of acute, chronic or resolved hepatitis B virus (HBV) infection of individuals with signs and symptoms of hepatitis or at risk for hepatitis B virus infection, including pregnant women, when used in conjunction with

		other laboratory results and clinical information. The Access anti-HBc Total 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.
	Calibrator: The ARCHITECT CORE Calibrator is used for the calibration of the ARCHITECT i System when the system is used for the qualitative detection of IgG and IgM antibodies to hepatitis B core antigen (anti-HBc) with the ARCHITECT CORE Reagent Kit. The performance of the ARCHITECT CORE Calibrator has not been established with any other anti-HBc assays.	Calibrator: The Access anti-HBc Total Calibrator is intended to calibrate the Access anti-HBc Total assay for the *in vitro* qualitative detection of hepatitis B virus core total antibodies (anti-HBc) in human serum and plasma using the DxI 9000 Access Immunoassay Analyzer.
	QC: The ARCHITECT CORE Controls are used for monitoring the performance of the ARCHITECT i System when used for the qualitative detection of IgG and IgM antibodies to hepatitis B core antigen (anti-HBc) with the ARCHITECT CORE Reagent Kit. The performance of the ARCHITECT CORE Controls has not been established with any other anti-HBc assays.	QC: The Access anti-HBc Total QC is intended for monitoring system performance of the Access anti-HBc Total assay. The Access anti-HBc Total QC is for use on the DxI 9000 Access Immunoassay Analyzer.
Analyte Measured	Anti-HBc IgG and IgM	same
Assay Type	Qualitative	same
Detection Method	Automated, chemiluminescent Microparticle Immunoassay (CMIA)	similar: automated, chemiluminescent
Reagent, Calibrator, and QC Format	Liquid, ready to use	same
Control(s)	2-levels, 1 Neg. Control, 1 Pos. Control	same
Sample Type	Serum and Plasma	same
Compatible Anticoagulants	Human serum, plasma (dipotassium EDTA, Lithium Heparin, Sodium Heparin)	Human serum, Serum separator tube, Plasma [Lithium Heparin, Lithium Heparin separator tube, Dipotassium EDTA, Tripotassium EDTA, Sodium Citrate, Acid Citrate Dextrose (ACD) Citrate Phosphate Dextrose (CPD)]
General Device Characteristic Differences		

Assay Type	noncompetitive	competitive
Sample Volume	75 µL	105 µL
Calibrator(s)	2-level Calibrator 1 (positive)	1-level Calibrator 1 (positive)
Instrumentation	ARCHITECT i Systems	DxI 9000 Access Immunoassay Analyzer
Target population	Adult and pediatrics	Adult, pediatrics, pregnant women
	As aid in the diagnosis of acute, chronic, or resolved hepatitis B virus (HBV) infection	As aid in the laboratory diagnosis of acute, chronic or resolved hepatitis B virus (HBV) infection of individuals with signs and symptoms of hepatitis or at risk for hepatitis B virus infection

VI Standards/Guidance Documents Referenced:

1. CLSI EP05-A3 (R2019): Evaluation of Precision of Quantitative Measurement Procedures; 2019.
2. CLSI EP07-A3: Interference Testing in Clinical Chemistry; 2018.
3. CLSI EP09c: Measurement Procedure Comparison and Bias Estimation Using Patient Samples, Third Edition; 2018.
4. CLSI EP24-A2: Assessment of the Diagnostic Accuracy of Laboratory Tests Using Receiver Operating Characteristic Curves; Approved Guideline – Second Edition; 2011.
5. CLSI EP25-A: Evaluation of Stability of *In Vitro* Medical Laboratory Reagents – Second Edition; 2023.
6. CLSI EP37: Supplemental Tables for Interference Testing in Clinical Chemistry – First Edition; 2018.
7. GP44-A4 (Formerly H18-A4): Procedures for the Handling and Processing of Blood Specimens for Common Laboratory Tests; Approved Guideline-Fourth Edition; 2014.
8. ISO 14971: Medical devices – Application of risk management of medical devices – Third Edition; 2019.
9. ISO 15223-1: Medical devices - Symbols to be used with information to be supplied by the manufacturer - Part 1: General requirements – Fourth Edition; 2021.
10. 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. <u>Precision/Reproducibility:</u>

A. Precision.

Within-laboratory precision of the Access anti-HBc Total assay was evaluated at one internal site on three Dxl 9000 Analyzers. Four serum and four plasma specimens (2 reactive and 2 non-reactive for each matrix) were tested in 3 replicates per run, 2 runs per day, for 20 days, using 3 lots of Access anti-HBc Total reagent kit and 2 Access anti-HBc Total Calibrator lots. The precision study results are summarized in Table 1.

Table 1. Access Anti-HBc Total within-laboratory precision study results

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	6.24	0.170	2.7	0.225	3.6	0.099	1.6	0.156	2.5	0.093	1.5	0.350	5.6
QC2	2,160	0.31	0.015	N/A	0.018	N/A	0.000	N/A	0.009	N/A	0.010	N/A	0.027	N/A
S1	2,160	5.14	0.146	2.8	0.209	4.1	0.048	0.9	0.138	2.7	0.122	2.4	0.318	6.2
S2	2,160	1.20	0.046	3.9	0.060	5.0	0.020	1.7	0.032	2.7	0.016	1.4	0.087	7.2
S3	2,160	0.85	0.031	3.7	0.044	5.2	0.018	2.2	0.021	2.4	0.011	1.3	0.061	7.2
S4	2,160	0.10	0.005	N/A	0.004	N/A	0.003	N/A	0.003	N/A	0.002	N/A	0.008	N/A
P1	2,160	5.21	0.135	2.6	0.158	3.0	0.138	2.6	0.141	2.7	0.107	2.1	0.306	5.9
P2	2,160	1.16	0.051	4.4	0.050	4.3	0.049	4.2	0.033	2.8	0.015	1.3	0.094	8.1
P3	2,160	0.82	0.035	4.3	0.029	3.5	0.040	4.8	0.022	2.7	0.010	1.2	0.065	7.9
P4	2,160	0.09	0.005	N/A	0.003	N/A	0.004	N/A	0.003	N/A	0.002	N/A	0.008	N/A

Note: %CV are not meaningful when S/CO approaches zero. Results are noted as N/A.

Within-laboratory precision of the Access anti-HBc Total 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 samples used for the within-laboratory precision study were tested in 3 replicates per run, 2 runs per day, for 20 days, using 1 reagent pack lot and 1 calibrator lot. The precision study results are summarized in Table 2.

Table 2. Access Anti-HBc Total within-laboratory precision study results on the Automation Line DxA 5000 total laboratory automation system

Sample	Mean (S/CO)	Repeatability (Within-Run)		Between-Run		Between-Day		Within Laboratory	
		SD (S/CO)	%CV	SD (S/CO)	%CV	SD (S/CO)	%CV	SD (S/CO)	%CV
QC1	6.71	0.217	3.2	0.168	2.5	0.108	1.6	0.295	4.4
QC2	0.32	0.015	4.5	0.016	4.9	0.000	0.0	0.022	N/A
S1	5.17	0.201	3.9	0.180	3.5	0.038	0.7	0.272	5.3
S2	1.18	0.048	4.1	0.051	4.3	0.029	2.4	0.076	6.4
S3	0.83	0.033	4.0	0.044	5.3	0.022	2.6	0.059	7.2
S4	0.10	0.006	6.3	0.005	5.6	0.002	2.0	0.008	N/A
P1	5.33	0.146	2.7	0.210	3.9	0.072	1.3	0.266	5.0
P2	1.15	0.050	4.4	0.057	4.9	0.016	1.4	0.077	6.7
P3	0.82	0.042	5.1	0.049	5.9	0.000	0.0	0.064	7.8
P4	0.09	0.006	6.8	0.005	5.4	0.000	0.0	0.008	N/A

B. Reproducibility

A 5-day reproducibility study was performed at 3 testing sites (1 instrument per site). Four serum and four plasma specimens (2 reactive and 2 non-reactive for each matrix) were tested using one lot of Access anti-HBc Total reagent kit, Access anti-HBc Total Calibrator, and Access anti-HBc Total QC. Samples were tested in 3 replicates per run, 2 runs per day, for 5 days. The reproducibility study results are summarized in Table 3.

Table 3. Access Anti-HBc Total reproducibility study results

Sample	N	Mean (S/CO)	Repeatability (Within Run)		Between-Run		Between-Day		Between-Site		Reproducibility	
			SD (S/CO)	%CV	SD (S/CO)	%CV	SD (S/CO)	%CV	SD (S/CO)	%CV	SD (S/CO)	%CV
S1	90	5.02	0.204	4.1%	0.041	0.8%	0.056	1.1%	0.076	1.5%	0.228	4.5%
S2	90	1.20	0.059	4.9%	0.005	0.4%	0.030	2.5%	0.043	3.6%	0.079	6.6%
S3	90	0.85	0.051	5.9%	0.000	0.0%	0.008	0.9%	0.027	3.1%	0.058	6.8%
S4	90	0.10	0.007	N/A	0.001	N/A	0.001	N/A	0.006	N/A	0.010	N/A
P1	90	5.21	0.172	3.3%	0.109	2.1%	0.031	0.6%	0.148	2.8%	0.254	4.9%
P2	90	1.15	0.065	5.6%	0.056	4.9%	0.000	0.0%	0.062	5.4%	0.105	9.2%
P3	90	0.81	0.037	4.5%	0.028	3.5%	0.022	2.7%	0.038	4.6%	0.064	7.8%
P4	90	0.09	0.007	N/A	0.003	N/A	0.001	N/A	0.005	N/A	0.009	N/A

Note: %CV are not meaningful when S/CO approaches zero. Results are noted as N/A.

2. Linearity:

N/A

3. Analytical Specificity/Interference:

A. Cross-reactivity

Potential cross-reactivity in the Access anti-HBc Total assay was evaluated using specimens with viral antibodies and from patients with related conditions. The anti-HBc total status of each specimen was verified using a commercially available comparator anti-HBc total assay. No cross-reactivity was observed. The cross-reactants, numbers of samples, and study results are summarized in Table 4.

Table 4. Cross-reactivity of Access anti-HBc Total assay

Category	Number of Samples Tested	Number of Reactive Samples by Access anti-HBc Total	Number of Nonreactive Samples by Access anti-HBc Total
Epstein-Barr virus (EBNA IgG or VCA IgG)	10	0	10
Cytomegalovirus (CMV)	10	0	10
Herpes simplex virus (HSV 1/2)	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

Category	Number of Samples Tested	Number of Reactive Samples by Access anti-HBc Total	Number of Nonreactive Samples by Access anti-HBc Total
Alcoholic liver disease	10	0	10
Primary biliary cirrhosis	10	0	10
Flavivirus (Zika)	10	0	10
Flavivirus (Dengue)	10	0	10
Flavivirus (West Nile)	10	0	10
Influenza post-vaccination	10	0	10
HAMA	10	1	9
Anti-nuclear antibody (ANA)	10	0	10
Rheumatoid Factor	10	0	10
Systemic lupus erythematosus (SLE)	10	0	10
Multiple Myeloma	10	0	10
Pregnancy multipara	10	0	10
Pregnancy first trimester	10	0	10
Pregnancy second trimester	10	0	10
Pregnancy third trimester	10	0	10
Syphilis	10	0	10
Toxoplasmosis	10	0	10
Transplant recipient	10	0	10
Dialysis patients	10	0	10
Hemophiliac / Clotting factor	10	0	10
anti-*E.coli*	10	0	10
Rubella	10	0	10
Varicella Zoster Virus (VZV)	10	0	10
Measles	10	0	10
Mumps	10	0	10

B. Interference

Potential interference of endogenous and exogenous substances was evaluated using three plasma samples: negative for anti-HBc (≥1.30 S/CO), high negative (~1.1-1.3 S/CO) and low positive (~0.7-0.9 S/CO). Each sample was spiked with each of the potential interfering substances, tested in 5 replicates, and compared to controls (sample without interferents). Of the compounds tested, none were found to cause interference using the highest test concentrations indicated in Table 5.

Table 5. Interfering Substances

Potential Interferent	Concentration Tested
Hemoglobin	500 mg/dL
Total Protein	15 g/dL
Bilirubin conjugated	40 mg/dL
Bilirubin unconjugated	40 mg/dL
Triglycerides (Intralipid)	19.20 mmol/L (2,000 mg/dL)
Aspirin (acetylsalicylic acid)	167 µmol/L
Salicylic acid	207 µmol/L

Potential Interferent	Concentration Tested
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
Cholesterol	400 mg/dL

C. Hook effect.

N/A

4. Assay Reportable Range:

N/A

5. Stability (Controls, Calibrators, or Methods):

Reagent Stability

Reagent real time stability, in-use stability, and stored curve stability studies supported the following stability claims:

Stability Study	Reagent	Storage temperature	Supported claim
Shelf-life	Access anti-HBc Total	2-10ºC	365 days
	Access anti-HBc Total Calibrator	2-10ºC	365 days
	Access anti-HBc Total QC	2-10ºC	296 days
Open vial	Access anti-HBc Total	2-10ºC	45 days
	Access anti-HBc Total Calibrator	2-10ºC	180 days
	Access anti-HBc Total QC	2-10ºC	62 days
Stored curve	Access anti-HBc Total	N/A*	56 days

*Stored curve stability study was executed with the calibration curve stored on the DxI 9000 Access Immunoassay Analyzer.

Sample Stability

A study was conducted to evaluate the effect of sample handling and storage conditions at room temperature (20 – 25°C), refrigerated (2 - 8°C), and frozen (≤ -18°C). It also evaluated sample stability after multiple freeze/thaw cycles. Sample stability studies support the following stability claims:

Storage Condition	Claimed Stability

Room Temp Storage (20-25º C)	Up to 3 Days
Refrigerated Storage (2-8º C)	Up to 7 Days
Frozen Storage (≤-20º C)	Up to 30 Days
Freeze/Thaw Cycles	No more than 4 cycles

6. Analytical Sensitivity:

A. Analytical sensitivity at cut-off

The Access anti-HBc Total assay was designed to have an analytical sensitivity of less than 1.40 IU/mL using the 1st International Standard (IS) material for Anti-HBc, NIBSC code: 95/522.

A series of dilutions were prepared using the 1st IS for Anti-HBc with target concentrations in the range of 0.1-1.0 IU/mL, using three reagent and three calibrator lots on two DxI 9000 Access Immunoassay Analyzers. The analytical sensitivity for each reagent/calibrator lot combination was determined using a quadratic model (2nd order polynomial) of log-transformed S/CO measurements versus the IS anti-HBc concentrations (IU/mL). The point estimate of the IS concentration corresponding to 1.00 S/CO was used in the analytical sensitivity estimation. The maximum overall analytical sensitivity results determined in this study are summarized below.

Standard	**Analytical Sensitivity**
1st International Standard NIBSC code: 95/522	0.69 IU/mL (95% CI: 0.69 - 0.69 IU/mL)

B. Seroconversion

Commercially available patient seroconversion panels were tested using the Access anti-HBc Total assay and a reference assay to determine the seroconversion sensitivity of the assay. Equivalent detection with no difference in bleed number was observed in 4 of the 7 panels and earlier detection by the Access anti-HBc Total assay was observed in 3 panels. The results are summarized in Table 6.

Table 6. Seroconversion Sensitivity Results

Panel ID	**First anti-HBc Total positive result from initial draw date**		**Access anti-HBc Total vs reference assay**
	Access anti-HBc Total assay (days)	**Reference assay (days)**	**Difference in bleed number for the first reactive bleed***
HBV-6281	41	41	0
HBV-9092	85	85	0
HBV-9093	49	49	0
HBV-9072	159	> 159**	≤ -1**
HBV-001	29	29	0
HBV-002	56	59	-1
HBV-004	65	71	-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 Total assay.

**The panel never seroconverted from a nonreactive status to a reactive status with the reference anti-HBc Total assay.

B Comparison Studies:

1. Method Comparison with Predicate Device:

A multi-center study was conducted using the DxI 9000 Access Immunoassay Analyzer to evaluate the ability of the Access anti-HBc Total assay to detect anti-HBc Total in serum specimens from the intended use population. The study consists of a qualitative method comparison agreement with a reference assay (FDA-approved Anti-HBc Total assay). A total of 2,391 prospectively collected specimens from individuals at increased risk for hepatitis B or with signs and symptoms of hepatitis were tested and included:

- 2,065 adult samples (non-pregnant)
- 155 pediatric samples (2-21 years)
- 171 pregnant women samples.

The HBV classification was determined for each specimen based on the reactivity patterns of 6 HBV serological marker results (HBsAg, HBeAg, anti-HBc IgM, total anti-HBc, anti-HBe, and anti-HBs).

The negative percent agreement (NPA) and positive percent agreement (PPA) results for the prospectively collected non-pregnant adults, pediatric non-pregnant, pregnant, and combined for all cohorts are presented in Tables 7-12.

Table 7. Percent Agreement between Access Anti-HBc Total and Comparator Anti-HBc Total Final Interpretation by HBV Disease Classification: Non-Pregnant Adult at Increased Risk and/or Signs and Symptoms Cohort (n=2,065)

HBV Classification	PPA		NPA	
	% (n/N)	95% CI	% (n/N)	95% CI
Acute	100.0% (1/1)	(20.7-100.0%)	100.0 (2/2)	(34.2-100.0%)
Recovery	99.5% (196/197)	(97.2-99.9%)	25.0 (1/4)	(4.6-69.9%)
Chronic	96.8% (92/95)	(91.1-98.9%)	0 (0/0)	N/A
Immune due to natural infection	97.5% (119/122)	(93.0-99.2%)	0 (0/0)	N/A
Immune due to HBV Vaccination	0 (0/0)	N/A	98.4% (692/703)	(97.2-99.1%)
Not previously infected	0 (0/0)	N/A	99.2 (922/929)	(98.5-99.6%)
Not interpretable/ Unknown profile[a]	100.0 (7/7)	(64.6-100.0%)	100.0 (3/3)	(43.9-100.0%)
Missing test data[b]	100.0 (1/1)	(20.7-100.0%)	100.0 (1/1)	(20.7-100.0%)
Total	**98.3% (416/423)**	**96.6-99.2%**	**98.7% (1,621/1,642)**	**98.1-99.2%**

[a] Samples were classified as "Not Interpretable" if their HBV seroprofile was predefined in the study protocol, and "Unknown" if not predefined. For data presentation, these are grouped as "Not Interpretable/Unknown", due to both groups having atypical seropatterns not aligning with HBV classification criteria.

[b] Samples were classified as “Missing Test Data” if insufficient volume was available to determine the HBV classification.

Table 8. Percent Agreement between Access Anti-HBc Total and Comparator Anti-HBc Total Final Interpretation by HBV Disease Classification: Pediatric Population (n=155)

HBV Classification	PPA		NPA	
	% (n/N)	95% CI	% (n/N)	95% CI
Recovery	100.0 (1/1)	(20.7-100.0%)	0 (0/0)	N/A
Immune due to natural infection	100.0 (2/2)	(34.2-100.0%)	0 (0/0)	N/A
Immune due to HBV Vaccination	0 (0/0)	N/A	100.0 (56/56)	(93.6-100.0%)
Not Previously Infected	0 (0/0)	N/A	100.0 (95/95)	(96.1-100.0%)
Not interpretable/ Unknown profile[a]	0 (0/0)	N/A	100.0 (1/1)	(20.7-100.0%)
Total	**100.0 (3/3)**	**(43.85-100.0%)**	**100.0 (152/152)**	**(97.54-100.0%)**

[a] Samples were classified as "Not Interpretable" if their HBV seroprofile was predefined in the study protocol, and "Unknown" if not predefined. For data presentation, these are grouped as "Not Interpretable/Unknown", due to both groups having atypical seropatterns not aligning with HBV classification criteria.

Analytical comparison between pediatrics and adult samples spiked with anti-HBc Total.
Thirty (30) samples from anti-HBc negative pediatric patients aged 2 to 21 were tested to determine if they provided equivalent results to anti-HBc negative adult human serum pool samples (controls) when samples were spiked with the same individual anti-HBc positive sample. Samples were spiked at a target anti-HBc value between 0.60 and 0.90 and tested with the Access Anti-HBc Total assay in replicates of three. The S/CO results for each pediatric sample were compared to the result obtained on each control sample and the difference between the pediatric sample and the control ranged from -0.052 to 0.165 S/CO.

Table 9. Percent Agreement between Access Anti-HBc Total and Comparator Anti-HBc Total Final Interpretation by HBV Disease Classification: Pregnant Population (n=171)

HBV Classification	PPA		NPA	
	% (n/N)	95% CI	% (n/N)	95% CI
Recovery	100.0 (2/2)	(34.2-100.0%)	0 (0/0)	N/A
Chronic	100.0 (1/1)	(20.7-100.0%)	0 (0/0)	N/A
Immune due to HBV Vaccination	0 (0/0)	N/A	100.0 (86/86)	(95.7-100.0%)
Not previously infected	0 (0/0)	N/A	100.0 (82/82)	(95.5-100.0%)
Total	**100.0 (3/3)**	**43.85-100.0%**	**100.0 (168/168)**	**97.76-100.0%**

Out of 171 specimens from pregnant subjects, 21 were from pregnant pediatrics. Comparison of Access Anti-HBc Total assay results to the reference results by trimester for the specimens is shown in the following Table.

Table 10. Pregnant Subjects Performance by Trimester

Trimester	Total	PPA		NPA	
		% (n/N)	95% CI	% (n/N)	95% CI
First	71	100.0 (2/2)	34.24 - 100.0	100.0 (69/69)	94.73 - 100.0
Second	67	100.0 (1/1)	20.65 - 100.0	100.0 (66/66)	94.50 - 100.0
Third	33	0 (0/0)	N/A	100.0 (33/33)	89.57 - 100.0
Overall	**171**	**100.0 (3/3)**	**43.85 - 100.0**	**100.0 (168/168)**	**97.76 - 100.0**

Analytical comparison between pregnant and adult non-pregnant samples spiked with anti-HBc Total.

Thirty (30) samples from anti-HBc negative pregnant patients were tested to determine if they provided equivalent results to anti-HBc negative adult human serum pool samples (controls) when samples were spiked with the same individual anti-HBc positive sample. These 30 samples were approximately distributed between the first, second and third trimester of pregnancy. Samples were spiked at target anti-HBc values between 0.60 and 0.90 S/CO and tested with the Access Anti-HBc Total assay in replicates of three. The S/CO results for each pregnant sample were compared to the result obtained on each control sample and the difference between the pregnant sample and the control ranged from -0.165 to 0.141 S/CO.

Table 11. Comparison of Access Anti-HBc Total Versus Comparator in all Population by HBV Classification (Adult, Pregnant, and Pediatric)

Cohort	Reference anti-HBc Total Assay				Total
	Reactive		Nonreactive		
	Access anti-HBc Total		Access anti-HBc Total		
	Nonreactive (N)	Reactive (N)	Nonreactive (N)	Reactive (N)	
Acute	0	1	2	0	**3**
Recovery	1	199	1	3	**204**
Chronic	3	93	0	0	**96**
Immune due to natural infection	3	121	0	0	**124**
Immune due to HBV Vaccination	0	0	834	11	**845**
Not Previously Infected	0	0	1,099	7	**1,106**
Not interpretable/Unknown profile[a]	0	7	4	0	**11**
Missing test data[b]	0	1	1	0	**2**
Total	**7**	**422**	**1,941**	**21**	**2,391**

[a] Samples were classified as "Not Interpretable" if their HBV seroprofile was predefined in the study protocol, and "Unknown" if not predefined. For data presentation, these are grouped as "Not Interpretable/Unknown", due to both groups having atypical seropatterns not aligning with HBV classification criteria.
[b] Samples were classified as “Missing Test Data” if insufficient volume was available to determine the HBV classification.

PPA and NPA by HBV classification for the study population is presented in the Table below.

Table 12. Percent Agreement between Access Anti-HBc Total and Comparator by HBV Disease Classification in all Population (Adult, Pregnant, and Pediatric)

HBV Classifications	Total	PPA % (N/N), [95% CI]	NPA % (N/N), [95% CI]
Acute	3	100.0% (1/1) [20.65 - 100.0%]	100.0% (2/2) [34.24 - 100.0%]
Recovery	204	99.5% (199/200) [97.22- 99.91%]	25.0% (1/4) [4.56 - 69.94%]
Chronic	96	96.9% (93/96) [91.21 - 98.93%]	N/A
Immune due to natural infection	124	97.6% (121/124) [93.13 - 99.17%]	N/A
Immune due to HBV Vaccination	845	N/A	98.7% (834/845) [97.68 - 99.27%]
Not Previously Infected	1,106	N/A	99.4% (1,099/1,106) [98.70 - 99.69%]
Not interpretable/ Unknown profile[a]	11	100.0% (7/7) [64.57 - 100.0%]	100.0% (4/4) [51.01 - 100.0%]
Missing test data[b]	2	100.0% (1/1) [20.65 - 100.0%]	100.0% (1/1) [20.65 - 100.0%]
Overall	**2,391**	**98.4% (422/429) [96.67 - 99.21%]**	**98.9% (1,941/1,962) [98.37 - 99.30%]**

[a] Samples were classified as "Not Interpretable" if their HBV seroprofile was predefined in the study protocol, and "Unknown" if not predefined. For data presentation, these are grouped as "Not Interpretable/Unknown", due to both groups having atypical seropatterns not aligning with HBV classification criteria.
[b] Samples were classified as “Missing Test Data” if insufficient volume was available to determine the HBV classification.

2. Matrix Comparison:

To verify equivalent performance between different matrices using the Access anti-HBc Total assay on the DxI 9000 Access Immunoassay Analyzer, 54 matched donor sets consisting of 9 specimen types each were evaluated. The results from the study demonstrate the equivalency between the reference sample type (serum without gel) and the 8 serum/plasma matrices evaluated (Table 13). The results support use of human serum [serum without gel and serum separator tubes (SST)], or plasma [lithium heparin, lithium heparin with gel, dipotassium (K2) EDTA, tripotassium (K3) EDTA, sodium citrate, Acid Citrate Dextrose (ACD), and Citrate Phosphate Dextrose (CPD)] sample types.

Table 13. Regression Statistics for Matrix Comparison

Tube Types	Slope	Intercept	r*
SST vs Serum no gel	0.998	-0.000	1.00
Li Heparin no Gel vs Serum no gel	1.015	0.004	1.00
Li Heparin Gel vs Serum no gel	1.016	0.008	1.00
K2 EDTA vs Serum no gel	0.985	0.013	1.00
K3 EDTA vs Serum no gel	0.999	0.016	1.00
Na Citrate vs Serum no gel	1.020	-0.001	1.00
ACD vs Serum no gel	1.021	-0.002	1.00
CPD vs Serum no gel	1.045	0.002	1.00

*r: Correlation coefficient

C Clinical Studies:

1. Clinical Sensitivity:

   N/A

2. Clinical Specificity:

   N/A

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

   N/A

D Expected Values/Reference Range:

The Access anti-HBc Total results for the study population for all clinical trial sites combined by age group and sex are summarized in the Table below. Samples were considered reactive if S/CO was < 1.00 upon testing and non-reactive if S/CO was ≥ 1.00.

Table 14. Expected Results of Access anti-HBc Total by Age and Sex

Access anti-HBc Total						
Age Range (years)	**Sex**	**Reactive**		**Nonreactive**		**Total**
		N	**%**	**N**	**%**	
2-12	Female	0	0	6	100	6
	Male	0	0	11	100	11
13-18	Female	1	2.9	33	97.1	34
	Male	0	0	24	100	24
19-21	Female	0	0	73	100	73
	Male	2	7.1	26	92.9	28
22-29	Female	6	2.0	296	98.0	302
	Male	4	3.6	106	96.4	110
30-39	Female	8	2.9	270	97.1	278
	Male	18	13.4	116	86.6	134
40-49	Female	21	10.8	173	89.2	194
	Male	42	25.8	121	74.2	163
50-59	Female	64	23.6	207	76.4	271
	Male	105	42.9	140	57.1	245
60-69	Female	47	27.6	123	72.4	170
	Male	90	45.7	107	54.3	197
70-79	Female	15	26.3	42	73.7	57
	Male	15	25.0	45	75.0	60
80-89	Female	2	20.0	8	80.0	10

	Male	3	16.7	15	83.3	18
90+	Female	0	0	1	100	1
	Male	0	0	5	100	5
Total		**443**	**18.5**	**1,948**	**81.5**	**2,391**

E Other Supportive Instrument Performance Characteristics Data:

Within-Assay Sample Carryover:
Testing was conducted to assess the sample-to-sample and sample-to-reagent pack carryover on the DxI 9000 Access Immunoassay Analyzer. Sample carryover testing was completed by running a sequence of alternating low (negative) and high anti-HBc serum samples. The acceptance criteria were met. Therefore, the Access anti-HBc Total assay is not susceptible to within-assay sample carryover.

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

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.