

SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Hepatitis B Surface Antigen (HBsAg)
Hepatitis B Surface Antigen Confirmatory

Device Trade Name: Access HBsAg
Access HBsAg Confirmatory
Access HBsAg Calibrator
Access HBsAg QC

Device ProCode: LOM

Applicant's Name and Address: Beckman Coulter, Inc.
1000 Lake Hazeltine Drive
Chaska, MN 55318

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P230015

Date of FDA Notice of Approval: October 17, 2025

II. INDICATIONS FOR USE

Access HBsAg

The Access HBsAg assay is a paramagnetic particle, chemiluminescent immunoassay for the *in vitro* qualitative detection of hepatitis B surface antigen (HBsAg) in human pediatric (7 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 (CDP)] using the DxI 9000 Access Immunoassay Analyzer.

The Access HBsAg assay is used for the laboratory diagnosis of acute or chronic hepatitis B virus (HBV) infection in individuals with signs and symptoms of hepatitis or at risk for hepatitis B virus infection, when used in conjunction with other serological and clinical information. The assay may also be used to screen for HBV infection in pregnant women to identify neonates who are at risk of acquiring hepatitis B during the perinatal period.

The Access HBsAg assay is for use on the DxI 9000 Access Immunoassay Analyzer only.

This assay has not been approved for use in the screening of blood, plasma, or tissue donors or cadaveric specimens.

Access HBsAg Confirmatory

The Access HBsAg Confirmatory assay is a paramagnetic particle, chemiluminescent immunoassay for the *in vitro* qualitative confirmation of the presence of hepatitis B surface antigen (HBsAg) in human pediatric (7 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 (CDP)] that have been found to be repeatedly reactive in the Access HBsAg assay using the Access DxI 9000 Immunoassay Analyzer.

The Access HBsAg Confirmatory assay is for use on the DxI 9000 Access Immunoassay System only.

Access HBsAg Calibrator

The Access HBsAg Calibrator is intended to calibrate the Access HBsAg and HBsAg Confirmatory assays for the *in vitro* qualitative detection and confirmation of hepatitis B surface antigen (HBsAg) in human serum and plasma using the DxI 9000 Access Immunoassay Analyzer.

Access HBsAg QC

The Access HBsAg QC is intended for monitoring system performance of the Access HBsAg and Access HBsAg Confirmatory assays. The Access HBsAg QC is for use on the DxI 9000 Access Immunoassay Analyzer.

III. CONTRAINDICATIONS

There are no known contraindications.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Access HBsAg, Access HBsAg Confirmatory, Access HBsAg Calibrator, and Access HBsAg QC labeling.

V. **DEVICE DESCRIPTION**

Kit Configurations and Components

The Access HBsAg assay (2 packs, 100 tests/pack) is for the qualitative determination of HBsAg, and is comprised of the following:

Table 1: Access HBsAg Reagent Pack Composition

Well	Contents	Ingredients
R1a	3.30 mL	Paramagnetic particles coated with streptavidin coupled to biotinylated monoclonal (mouse) HBsAg antibodies in TRIS buffer, surfactant, protein (bovine), < 0.1% sodium azide and 0.1% ProClin* 300.
R1b	3.00 mL	MES buffer, protein (bovine), < 0.1% sodium azide, and 0.1% ProClin 300.
R1c	3.20 mL	MES buffer, polyclonal (caprine) HBsAg antibody alkaline phosphatase conjugate, surfactant, protein (bovine, caprine and mouse), < 0.1% sodium azide and 0.1% ProClin 300.

*ProClin™ is a trademark of LANXESS Corp.

The Access HBsAg Confirmatory assay (2 packs, 50 determinations/pack) is for the confirmation of the presence of HBsAg, and is comprised of the following:

Table 2: Access HBsAg Confirmatory Reagent Pack Composition

Well	Contents	Ingredients
R1a	3.30 mL	Paramagnetic particles coated with streptavidin coupled to biotinylated monoclonal (mouse) HBsAg antibodies in TRIS buffer, surfactant, protein (bovine), < 0.1% sodium azide and 0.1% ProClin* 300.
R1b	2.10 mL	MES buffer, protein (bovine), < 0.1% sodium azide, and 0.1% ProClin 300.
R1c	3.20 mL	MES buffer, polyclonal (caprine) HBsAg antibody alkaline phosphatase conjugate, surfactant, protein (bovine, caprine and mouse), < 0.1% sodium azide and 0.1% ProClin 300.
R1d	1.20 mL	MES buffer, polyclonal (equine) HBsAg antibody, protein (bovine), < 0.1% sodium azide and 0.1% ProClin 300.

*ProClin™ is a trademark of LANXESS Corp.

The Access HBsAg Calibrator contains one level (positive for HBsAg) calibrator that is ready to use (C1): 2.0 mL/vial.

Table 3: Access HBsAg Calibrator Composition

Description	Contents	Ingredients
C1	1 vial	TRIS buffer with HBs antigen (human), protein (bovine), < 0.1% sodium azide, and 0.5% ProClin* 300.
Calibration Card	2 cards	Card 1 is for use with the Access HBsAg assay (REF C39422) Card 2 is for use with the Access HBsAg Confirmatory assay (REF C39425)

*ProClin™ is a trademark of LANXESS Corp.

The Access HBsAg QC set contains two controls (negative and positive) that are ready to use (QC1-QC2): 4.0 mL/vial, 3 vials each level.

Table 4: Access HBsAg QC Composition

Description	Contents	Ingredients
QC1	3 vials	Human serum negative for HBsAg, < 0.1% sodium azide, and 0.5% ProClin* 300.
QC2	3 vials	TRIS Buffer, human serum, HBs antigen, protein (bovine), < 0.1% sodium azide, and 0.5% ProClin 300.
QC Value Card	2 cards	Card 1 is for use with the Access HBsAg assay (REF C39422) Card 2 is for use with the Access HBsAg Confirmatory assay (REF C39425)

*ProClin™ is a trademark of LANXESS Corp.

In addition, the following components are required.

1. UniCel DxI Wash Buffer II is used to dilute patient samples for testing with the Access HBsAg Confirmatory assay.
2. The Access HBsAg and Access HBsAg Confirmatory assay protocol files (APF) must be installed on the DxI Access 9000 Immunoassay Analyzer prior to performing the assays.
3. The DxI Access 9000 Immunoassay Analyzer is designed to perform fully automated immunoassay tests based on the use of chemiluminescent detection technology, cleared under K221225.

Assay Principle and Format

Access HBsAg

The Access HBsAg assay is a one-step enzyme immunoassay. Paramagnetic particles coated with monoclonal HBsAg antibodies, alkaline phosphatase coupled to polyclonal HBsAg antibodies and sample are added to a reaction vessel. HBsAg present in the patient sample is bound by the anti-HBsAg coated on the paramagnetic particles and the anti-HBsAg-alkaline phosphatase conjugate. After incubation in a reaction vessel, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. A chemiluminescent substrate is added to the vessel and light generated by the reaction is measured with a luminometer. The light production is compared to the cut-off value defined during calibration on the instrument. Qualitative assessment is automatically determined from a stored calibration.

Access HBsAg Confirmatory

The Access HBsAg Confirmatory assay uses the principle of neutralization by an excess of HBsAg-specific antibodies (neutralization reagent) to confirm the presence of HBsAg in samples found repeatedly reactive in the Access HBsAg assay. The confirmatory assay reports percent neutralization (suppression) of a control assay with a neutralization reagent.

Paramagnetic particles coated with monoclonal HBsAg antibodies, alkaline phosphatase coupled to polyclonal HBsAg antibodies and sample are added to two separate reaction vessels, one containing neutralization reagent, and the other containing diluent (control). If HBsAg is present in the sample, the HBsAg specific antibodies of the neutralization reagent bind to the antigenic determinants which can no longer bind to the antibodies of the solid phase and conjugate. After incubation in a reaction vessel, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. A chemiluminescent substrate is added to each vessel and light generated by the reaction is measured with a luminometer. Both neutralization and diluent (control) tests are automatically run on the system. Percent neutralization is determined by comparison of the light generated with the neutralization reagent to that of the diluent (control).

Access HBsAg Calibrator

The Access HBsAg Calibrator is used to establish calibration (determine the cut-off value) for the Access HBsAg and Access HBsAg Confirmatory assays. By comparing the light intensity generated by a sample to the cut-off value, the presence or absence of hepatitis B virus surface antigen in the sample is determined.

Access HBsAg QC

Quality control (QC) materials simulate the characteristics of patient samples and are essential for monitoring the system performance of the Access HBsAg and Access HBsAg Confirmatory assays. In addition, they are an integral part of good laboratory practices. When performing assays with Access reagents for HBsAg, include quality control materials to validate the integrity of the assays. The assayed values should fall within the acceptable range if the test system is working properly.

Interpretation of Results

Access HBsAg

Test results are determined automatically by the system software. Results (Signal/Cut-off (S/CO)) are reported to be “reactive” or “nonreactive” as a function of their relationship with the “cut-off” (signal “greater than or equal to” or “less than” the cut-off value).

The high positive cut-off value (≥ 100.00 S/CO of HBsAg) for not performing repeat testing on Access HBsAg or confirmation testing on the Access HBsAg Confirmatory was determined using a population of reactive and nonreactive clinical samples. The cut-off was validated by comparing results from samples with initial S/CO values ≥ 100.00 with the final result using the Access HBsAg Confirmatory assay, as well as the final interpretation using commercially available reference HBsAg Qualitative and reference HBsAg Confirmatory assays. In this study, 399/423 (94.3%) samples initially reactive with Access HBsAg assay fell into the ≥ 100.00 S/CO range and 100.0% (399/399) were confirmed positive using the Access HBsAg Confirmatory assay. Positive percent agreement (PPA) of the Access HBsAg assay with the HBsAg reference assay final interpretation was also 100.0% with a lower bound 2-sided 95% score confidence interval of 99.0%.

Table 5: Access HBsAg Assay Results Interpretation

	Result (S/CO)	Interpretation	Reporting Instructions	Retest Procedure
Initial Results	< 1.00	Nonreactive	Report result as nonreactive for HBsAg	No retest required
	≥ 1.00 to < 100.00	Reactive	Report as initial reactive for HBsAg	Retest in duplicate
	≥ 100.00	Reactive	Report as positive (reactive) for HBsAg	No retest or additional confirmatory testing required
Duplicate Retest Results	Both results < 1.00	Nonreactive	Report result as nonreactive for HBsAg	No retest required
	One or both results ≥ 1.00	Reactive	Report result as repeat reactive for HBsAg	Confirm repeat reactive result in Access HBsAg Confirmatory assay (REF C39425). Samples that are confirmed using the neutralization reagent can be considered positive for the presence of HBsAg.

Access HBsAg Confirmatory

Access HBsAg Confirmatory test results are determined automatically by the system software. The presence of HBsAg in a reactive sample is confirmed if the calculations performed by the DxI 9000 Access Immunoassay Analyzer show a Signal/Cut-off (S/CO) ratio that is ≥ 1.00 , and a percent neutralization (%NT) that is $\geq 50\%$.

Samples with a S/CO ratio that is ≥ 1.00 and $< 50\%$ neutralization may be diluted up to 1:62,500, as indicated in the following table.

Table 6: Access HBsAg Confirmatory Assay Results Interpretation

Sample	Result (S/CO)	Percent Neutralization (%NT)	Reporting Instructions	Retest Procedure
Neat sample	< 1.00	Not applicable	Nonreactive for the presence of HBsAg	No retest required
	≥ 1.00	$\geq 50\%$	Confirmed positive for the presence of HBsAg	No retest required
	≥ 1.00	$< 50\%$	Not Confirmed	Dilute sample 1:250 and run in Access HBsAg Confirmatory assay
1: 250 diluted sample	< 1.00	Not applicable	Nonreactive for the presence of HBsAg	No retest required
	≥ 1.00	$\geq 50\%$	Confirmed positive for the presence of HBsAg	No retest required
	≥ 1.00	$< 50\%$	Not Confirmed	Dilute sample 1:62,500 and run in Access HBsAg Confirmatory assay
1:62,500 diluted sample	< 1.00	Not applicable	Nonreactive for the presence of HBsAg	No retest required
	≥ 1.00	$\geq 50\%$	Confirmed positive for the presence of HBsAg	No retest required

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the detection of hepatitis B virus (HBV) surface antigen (HBsAg). There are currently several FDA approved *in vitro* diagnostic tests commercially available for serological markers of hepatitis B virus (HBV) which, when used in conjunction with a patient's medical history, clinical examination, and other laboratory findings, may be used as an aid in the diagnosis of HBV infection in patients with symptoms of hepatitis or who may be at risk for HBV infection. The assay may be used to screen for hepatitis B infection in pregnant women to identify neonates at high risk of acquiring HBV during perinatal period. 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 their expectations and lifestyle.

VII. MARKETING HISTORY

The Access HBsAg, Access HBsAg Confirmatory, Access HBsAg Calibrator, and Access HBsAg QC have not been marketed in the United States but is legally marketed in the European Union. The Access HBsAg, Access HBsAg Confirmatory, Access HBsAg Calibrator, and Access HBsAg QC have not been withdrawn from marketing for any reason related to its safety or effectiveness.

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

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

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

For the specific adverse events that occurred in the clinical study, please see Section X.D.1 below.

IX. SUMMARY OF NON-CLINICAL STUDIES

A. Laboratory Studies

1. Cut-Off Determination

The Access HBsAg and the Access HBsAg Confirmatory assays utilize a signal to cut-off ratio to define sample HBsAg status. The ratio of relative light units (RLUs) to an established cut-off determined during the assay calibration on the instrument indicates the presence or absence of HBsAg. The cut-offs of the Access HBsAg and the Access HBsAg Confirmatory assays were established by testing a total of 3,750 samples including characterized HBsAg positive samples, HBsAg negative samples, and samples. The evaluation was based on CLSI EP24-A2, *Assessment of the Diagnostic Accuracy of Laboratory Tests Using Receiver Operating Characteristic Curves; Approved Guideline – 2nd Edition*. Receiver Operating Characteristics (ROC) analyses were performed on the results of the specimens tested. The assays' cut-offs were evaluated with the observed results to demonstrate that their selection represent the best compromise between diagnostic specificity and diagnostic sensitivity. ROC curve analysis provided sensitivity (true positive proportion) and specificity (true negative proportion) values based on the manufacturer's working calibrator (WC-1) S/CO. The cut-off for the Access HBsAg assay is 1.0 S/CO. The cutoff for the Access HBsAg confirmatory assay is 1.0 S/CO with a percent neutralization ration (NR%) of $\geq 50\%$.

2. Analytical Sensitivity at the Cut-off (1.0 S/CO)

The ability of the Access HBsAg and Access HBsAg Confirmatory assays to detect low concentrations of the Third International Standard (IS) material for HBsAg, NIBSC code: 12/226 was evaluated.

The IS material was reconstituted according to manufacturer's instructions with 1 mL water to obtain a stock solution (47.30 IU/mL). A dilution series of six serum and six plasma levels were prepared with spiked amounts of the IS stock solution into each negative matrix to target HBsAg sample concentrations ranging from 0.01 – 0.1 IU/mL. Each dilution was tested in triplicate using three lots each of Access HBsAg assay, Access HBsAg Confirmatory assay, and Access HBsAg Calibrator. The analytical sensitivity for each sample type and reagent/calibrator lot combination was determined by a linear fit regression of sample S/CO values versus the IS stated concentrations (IU/mL). The point estimate of the IS concentration corresponding to 1.00 S/CO was used in the analytical sensitivity estimation. For each assay, the final analytical sensitivity is the maximum analytical sensitivity of all the reagent pack lot/calibration combinations tested.

The Access HBsAg and Access HBsAg Confirmatory assays were designed to have an analytical sensitivity of less than or equal to 0.03 IU/mL using the same IS material for HBsAg (HBV genotype B4, HBsAg subtypes ayw1/adw2) NIBSC code: 12/226. The overall results obtained are summarized below.

Access HBsAg assay: 0.025 IU/mL (95% CI: 0.024 – 0.026 IU/mL)

Access HBsAg Confirmatory assay: 0.019 IU/mL (95% CI: 0.018 – 0.020 IU/mL).

3. Limit of Detection

A limit of detection (LoD) study was conducted on the DxI 9000 Access Immunoassay Analyzer following methods described in CLSI guideline EP17-A2 using dilutions of the 3rd International standard material, NIBSC code: 12/226. Five (5) dilutions in serum and five (5) dilutions in plasma were prepared ranging from 0.020 IU/mL to 0.024 IU/mL, and each dilution level was tested across three reagent lots.

The LoD was determined for serum and plasma for each reagent lot by modeling the relationship between the percent of replicates detected ($S/CO \geq 1.00$) and sample concentration using the Probit approach to calculate the concentration corresponding to 95% probability of detection. The maximum observed LoD value across reagent lots was 0.024 IU/mL for both plasma and serum sample types.

4. Genotype and Subtype Detection

Genotype detection was evaluated using two commercially available genotype panels (22 samples) and two patient samples containing genotypes A through H. A total of 24 panel members (A (4), B (3), C (4), D (4), E (2), F (3), G (1) and H (3)) were tested using the Access HBsAg and Access HBsAg Confirmatory assays. Fifteen of these samples were from the 1st International Reference Panel for Hepatitis B Virus (HBV) Genotypes for Hepatitis B Virus Surface Antigen (HBsAg) assays, PEI Code 6100/09.

A total of 9 commercially available subtypes, (adw2 (1), adw4 (1), adr (1), ayw1 (1), ayw2 (1), ayw3 (2), ayw4 (1), and ayr (1), were tested using the Access HBsAg and Access HBsAg Confirmatory assays.

Each sample was tested in a single replicate using one DxI 9000 Access Immunoassay Analyzer, one lot of Access HBsAg, one lot of Access HBsAg Confirmatory, and three lots of Access HBsAg Calibrator run in duplicate. All genotypes and subtypes were found to be reactive using the Access HBsAg assay, verified reactive using the reference HBsAg assay, and confirmed reactive for the presence of HBsAg using the Access HBsAg Confirmatory assay.

5. HBsAg Mutant Detection

A total of thirty HBsAg mutant samples (10 native and 20 recombinants internally created and verified by DNA sequencing), containing modifications between HBsAg amino acids 100 through 170 and representing mutants commonly reported in literature, were evaluated in singlicate with one lot each of the Access

All mutant HBsAg samples were recognized (100.0%) using the Access HBsAg assay, verified reactive with the reference assay, and confirmed reactive with HBsAg assay, Access HBsAg Confirmatory assay and HBsAg Calibrator on one DxI 9000 Immunoassay Analyzer. These same thirty samples were also tested with the reference assays (Qualitative and Confirmatory).

Access HBsAg Confirmatory and reference confirmatory assays. The list of all mutants tested and detected as reactive are listed in Table 7.

Table 7: HBsAg Mutations Evaluated (Native and Recombinant)

Mutant Type	Mutation
Native	Q129R+G130N, T126N, G130R+S132Y, P120S+F134I, T126A, Q129H+D144A, T118A (2), Y137F, M133L
Recombinant	P142S, S143L, G145R, C137W, P142S+G145R, 122NT, C124R, D144A, F134H, G130N, K122T, L109I, M133T, P127T, Y161F, Q129H, T123N, T126S, T131A, Y100C

6. Within Assay Sample Carryover (Intra-Assay)

The study was performed to evaluate the susceptibility of the Access HBsAg assay to within-assay sample carryover. High sample carryover testing was completed by running a sequence of alternating low (negative) and high HBsAg serum samples. Carryover testing was performed using one lot each of Access HBsAg and Access HBsAg Calibrator on one DxI 9000 Access Immunoassay Analyzer.

The acceptance criteria were met. Therefore, the Access HBsAg assay is not susceptible to within-assay sample carryover.

7. Interfering Substances (Endogenous/Exogenous)

The study was performed using a paired differences approach, as described in CLSI EP07, *Interference Testing in Clinical Chemistry; Approved Guideline – 3rd Edition*. Each substance was tested with matched samples (Control and Test for each interferent) run on the same day at three analyte levels (negative, low positive, and moderate positive) in seven replicates using one DxI 9000 Access Immunoassay Analyzer, one lot each of Access HBsAg, Access HBsAg Confirmatory, and Access HBsAg Calibrator. No significant interference was observed at the following concentrations. Refer to Table 8.

Table 8: Interfering Substances

Substance	Highest Concentration Added
Hemoglobin	1,000 mg/dL
Total protein	15 g/dL
Bilirubin Conjugated	43 mg/dL
Bilirubin Unconjugated	43 mg/dL
Intralipid	38.54 mg/mL (37 mmol/L)
Biotin	3,510 ng/mL
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	862.26 µmol/L
Sertraline	3.03 µmol/L

8. Cross reactivity (Analytical Specificity) and Microbial Interference
The study was conducted per CLSI EP07, *Interference Testing in Clinical Chemistry-Approved Guideline, 3rd Edition* to evaluate the Access HBsAg and Access HBsAg Confirmatory assays for potential cross-reactivity in specimens from individuals with various medical conditions. Confirmation of cross-reactivity status of serum or plasma samples was obtained from the certificate of analysis (CoA) of each stock sample.

A total of 401 HBsAg negative samples were tested using the Access HBsAg assay, and a total of 80 HBsAg positive samples were tested using the Access HBsAg Confirmatory assay. Sample status was verified using a reference HBsAg assay to confirm an initial negative result. For the Access HBsAg assay, viral antigen samples were diluted in normal human serum, and bacterial samples were prepared by spiking HBsAg negative samples with bacterial cultures before testing. For the Access HBsAg Confirmatory assay, viral antigen samples and bacterial samples were diluted in normal human serum spiked with HBsAg positive samples before testing.

All negative samples remained unimpacted in the presence of cross reactants. All HBsAg-spiked samples were found reactive and were confirmed with the Access HBsAg Confirmatory assay. Results are presented in Table 9.

Table 9: Cross Reactivity (Analytical Specificity)

Category	Access HBsAg and Reference HBsAg Assay Final Interpretation			Access HBsAg Confirmatory Final Interpretation		
	Samples tested	Number of Reactive samples	Number of Non-reactive samples	Number of spiked samples tested	Number of Reactive and Confirmed	Number of Non-reactive and Non-confirmed
Epstein-Barr Virus (EBV IgG)	10	0	10	2	2	0
Cytomegalovirus (CMV IgG and IgM)	10	0	10	2	2	0
Herpes Simplex Virus (HSV 1/2 IgG)	10	0	10	2	2	0
Human Immunodeficiency Virus (anti-HIV-1/2)	10	0	10	2	2	0
Hepatitis A Virus (HAV)	10	0	10	2	2	0
Hepatitis C Virus (anti-HCV)	10	0	10	2	2	0
Hepatitis E Virus (HEV)	10	0	10	2	2	0
Alcoholic Liver Disease	10	0	10	2	2	0
Primary Biliary Cirrhosis	10	0	10	2	2	0
Flavivirus (Zika)	11	0	11	2	2	0
Flavivirus (Dengue)	8	0	8	2	2	0
Flavivirus (Zika + Dengue)	2	0	2	N/A	N/A	N/A
Flavivirus (West Nile)	10	0	10	2	2	0
Influenza Post Vaccination	10	0	10	2	2	0
HAMA	10	0	10	2	2	0
Anti-Nuclear Antibody (ANA)	10	0	10	2	2	0
Rheumatoid Factor	10	0	10	2	2	0
Systemic Lupus Erythematosus (SLE)	10	0	10	2	2	0
Pregnancy Multipara	10	0	10	2	2	0
Pregnancy First Trimester	10	0	10	2	2	0
Pregnancy Second Trimester	10	0	10	2	2	0
Pregnancy Third Trimester	10	0	10	2	2	0
Syphilis	10	0	10	2	2	0
Toxoplasmosis (Anti-Toxo IgG)	10	0	10	2	2	0
Transplant / Transplant Recipient	10	0	10	2	2	0
Dialysis patients	10	0	10	2	2	0
Hemophiliac / Clotting Factor	10	0	10	2	2	0
<i>S.aureus</i>	10	0	10	2	2	0
<i>P.aeruginosa</i>	10	0	10	2	2	0
<i>E.coli</i>	10	0	10	2	2	0

In addition, Access HBsAg and Access HBsAg Confirmatory assays were evaluated for 11 other disease categories by spiking 10 negative samples with antigen for each of the following categories: Cytomegalovirus (CMV), Epstein-Bar virus (EBV), Hepatitis A Virus (HAV), Hepatitis C Virus (HCV), Hepatitis E Virus (HEV), Human Immunodeficiency Virus (HIV), Herpes Simplex virus (HSV1/2), Rubella, Varicella Zoster Virus (VZV), Toxoplasmosis, and Syphilis. No cross reactivity was observed.

9. Sample Type Equivalency

The study was conducted using a protocol based on CLSI EP09c, *Measurement Procedure Comparison and Bias Estimation Using Patient Samples Approved Guideline – 3rd Edition*, to establish the equivalence of serum and plasma specimens. Matched sample sets from 80 individuals were used to create test samples for use in this study. A total of 40 of the matched sets of HBsAg negative samples were tested as true negative samples in the study, and the remaining 40 sets were used to prepare positive samples. Serum (without gel) served as the reference sample type. The samples from each sample set were tested in two replicates using one lot each of Access HBsAg, Access HBsAg Confirmatory, and Access HBsAg Calibrator on one DxI 9000 Access Immunoassay Analyzer. The results from reactive samples tested with the Access HBsAg assay were verified with the Access HBsAg Confirmatory assay to confirm the “reactive” status of the positive samples.

The results from the study demonstrate the equivalency between the reference sample type and the eight serum/plasma matrices evaluated. The results support the use of human serum (serum without gel and serum separator tubes) or plasma (lithium heparin, lithium heparin separator tube, dipotassium (K₂) EDTA, tripotassium (K₃) EDTA, sodium citrate, Acid Citrate Dextrose (ACD), and Citrate Phosphate Dextrose (CPD)) to detect hepatitis B virus surface antigen using Access HBsAg and Access HBsAg Confirmatory assays. Results are presented in Table 10.

Table 10: Sample Type Equivalence

Sample Type	Slope (95% Confidence Interval: Lower 95% CI – Upper 95% CI)	Correlation Coefficient (r)
Serum	N/A	N/A
Serum separator tube	1.02 (1.00 – 1.04)	1.00
Plasma Lithium Heparin	0.99 (0.97 – 1.01)	1.00
Plasma Lithium Heparin separator tube	0.99 (0.98 – 1.01)	1.00
Plasma K ₂ EDTA	0.99 (0.97 - 1.00)	1.00
Plasma K ₃ EDTA	0.99 (0.97 - 1.03)	1.00
Plasma Sodium Citrate	1.00 (0.98 - 1.01)	1.00
Plasma ACD	0.96 (0.95 – 0.98)	1.00
Plasma CPD	1.00 (0.98 - 1.02)	1.00

10. Hook Effect

The purpose of this study was to determine whether high levels of HBsAg in patient specimens result in a hook effect impacting the results reported with the Access HBsAg and Access HBsAg Confirmatory assays on the DxI 9000 Immunoassay Analyzer. The highest available HBsAg positive human specimens at concentrations of 3.01 mg/mL HBsAg Ad and 2.52 mg/mL HBsAg Ay were used as positive stocks for this study. A series of ten-fold dilutions of the high positive samples were prepared using negative serum. The samples were tested in three replicates using one DxI 9000 Access Immunoassay Analyzer and one lot each of Access HBsAg, Access HBsAg Confirmatory, and Access HBsAg Calibrator. The Access HBsAg and Access HBsAg Confirmatory assays do not demonstrate any “hook” effect up to 2.5 mg/mL.

11. Within Laboratory Precision (20 days)

A precision study was performed to evaluate the precision performance of the Access HBsAg assay based on guidance from the CLSI EP05-A3, *Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – 3rd Edition*. The study design included two test runs per day over 20 test days. A ten-member panel of serum (S1-S5), plasma (P1-P5) patient samples and one lot of QC (QC1-QC2) were assayed in each run with patient samples tested in triplicate. Three lots of Access HBsAg reagents, two lots of calibrators and two lots of QC were tested on one DxI 9000 Access Immunoassay Analyzer for the study. The results presented in the following table are overall results.

The assay was designed to have within-laboratory imprecision of ≤ 0.100 S/CO SD at concentrations of < 1.00 S/CO and $\leq 10.0\%$ CV at concentrations ≥ 1.00 S/CO.

Table 11: Precision

Sample	Mean (S/CO)	N	Repeatability		Between-Run		Between-Day		Within Laboratory (Total)	
			(Within-Run)							
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
QC1	0.12	1,440	0.00	N/A	0.00	N/A	0.00	N/A	0.01	N/A
QC2	2.90	1,440	0.05	1.7	0.03	1.1	0.06	1.9	0.15	5.3
P1	0.12	1,440	0.00	N/A	0.00	N/A	0.00	N/A	0.01	N/A
P2	1.28	1,440	0.02	1.5	0.01	1.1	0.02	1.7	0.07	5.3
P3	3.18	1,440	0.05	1.5	0.05	1.7	0.05	1.4	0.17	5.2
P4	6.23	1,440	0.10	1.7	0.08	1.4	0.11	1.8	0.34	5.4
P5	156.97	1,440	2.63	1.7	1.97	1.3	2.42	1.5	10.88	6.9
S1	0.11	1,440	0.00	N/A	0.00	N/A	0.00	N/A	0.01	N/A
S2	1.23	1,440	0.02	1.5	0.01	1.1	0.02	1.7	0.06	5.1
S3	2.91	1,440	0.04	1.5	0.03	1.2	0.05	1.6	0.15	5.1
S4	4.51	1,440	0.07	1.6	0.05	1.1	0.08	1.7	0.23	5.1
S5	152.09	1,440	2.53	1.7	1.59	1.0	2.56	1.7	10.33	6.8

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

12. Analyte Detection in Serum (Seroconversion)

The study was conducted to determine the seroconversion sensitivity of the Access HBsAg and Access HBsAg Confirmatory assays. Thirty HBV seroconversion panels obtained from commercial vendors were tested on the DxI 9000 Access Immunoassay Analyzer using the Access HBsAg and Access HBsAg Confirmatory assays. The same panels were tested with the qualitative reference assay and samples found reactive were also tested using the confirmatory reference assay. The Access HBsAg assay shows detection of analyte equal to the reference assay for all panels except three. The Access HBsAg assay detected analyte and exhibited a reactive status one draw later than the reference assay in panels HBV6278 and PHM939, while it detected two draws later than the reference assay in panel HBV6290. All bleeds detected by Access HBsAg assay as reactive were confirmed reactive by the Access HBsAg Confirmatory assay. Results are summarized in the following table.

Table 12: Seroconversion

Panel ID	HBsAg Positive Result from Initial Draw Date		Access HBsAg vs. Reference Assay
	Access HBsAg (days)	Reference Assay (days)	Difference in Bleed Number*
SCP-HBV-002	16	16	0
SCP-HBV-004	18	18	0
SCP-HBV-006	13	13	0
HBV6273	14	14	0
HBV6275	7	7	0
HBV6277	33	33	0
HBV6278	12	8	+1
HBV6279	26	26	0
HBV6280	13	13	0
HBV6282	19	19	0
HBV6283	26	26	0
HBV6284	50	50	0
HBV6285	40	40	0
HBV6286	33	33	0
HBV6290	21	14	+2
HBV6291	27	27	0
HBV9099	16	16	0
HBV11000	21	21	0
HBV11001	44	44	0
HBV11003	142	142	0
HBV11007	34	34	0
HBV11011	103	103	0
HBV11012	18	18	0
HBV11017	40	40	0
HBV11029	35	35	0
HBV11052	37	37	0
HBV11056	33	33	0
PHM937	2	2	0
PHM939	11	3	+1
PHM941	7	7	0

* The difference in bleed number is compared to the reference assay. For example, +1 indicates that the reference assay required 1 less bleed before reactivity was determined compared to the Access HBsAg assay.

13. Reproducibility

A 5-day reproducibility study was performed based on CLSI EP05-A3, *Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – 3rd Edition*. A ten-member panel of patient samples, including serum (S1-S5) and plasma (P1-P5) samples were assayed at three external clinical sites using one lot of Access HBsAg reagent kits, on three instruments. Each panel member was assayed in replicates of three with two runs per day. The results are summarized in Table 13.

Table 13: Combined Site Reproducibility

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	0.11	0.02	N/A	0.00	N/A	0.00	N/A	0.01	N/A	0.02	N/A
S2	90	1.23	0.12	9.9	0.01	0.8	0.04	2.9	0.06	4.7	0.14	11.4
S3	90	2.94	0.32	10.8	0.05	1.8	0.07	2.2	0.04	1.5	0.33	11.2
S4	90	4.56	0.44	9.6	0.00	0.0	0.16	3.6	0.20	4.4	0.51	11.2
S5	90	155.93	19.45	12.5	5.48	3.5	4.29	2.8	2.29	1.5	20.79	13.3
P1	90	0.12	0.02	N/A	0.00	N/A	0.00	N/A	0.01	N/A	0.02	N/A
P2	90	1.28	0.13	10.3	0.00	0.0	0.02	1.7	0.03	2.1	0.14	10.7
P3	90	3.20	0.34	10.5	0.04	1.1	0.03	0.9	0.06	1.7	0.34	10.7
P4	90	6.34	0.57	9.0	0.09	1.4	0.07	1.1	0.11	1.8	0.59	9.3
P5	90	159.12	17.86	11.2	5.79	3.6	3.46	2.2	2.86	1.8	19.3	12.1

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

14. 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 (\leq -18°C). It also evaluated sample stability after multiple freeze/thaw cycles. The data demonstrated that samples may be used with the Access HBsAg and Access HBsAg Confirmatory assays when:

1. Stored at 2-8°C for up to 6 days
2. Stored at 20-25°C for up to 72 hours
3. Stored at -20°C or colder for up to 30 days. Do not thaw more than 5 times.

15. Reagent Stability Studies

Real Time Stability: A stability study was performed to establish the shelf-life of Access HBsAg, Access HBsAg Confirmatory, Access HBsAg Calibrator, and Access HBsAg QC with three lots, each stored at the recommended storage temperature of 2-10°C throughout the study duration. The study demonstrated that reagents are stable when stored at 2-10°C as follows:

1. Access HBsAg reagent pack – 120 days
2. Access HBsAg Confirmatory reagent pack – 120 days
3. Access HBsAg Calibrator – 90 days
4. Access HBsAg QC – 318 days

In-Use Stability: A stability study was performed to verify the performance of Access HBsAg, Access HBsAg Confirmatory, Access HBsAg Calibrator, and Access HBsAg QC at the recommended open storage conditions (2-10°C). The results showed that Access HBsAg and Access HBsAg Confirmatory are stable for 56 days after initial use, Access HBsAg Calibrator is stable for 180 days after initial use, and Access HBsAg QC are stable for 90 days after initial use.

Stored Curve Stability: The stability study was performed to establish the stored curve stability of the Access HBsAg and Access HBsAg Confirmatory assays on the DxI 9000 Access Immunoassay Analyzer. The results showed that, for the Access HBsAg and the Access HBsAg Confirmatory assays, calibration is required every 56 days.

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 of the Access HBsAg and Access HBsAg Confirmatory for the detection of hepatitis B surface antigen using samples that would routinely be tested for hepatitis in the US. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

A multi-center study was conducted between 2019 and 2025 at three clinical testing sites in the United States. Specimens were collected from a total of forty-two (42) sites and 4 vendors. A total of 3,614 specimens were tested and analyzed with the Access HBsAg assay and a reference HBsAg assay from the following categories:

- 3,150 prospective samples:
 - 2,474 adult samples (non-pregnant)
 - 181 pediatric samples
 - 495 pregnant women samples
- 464 retrospective specimens from known positive, acute or chronically ill adult subject specimens were tested and analyzed with the Access HBsAg assay and a Comparator HBsAg assay.

The prospective study population was as follows:

- The majority of patients were female (65% female and 35% male).
- 62.6% White, 26.7% Black or African American, 1.4% Asian, 1.4% American Indian or Alaska Native, 0.2% Native Hawaiian or other Pacific Islander, and 7.7% from unknown/other or unwilling to answer. 28.9% of the prospective study population was of Hispanic ethnicity.
- Patients in the prospective population were from the following states: Arizona (586, 18.6%), California (1, 0.0%), Connecticut (148, 4.7%), Florida (457, 14.5%), Georgia (118, 3.7%), Indiana (90, 2.9%), North Carolina (5, 0.2%), New Jersey (90, 2.9%), New York (518, 16.4%), Ohio (54, 1.7%), Pennsylvania (201, 6.4%), South Carolina (95, 3.0%), Tennessee, (225, 7.1%), Texas (392, 12.4%), and Virginia (170, 5.4%).

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the Access HBsAg and Access HBsAg Confirmatory study was limited to patients who met the following inclusion:

- Subjects 2 years of age or older
- Subjects willing and able to donate required blood sample
- Subjects or legal guardian has signed the Informed Consent Form (a minor may need to sign an Assent Form if required by IRB)
- Subjects belong to one or more of the below categories:
 - a. Person with an increased risk for hepatitis and/or with signs or symptoms of hepatitis

- b. Pregnant person of any age for typical pre-natal HBV screening (low risk)
- Purchased HBV positive samples from acute and chronically ill subjects

Patients were not permitted to enroll in the Access HBsAg and Access HBsAg Confirmatory study if they met any of the following exclusion criteria:

- Subject who previously participated in the study.
- Subject who has received any experimental or investigational drugs or treatments pertaining to hepatitis B within 4 weeks of phlebotomy.

Subject samples that did not meet the required volume of sample were excluded from testing.

2. Follow-up Schedule

A follow-up schedule was not required for the study.

3. Clinical Endpoints

With regards to safety and effectiveness, the clinical endpoints are described in Section X.D.2.

B. Accountability of PMA Cohort

At the time of database lock, 3,593 subjects were prospectively enrolled and 472 retrospective samples were collected in the PMA study, 88% patients are available for analysis at the completion of the study.

HBV Classification

The HBV classification was determined for each specimen based on the reactivity patterns of the 4 HBV serological marker results (HBsAg, anti-HBc IgM, total anti-HBc, and anti-HBs), shown in Table 14 below.

Table 14: HBV Disease Staging by Serological Marker Results – 4 Markers

HBV Disease Staging	HBsAg ^a	Anti-HBc IgM	Anti-HBc Total	Anti-HBs
Early Acute	+	-	-	-
Acute	+	+	+	-
	+	I	+	-
Recovering Acute/Undetectable	-	+	+	-
Recovering Acute	-	+	+	+
Chronic	+	-	+	+
	+	-	+	-
Immune due to Natural Infection	-	-	+	+

HBV Disease Staging	HBsAg ^a	Anti-HBc IgM	Anti-HBc Total	Anti-HBs
Immune due to HBV Vaccination	-	-	-	+
Susceptible	-	-	-	-
Uninterpretable	-	-	+	-
	-	-	+	I
	-	-	-	I
	-	I	+	+
	-	+	-	-

+ = Positive/Reactive; - = Negative; I = Indeterminate

^a HBsAg results indicated as + were repeatedly reactive and confirmed by neutralization as required by the manufacturer's Instructions for Use.

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for an HBsAg detection study performed in the US. Demographics for the different study cohorts are shown in the following tables.

The following table summarizes the samples analyzed by gender and age for both the prospective and retrospective (purchased positives from acute or chronically ill patients) enrollment populations.

Table 15: Analyzed Samples by Gender and Age (Prospective and Purchased Positive Subjects)

Age Range (years)	Prospective		Retrospective		Total
	Female	Male	Female	Male	
7-12*	14	19	0	0	33
13-18	43	24	0	0	67
19-21	109	32	0	0	141
22-29	520	126	40	103	789
30-39	480	167	44	106	797
40-49	260	174	27	64	525
50-59	340	270	18	28	656
60-69	207	203	9	16	435
70-79	62	64	1	4	131
80-89	13	17	1	0	31
90+	1	5	0	0	6
Unknown	0	0	1	2	3
Total	2,049	1,101	141	323	3,614

*Four (4) subjects outside of the pediatric intended use population of 7-21 are included in this analysis.

Analyzed samples by race and enrollment cohort (prospective subjects only) are presented in the following table.

Table 16: Analyzed Samples by Race and Cohort (Prospective Subjects Only)

Race	Adults (Non-Pregnant)		Pediatrics (Non-Pregnant)		Pregnant		All Subjects	
	N	%	N	%	N	%	N	%
American Indian or Alaska Native	28	0.9%	5	0.2%	11	0.3%	44	1.4%
Asian	34	1.1%	0	0.0%	9	0.3%	43	1.4%
Black or African American	700	22.2%	38	1.2%	105	3.3%	843	26.7%
Native Hawaiian or other Pacific Islander	2	0.1%	0	0.0%	3	0.1%	5	0.2%
Other	158	5.0%	7	0.2%	27	0.9%	192	6.1%
Unknown	17	0.5%	4	0.1%	9	0.3%	30	1.0%
Unwilling to specify	17	0.5%	2	0.1%	0	0.0%	19	0.6%
White	1,518	48.2%	125	4.0%	331	10.5%	1,974	62.6%
Total	2,474	78.5%	181	5.7%	495	15.7%	3,150	100.0%

Analyzed prospective samples for Hispanic and Non-Hispanic subjects by enrollment cohort are presented in the following table.

Table 17: Analyzed Hispanic and Non-Hispanic Subject Samples by Cohort (Prospective Subjects Only)

Ethnicity	Adults (Non-Pregnant)		Pediatrics (Non-Pregnant)		Pregnant		All Subjects	
	N	%	N	%	N	%	N	%
Not Hispanic or Latino	1,760	55.9%	70	2.2%	389	12.3%	2,219	70.4%
Unknown or unwilling to specify	13	0.4%	0	0.0%	7	0.2%	20	0.6%
Hispanic or Latino	701	22.3%	111	3.5%	99	3.1%	911	28.9%
Total	2,474	78.5%	181	5.7%	495	15.7%	3,150	100.0%

The overall study population included 3,614 specimens, consisting of 3,150 serum samples that were prospectively collected, and an additional 464 pre-characterized retrospective samples (serum and plasma) collected from patients with acute or chronic HBV infection. Of the 3,150 specimens prospectively collected, 2,474 were from non-pregnant adults classified as increased risk for hepatitis due to lifestyle, behavior, occupation, or known exposure events, or individuals with signs and symptoms of hepatitis. 495 prospective specimens were from the pregnant screening population, of which 183 also were increased risk and/or showed signs and symptoms of hepatitis. Specimens from the pregnant population included 202 from the first trimester, 180 from the second trimester, and 113 from the third trimester. In addition, 181 prospective specimens were collected from the pediatric increased risk and/or signs & symptoms population. The table below summarizes the number of specimens in each population.

Table 18: Summary of Specimens Used for the Access HBsAg Study

	Adult (non-pregnant) (n = 2,938)		Pregnant (n = 495)		Pediatric (non-pregnant)
	IR/S&S*	Pre-characterized acute/chronic HBV infection	IR/S&S	Low risk	IR/S&S
Prospective (n=3,150)	2,474	N/A	183	312	181
Retrospective (n=464)	N/A	464	N/A	N/A	N/A
Total	3,614				

*IR/S&S = Increased Risk and/or Signs & Symptoms

The Access HBsAg results for the prospective population for all clinical trial sites combined by age group and gender are summarized in the table below. Samples were considered nonreactive if S/CO was < 1.00 upon initial testing and reactive if S/CO was ≥ 1.00 during initial testing and repeat reactive if 2 of 3 replicates were ≥ 1.00 S/CO after duplicate testing.

Table 19: Distribution of Access HBsAg Assay Repeat Reactive and Nonreactive Results Among the Prospective Cohort by Age Group and Gender

Age Range (years)	Gender	Access HBsAg				Total
		Reactive		Nonreactive		
		N	%	N	%	
7-12*	Female	0	0.00	14	0.44	14
	Male	0	0.00	19	0.60	19
13-18	Female	0	0.00	43	1.37	43
	Male	0	0.00	24	0.76	24
19-21	Female	0	0.00	109	3.46	109
	Male	0	0.00	32	1.02	32
22-29	Female	1	0.03	519	16.48	520
	Male	0	0.00	126	4.00	126
30-39	Female	2	0.06	478	15.17	480
	Male	2	0.06	165	5.24	167
40-49	Female	3	0.10	257	8.16	260
	Male	3	0.10	171	5.43	174
50-59	Female	4	0.13	336	10.67	340
	Male	5	0.16	265	8.41	270
60-69	Female	0	0.00	207	6.57	207
	Male	5	0.16	198	6.29	203
70-79	Female	0	0.00	62	1.97	62
	Male	1	0.03	63	2.00	64
80-89	Female	0	0.00	13	0.41	13
	Male	0	0.00	17	0.54	17
90+	Female	0	0.00	1	0.03	1
	Male	0	0.00	5	0.16	5
Total		26	0.83	3,124	99.17	3,150

*Four (4) subjects outside of the pediatric intended use population of 7-21 are included in this analysis.

Pregnant Females

495 serum samples were prospectively collected from a U.S. pregnant screening population, including 183 with at-risk factors for hepatitis and/or signs and symptoms of hepatitis. Samples were tested using the Access HBsAg assay and the reference HBsAg qualitative and reference HBsAg confirmatory assay to provide a final interpretation. Access HBsAg samples were considered nonreactive if S/CO was < 1.00 upon initial testing and repeat reactive if S/CO was ≥ 1.00 during initial testing and if at least 2 of 3 replicates were ≥ 1.00 S/CO after duplicate testing. The results of HBsAg testing at all sites combined is presented in the following table.

Table 20: Pregnant Subjects Reference HBsAg Assay with Confirmation by Trimester

Pregnancy Cohort	Trimester	Reference HBsAg with Reference HBsAg Confirmatory assay result				Total (N)
		Reactive		Nonreactive		
		Access HBsAg				
		Repeat Reactive (N)	Nonreactive (N)	Repeat Reactive (N)	Nonreactive (N)	
Pregnancy Screening (IR/S&S*) n = 183	First	1	0	0	74	75
	Second	0	0	0	71	71
	Third	0	0	0	37	37
Pregnancy Screening (Low Risk) n = 312	First	0	0	0	127	127
	Second	0	0	0	109	109
	Third	0	0	0	76	76
Total	Total	1	0	0	494	495

*IR/S&S = Increased Risk and/or Signs & Symptoms

Pediatrics

181 serum samples were prospectively collected from an at-risk and signs and symptoms U.S. pediatric non-pregnant population. Samples were tested using the Access HBsAg assay and the reference HBsAg qualitative and reference HBsAg confirmatory assay to provide a final interpretation. No reactive samples were found with Access HBsAg; therefore, no Access HBsAg Confirmatory testing was required. Negative percent agreement between the Access HBsAg assay and the reference HBsAg assay in pediatric samples was calculated. The results are presented in the following table.

Table 21: Pediatric Performance

PPA		NPA	
% (n/N)	95% CI	% (n/N)	95% CI
N/A	N/A	100.0 (181/181)	97.9-100.0

Access HBsAg results for each classification were compared with the final interpretation from the same reference HBsAg assay used for classification in the table above. The results are described in the table below.

Table 22: Comparison of Access HBsAg assay versus HBsAg Reference Assay - All Populations by HBV Classification

	Reference HBsAg with Reference HBsAg Confirmatory Assay Result				Total		
	Reactive		Nonreactive				
	Access HBsAg						
Cohort	Nonreactive (N)	Repeat Reactive (N)	Nonreactive (N)	Repeat Reactive (N)	Prospective (N)	Retrospective (N)	Total (N)
Early Acute	0	3	0	0	3	0	3
Acute	0	17	0	0	2	15	17
Recovering Acute	0	0	4	0	4	0	4
Chronic	1 ^a	393	0	0	18	376	394
Immune due to Natural Infection	0	0	264	2	226	40	266
Immune due to HBV Vaccination	0	0	1,164	1 ^b	1,163	2	1,165
Susceptible	0	0	1,552	0	1,549	3	1,552
Uninterpretable	0	0	203	5 ^c	183	25	208
Missing Classification	1 ^d	2	2	0	2	3	5
Total	2	415	3,189	8	3,150	464	3,614

^a Sample tested PCR negative by certificate of analysis.

^b Sample tested nonreactive using the Access HBsAg Confirmatory assay.

^c Three of five samples were confirmed reactive using the Access HBsAg Confirmatory assay: available seroprofile information for these samples may indicate a low level of HBsAg that was not detected by the reference assay. The remaining two samples tested nonreactive with Access HBsAg Confirmatory.

^d Sample tested PCR negative by supplementary testing and by certificate of analysis.

D. Safety and Effectiveness Results

1) Safety Results

With regard to safety, as an *in vitro* diagnostic test, the Access HBsAg assay involves taking a sample of plasma or serum from a patient. The test therefore presents no more safety hazard to an individual being tested than other tests where blood samples were drawn.

There were no adverse events or device deficiencies reported during the conduct of the study.

2) Effectiveness Results

Effectiveness of the Access HBsAg and Access HBsAg Confirmatory assays were evaluated by comparing the final interpretation of Access HBsAg assay and Access HBsAg Confirmatory assay to the subject's final HBsAg status as determined by the Comparator assay(s) on the same blood samples. Pre-specified endpoints were overall diagnostic effectiveness measured as positive percent agreement (PPA) and negative percent agreement (NPA) of the Access HBsAg assay compared to final HBsAg sample status as determined by the comparator assay(s).

Primary Endpoint

The primary endpoint evaluated for the Access HBsAg Confirmatory assay is as follows:

- 1) PPA for positive subjects from the overall population (HBsAg repeat reactive samples)
 - The overall population includes all prospectively enrolled adult and pregnant subjects and purchased positive samples from acute and chronically infected adult patients.

The following pass criteria will be used for pass criteria for Primary Endpoints of the Access HBsAg assay:

- 1) $PPA \geq 98.0\%$ on overall population with lower bound of a 95% 2-sided score confidence interval of $PPA > 95\%$ for positive samples from HBV infected subjects
- 2) $NPA \geq 98.0\%$ on overall population (excluding purchased positive samples from acute and chronically infected adult patients) with lower bound of a 95% 2-sided score confidence interval of $NPA > 95\%$ for negative samples
- 3) Lower bound of a 95% 2-sided score confidence interval of $NPA > 98\%$ in all pregnant subjects

The Access HBsAg Confirmatory assay will have the following pass criteria for primary endpoint:

- $PPA \geq 99.5\%$ on overall population with lower bound of a 95% 2-sided score confidence interval of $PPA > 95\%$

Primary Endpoint - PPA & NPA in Overall Population

PPA (calculated on Access HBsAg assay only and Comparator HBsAg and confirmatory assays) and NPA (calculated on Access HBsAg assay only and Comparator HBsAg and confirmatory assays) for the overall population are shown in Table 23. The PPA overall population includes all subjects at-risk and/or with signs and symptoms, including the adult and pregnant population and purchased positive samples from acute and chronically ill adult patients that were HBsAg reactive by the Comparator during this study. No pediatrics are included as there were no HBsAg positive pediatric samples in this study. The NPA overall population includes All adult (at-risk and/or with signs and symptoms), pediatric (at-risk and/or with signs and symptoms) and pregnant (with or without documented risk factors and/or signs and symptoms) subjects and purchased HBV positive samples from acute and chronically infected adult patients that were HBsAg negative by the Comparator assay.

Table 23: Overall Population PPA & NPA

Cohort	PPA		NPA	
	% (n/N)	95% CI	% (n/N)	95% CI
Overall Population	99.5% (415/417) ^a	98.3-99.9%	99.7% (3,189/3,197)	99.5-99.9%

^a The two samples that were found nonreactive using the Access HBsAg assay tested PCR negative by certificate of analysis or supplementary testing.

Primary Endpoint – NPA in Pregnant Population

Pregnant subjects NPA (calculated with Access HBsAg assay only and compared the final HBsAg sample status) is shown in Table 24. Pregnant subject population includes all adult and pediatric Pregnant subjects with or without documented risk factors and/or signs and symptoms and vaccinated Pregnant subjects.

Table 24: Pregnant Subjects NPA

Cohort	NPA	
	% (n/N)	95% CI
Pregnant	100.0% (494/494)	99.2-100.0%

Primary Endpoint – HBsAg Repeat Reactive Samples with Confirmatory Test PPA

Primary endpoint PPA on 415 confirmed HBsAg positive samples from the overall population (including purchased positive samples from acute and chronically ill adult patients), with the Access HBsAg assay and the Access HBsAg Confirmatory assay compared to the Comparator HBsAg confirmatory assay, is shown in Table 25.

Table 25: Repeat Reactive HBsAg Samples Requiring Confirmatory Assay PPA

Cohort	PPA	
	% (n/N)	95% CI
Overall Population	100.0% (415/415)	99.1-100.0%

The following table provides a subanalysis of samples where the Access HBsAg initial results were reactive ($1.00 \leq S/CO < 100.00$) and required repeat testing and confirmation.

Table 26: Access HBsAg Initial Reactive Results ($S/CO \geq 1.00$ and < 100.00) and Required Repeat Testing

HBV Classification	Reference HBsAg with Reference HBsAg Confirmatory Assay Result				Total
	Reactive		Nonreactive		
	Access HBsAg with Confirmatory				
	Initial Reactive (N)	Nonreactive (N)	Initial Reactive (N)	Nonreactive (N)	
Early Acute	1	0	0	0	1
Acute	1	0	0	0	1
Chronic	13	0	0	0	13
Immune due to Natural Infection	0	0	2	0	2
Immune due to HBV Vaccination	0	0	0	1	1
Uninterpretable	0	0	3 ^a	2	5
Missing Classification	1	0	0	0	1
Total	16	0	5	3	24

^a Samples were confirmed reactive using Access HBsAg Confirmatory: available seroprofile information for these samples may indicate a low level of HBsAg that was not detected by the reference assay.

The following table provides a sub analysis of results from positive samples where no repeat or confirmatory testing was required using the high positive cut-off (S/CO \geq 100.00).

Table 27: Access HBsAg Initial Reactive Results (S/CO \geq 100.00) using the High Positive Cutoff

HBV Classification	Reference HBsAg with Reference HBsAg Confirmatory assay result				Total
	Reactive		Nonreactive		
	Access HBsAg				
	Reactive (N)	Nonreactive (N)	Reactive (N)	Nonreactive (N)	
Early Acute	2	0	0	0	2
Acute	16	0	0	0	16
Chronic	380	0	0	0	380
Missing Classification	1	0	0	0	1
Total	399	0	0	0	399

Secondary Endpoint

Secondary endpoint NPA on both pediatric at-risk and/or signs and symptoms subjects (n=181) and pediatric pregnant subjects at-risk and/or with signs and symptoms (n=22) for a total of 203 subjects with Access HBsAg Assay only compared to the final HBsAg sample status, is shown in Table 28.

Table 28: Pediatric Subjects NPA

Cohort	NPA	
	% (n/N)	95% CI
Pediatric At-Risk or S&S	100.0% (203/203)	98.1-100.0%

3) Subgroup Analyses

The analysis of effectiveness was based on the 3,614 evaluable patients. Key effectiveness outcomes are presented in Section X.D.2 above. Subgroup analyses for each cohort discussed above are presented below.

The following tables compare the Access HBsAg assay results with the results obtained on an FDA-approved HBsAg reference assay by HBV disease classification for the different cohorts tested.

The distribution of Access HBsAg assay repeat reactive and non-reactive results by age and gender of the overall prospective population are presented below in Table 29.

Table 29: Distribution of Access HBsAg Assay Repeat Reactive and Nonreactive Results Among the Prospective Cohort by Age Group and Gender

Age Range (years)	Gender	Access HBsAg Assay				Total
		Repeat Reactive		Nonreactive		
		N	%	N	%	
7-12*	Female	0	0.00%	14	0.44%	14
	Male	0	0.00%	19	0.60%	19
13-18	Female	0	0.00%	43	1.37%	43
	Male	0	0.00%	24	0.76%	24
19-21	Female	0	0.00%	109	3.46%	109
	Male	0	0.00%	32	1.02%	32
22-29	Female	1	0.03%	519	16.48%	520
	Male	0	0.00%	126	4.00%	126
30-39	Female	2	0.06%	478	15.17%	480
	Male	2	0.06%	165	5.24%	167
40-49	Female	3	0.10%	257	8.16%	260
	Male	3	0.10%	171	5.43%	174
50-59	Female	4	0.13%	336	10.67%	340
	Male	5	0.16%	265	8.41%	270
60-69	Female	0	0.00%	207	6.57%	207
	Male	5	0.16%	198	6.29%	203
70-79	Female	0	0.00%	62	1.97%	62
	Male	1	0.03%	63	2.00%	64
80-89	Female	0	0.00%	13	0.41%	13
	Male	0	0.00%	17	0.54%	17
90+	Female	0	0.00%	1	0.03%	1
	Male	0	0.00%	5	0.16%	5
Total		26	0.83%	3,124	99.17%	3,150

*Four (4) subjects outside of the pediatric intended use population of 7-21 years are included in this analysis

The results are summarized in Table 30, categorized by HBV classification for the entire population.

Table 30: PPA and NPA between the Access HBsAg Assay Results and the Reference HBsAg Assay

Cohort	PPA		NPA	
	% (n/N)	95% CI	% (n/N)	95% CI
Early Acute	100.0% (3/3)	43.9-100.0%	N/A	N/A
Acute	100.0% (17/17)	81.6-100.0%	N/A	N/A
Recovering Acute	N/A	N/A	100.0% (4/4)	51.0-100.0%
Chronic	99.7% (393/394) ^a	98.6-100.0%	N/A	N/A
Immune due to Natural Infection	N/A	N/A	99.2% (264/266)	97.3-99.8%
Immune due to HBV Vaccination	N/A	N/A	99.9% (1,164/1,165) ^b	99.5-100.0%
Susceptible	N/A	N/A	100.0% (1,552/1,552)	99.8-100.0%
Uninterpretable	N/A	N/A	97.6% (203/208) ^c	94.5-99.0%
Missing Classification	66.7% (2/3) ^d	20.8-93.9%	100.0% (2/2)	34.2-100.0%
Total	99.5% (415/417)	98.3-99.9%	99.7% (3,189/3,197)	99.5-99.9%

^a The one sample found nonreactive using Access HBsAg also tested PCR negative by certificate of analysis.

^b The one sample found repeat reactive using Access HBsAg was found nonreactive using Access HBsAg Confirmatory.

^c Of five samples found repeat reactive with Access HBsAg, three were confirmed reactive using Access HBsAg Confirmatory; available seroprofile information for these samples may indicate a low level of HBsAg that was not detected by the reference assay. The remaining two samples tested nonreactive with Access HBsAg Confirmatory.

^d The one sample found nonreactive using Access HBsAg was found PCR negative by supplementary testing and by certificate of analysis.

The positive percent agreement between the Access HBsAg assay repeat reactive results and the reference assay final interpretation for the prospective, retrospective and combined populations is summarized in the following table.

Table 31: Comparison of Prospective and Retrospective Cohorts

Cohort	PPA		NPA	
	% (n/N)	95% CI	% (n/N)	95% CI
Prospective	100.0 (23/23)	85.7-100.0	99.7 (3,189/3,197)	99.5-99.9
Retrospective	99.5 (392/394) ^a	98.2-99.9	N/A	N/A
Combined	99.5 (415/417)	98.3-99.9	N/A	N/A

^a The two samples found nonreactive using Access HBsAg tested PCR negative by certificate of analysis or supplementary testing.

Pregnant Female Population

Four hundred and ninety-five (495) specimens were from pregnant women. Positive percent agreement (PPA) and negative percent agreement (NPA) between the Access HBsAg assay and the reference HBsAg assay in pregnant samples was calculated. The results are summarized in Table 32, categorized by trimester.

Table 32: Pregnant Population - PPA and NPA between the Access HBsAg Assay Results and the Reference HBsAg Assay

Pregnancy Cohort	PPA		NPA	
Trimester	% (n/N)	95% CI	% (n/N)	95% CI
First	100.0% (1/1)	20.7-100.0%	100.0% (201/201)	98.1-100.0%
Second	0.0% (0/0)	N/A	100.0% (180/180)	97.9-100.0%
Third	0.0% (0/0)	N/A	100.0% (113/113)	96.7-100.0%
Total	100.0% (1/1)	20.7-100.0%	100.0% (494/494)	99.2-100.0%

Pediatric Population

One hundred and eighty-one (181) serum samples were prospectively collected from an at-risk and signs and symptoms U.S. pediatric non-pregnant population. Samples were tested using the Access HBsAg assay and the reference HBsAg qualitative and reference HBsAg confirmatory assay to provide a final interpretation. No positive samples were obtained and negative percent agreement between the Access HBsAg assay and the reference HBsAg assay in pediatric samples was calculated. The results are summarized in Table 33.

Table 33: Pediatric Population - PPA and NPA between the Access HBsAg Assay Results and the Reference HBsAg assay

PPA		NPA	
% (n/N)	95% CI	% (n/N)	95% CI
N/A	N/A	100.0% (181/181)	97.9-100.0%

4) Pediatric Extrapolation

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

XI. 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 10 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.

XII. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

Analytical comparison between pregnant and adult non-pregnant samples spiked with HBsAg

Thirty (30) samples from HBsAg negative pregnant patients were tested to determine if they provided equivalent results to HBsAg negative adult human serum pool samples (controls) when samples were spiked with the same individual HBsAg positive sample. These 30 samples included two specimens from women in the 1st trimester, 16 from the 2nd trimester, and 12 from the 3rd trimester of pregnancy.

Samples were spiked at target HBsAg values between 2.00 and 4.00 S/CO and tested with the Access HBsAg and Access HBsAg Confirmatory assays in replicates of five. The S/CO results for each pregnant sample were compared to the result obtained on each control sample and ranged from -6% to 13%. All samples were confirmed reactive with the Access HBsAg Confirmatory assay.

Analytical comparison between pediatrics and adult samples spiked with HBsAg

Thirty (30) samples from HBsAg negative pediatric patients aged 7 to 20 were tested to determine if they provided equivalent results to HBsAg negative adult human serum pool samples (controls) when samples were spiked with the same individual HBsAg positive sample.

Samples were spiked at a target HBsAg value between 2.00 and 4.00 S/CO and tested with the Access HBsAg and Access HBsAg Confirmatory assays in replicates of five. The S/CO results for each pediatric sample were compared to the result obtained on each control sample and ranged from -13% to 6%. All samples were confirmed reactive with Access HBsAg Confirmatory assay.

XIII. 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.

XIV. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The effectiveness of the Access HBsAg assay for the qualitative detection of hepatitis B surface antigen in human adult and pediatric (7 years to 21 years of age) serum and plasma is supported by the clinical study results. The results of this test may be used as an aid in the diagnosis of HBV infection in patients at risk or with signs and symptoms of hepatitis. The assay may also be used to screen for hepatitis B virus (HBV) infection in pregnant women to identify neonates who are at risk for acquiring hepatitis B during the perinatal period. See Section X.D.2 for Effectiveness Results.

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 Access HBsAg assay, when used according to the manufacturer's instructions, can aid the physician in the diagnosis of HBV infection and screen for HBV infection in pregnant women to identify neonates who are at risk for acquiring hepatitis B during the perinatal period.

C. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in the clinical study conducted to support PMA approval as described above. The benefits of the assay are the determination, in conjunction with other serological and clinical information, the appropriate diagnosis and treatment of 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 reduced morbidity and mortality in these patients. Additionally, diagnosis and appropriate treatment can potentially decrease transmission and disease burden in the general population as well as in populations at high risk for hepatitis B infection. Accurate diagnosis of HBV infection also leads clinicians to evaluate and subsequently treat patients for human immunodeficiency virus (HIV) and hepatitis C virus (HCV) if indicated as these viruses share common risk factors and modes of transmission with HBV, and patients are often co-infected.

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

Risks of a false positive test include improper patient management, including further investigation of hepatitis B infection with other laboratory tests to determine if a patient is acutely or chronically infected. It is possible that a clinician would decide to treat hepatitis B infection with antiviral medications in a patient without hepatitis B infection. Antiviral medication has risks including toxicity and more rarely allergic

reactions. Over time, viral resistance in patients who are co-infected but undiagnosed with other viruses using the same antiviral medication, such as HIV, can lead to viral resistance, however the likelihood of an undiagnosed co-infection in a patient tested for hepatitis B is exceedingly unlikely. These risks are likely mitigated by the fact that this test would then be part of a panel, and incongruous test results in a hepatitis panel would lead a clinician to retest the patient before starting treatment.

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

D. 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 that for the claimed intended use the probable benefits outweigh the probable risks.

E. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The probable clinical benefits outweigh the potential risks for the proposed assay considering the performance of the device in the clinical study and the low risk and associated risk mitigations in clinical practice. The proposed assay labeling will facilitate accurate assay implementation and interpretation of results. The clinical performance observed 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 and as an aid in determination of HBV infection.

XV. CDRH DECISION

CDRH issued an approval order on October 17, 2025

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

XVI. 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.