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: ARCHITECT HBsAg NEXT Qualitative Reagent Kit
ARCHITECT HBsAg NEXT Confirmatory Reagent Kit
ARCHITECT HBsAg NEXT Qualitative Calibrators
ARCHITECT HBsAg NEXT Qualitative Controls
ARCHITECT HBsAg NEXT Confirmatory Manual Diluent

Device Procode: LOM

Applicant's Name and Address: Abbott Laboratories
Abbott Diagnostics Division
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Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P210003

Date of FDA Notice of Approval: August 10, 2022

II. INDICATIONS FOR USE

ARCHITECT HBsAg NEXT Qualitative Reagent Kit
The HBsAg Next Qualitative assay is a chemiluminescent microparticle immunoassay (CMIA) for the qualitative detection of Hepatitis B surface antigen (HBsAg) in human adult and pediatric (2 years to 21 years of age) serum, serum separator tube, and plasma (dipotassium EDTA, tripotassium EDTA, lithium heparin, lithium heparin separator, sodium heparin) on the ARCHITECT i System.

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. Assay results, in conjunction with other laboratory results and clinical information, may be used to provide presumptive evidence of infection with HBV (state of infection or associated disease not determined) in persons with signs and symptoms of hepatitis and in persons at risk for hepatitis B infection.

WARNING: Not approved for use in screening blood, plasma, tissue donors, or cadaveric specimens.

ARCHITECT HBsAg NEXT Confirmatory Reagent Kit
The HBsAg Next Confirmatory assay is a chemiluminescent microparticle immunoassay (CMIA) used for the qualitative confirmation of the presence of hepatitis B surface antigen (HBsAg) in human adult and pediatric (2 years to 21 years of age) serum, serum separator, and plasma (dipotassium EDTA, tripotassium EDTA, lithium heparin, lithium heparin separator, sodium heparin) by means of specific antibody neutralization on the ARCHITECT i System

Assay results, in conjunction with other laboratory results and clinical information, may be used to provide presumptive evidence of infection with the hepatitis B virus (HBV) (state of infection or associated disease not determined) in persons with signs and symptoms of hepatitis and in persons at risk for hepatitis B infection.
It is intended to be used for the confirmation of samples found to be repeatedly reactive by HBsAg Next Qualitative.

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WARNING: Not approved for use in screening blood, plasma, tissue donors, or cadaveric specimens. The effectiveness of the ARCHITECT HBsAg Next Confirmatory assay for use in screening blood, plasma, or tissue donors has not been established.

ARCHITECT HBsAg NEXT Qualitative Calibrators
The HBsAg Next Qualitative Calibrators are for the calibration of the ARCHITECT i System when used for qualitative determination and confirmation of the presence of hepatitis B surface antigen (HBsAg) in human serum and plasma.

ARCHITECT HBsAg NEXT Qualitative Controls
The HBsAg Next Qualitative Controls are for the estimation of test precision and the detection of systematic analytical deviations of the ARCHITECT i System when used for the qualitative detection and for the confirmation of the presence of hepatitis B surface antigen (HBsAg) in human serum and plasma.

ARCHITECT HBsAg NEXT Confirmatory Manual Diluent
The HBsAg Next Confirmatory Manual Diluent is used for manually diluting specimens for testing on the ARCHITECT i System.

III. CONTRAINDICATIONS

There are no known contraindications.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the ARCHITECT HBsAg NEXT Qualitative Reagent Kit, ARCHITECT HBsAg NEXT Confirmatory Reagent Kit, ARCHITECT HBsAg NEXT Qualitative Calibrators, ARCHITECT HBsAg NEXT

Qualitative Controls, ARCHITECT HBsAg NEXT Confirmatory Manual Diluent labeling.

V. DEVICE DESCRIPTION

Kit Configurations and Components

For the qualitative determination of HBsAg, the ARCHITECT HBsAg Next Qualitative Reagent Kit is comprised of the following components:

- ARCHITECT HBsAg Next Qualitative Microparticles: 1 bottle (6.6 mL per 100-test bottle/27.0 mL per 500-test bottle) or 4 bottles (27.0 mL per 2000-test bottle) of anti-HBs (mouse, monoclonal, IgM, IgG) coated microparticles in MES buffer with protein (bovine) stabilizer. Minimum concentration: 0.08% solids. Preservatives: ProClin 300 and ProClin 950.
    - ARCHITECT HBsAg Next Qualitative Conjugate: 1 bottle (3.3 mL per 100-test bottle/13.5 mL per 500-test bottle) or 4 bottles (13.5 mL per 2000-test bottle) of anti-HBs (goat, IgG) acridinium-labeled conjugate in phosphate buffer with protein (bovine, goat, mouse) stabilizers. Minimum concentration: 0.75 µg/mL. Preservatives: ProClin 300 and ProClin 950.
    - ARCHITECT HBsAg Next Qualitative Assay Specific Diluent: 1 bottle (3.3 mL per 100-test bottle/13.5 mL per 500-test bottle) or 4 bottles (13.5 mL per 2000-test bottle) contains phosphate buffer with protein (bovine) stabilizer. Preservatives: ProClin 300 and ProClin 950.
    - ARCHITECT HBsAg Next Qualitative Ancillary Wash Buffer: 1 bottle (5.9mL per 100-test bottle/26.3 mL per 500-test bottle) or 4 bottles (26.3 mL per 2000-test bottle) contains MES buffer. Preservatives: ProClin 300 and ProClin 950.

For the confirmation of the presence of HBsAg, the ARCHITECT HBsAg Next Confirmatory Reagent Kit is comprised of the following components:

- ARCHITECT HBsAg Next Confirmatory Microparticles: 1 bottle (6.6 mL per 100-test bottle) of anti-HBs (mouse, monoclonal, IgM, IgG) coated microparticles in MES buffer with protein (bovine) stabilizer. Minimum concentration: 0.08% solids. Preservatives: ProClin 300 and ProClin 950.
    - ARCHITECT HBsAg Next Confirmatory Conjugate: 1 bottle (3.3 mL per 100-test bottle) of anti-HBs (goat, IgG) acridinium-labeled conjugate in phosphate buffer with protein (bovine, goat, mouse) stabilizers. Minimum concentration: 0.75 µg/mL. Preservatives: ProClin 300 and ProClin 950.

- ARCHITECT HBsAg Next Confirmatory Assay Specific Diluent: 1 bottle (3.3 mL per 100-test bottle) contains phosphate buffer with protein (bovine) stabilizer. Preservatives: ProClin 300 and ProClin 950.
- ARCHITECT HBsAg Next Confirmatory Pre-Treatment 1: 1 bottle (2.4 mL per 100-test bottle) contains recalcified sheep plasma reactive for anti-HBs and recalcified human plasma. Preservatives: ProClin 950 and sodium azide.
- ARCHITECT HBsAg Next Confirmatory Pre-Treatment 2: 1 bottle (2.4 mL per 100-test bottle) contains recalcified human plasma and recalcified sheep plasma. Preservatives: ProClin 950 and sodium azide.
- ARCHITECT HBsAg Next Confirmatory Ancillary Wash Buffer: 1 bottle (5.9mL per 100-test bottle) contains MES buffer. Preservatives: ProClin 300 and ProClin 950.

The ARCHITECT HBsAg Next Qualitative Calibrators contain:

- 2 Bottles (4.0 mL each) of ARCHITECT HBsAg Next Qualitative Calibrators 1 and 2. Calibrator 1 contains recombinant HBsAg (subtype *ad*) in phosphate buffer with protein (bovine) stabilizer. Calibrator 2 contains phosphate buffer with a protein (bovine) stabilizer. Preservatives: ProClin 300 and ProClin 950.

The ARCHITECT HBsAg Next Qualitative Controls contain:

- 2 Bottles (8.0 mL each) of ARCHITECT HBsAg Next Qualitative Controls. Negative and Positive. ARCHITECT HBsAg Next Qualitative Negative Control contains recalcified human plasma. Preservatives: ProClin 950 and sodium azide. ARCHITECT HBsAg Next Qualitative Positive Control. contains inactivated purified human HBsAg (subtype *ad/ay*) in phosphate buffer with a protein (bovine) stabilizer. Preservatives: ProClin 300 and ProClin 950.

The ARCHITECT HBsAg Next Confirmatory Manual Diluent contain:

- 1 Bottle (100 mL each) of ARCHITECT HBsAg Next Confirmatory Manual Diluent contains recalcified human plasma. Preservatives: ProClin 950 and sodium azide.

In addition, the following components are required for the ARCHITECT HBsAg Next Qualitative and the ARCHITECT HBsAg Next Confirmatory Reagent Kits:

- The ARCHITECT HBsAg Next Qualitative and ARCHITECT HBsAg Next Confirmatory assay files must be installed on the ARCHITECT i System with i2000SR Induction Heating installed on the system prior to performing the assays.

- ARCHITECT *i* System is an analyzer designed to perform fully-automated immunoassay tests based on the use of CMIA detection technology.
- ARCHITECT *i* Pre-Trigger Solution contains 1.32% (w/v) hydrogen peroxide.
- ARCHITECT *i* Trigger Solution contains 0.35 N sodium hydroxide.
- ARCHITECT *i Wash Buffer contains phosphate buffered saline solution. Preservatives: antimicrobial agents.*

Assay Principle and Format

HBsAg Next Qualitative
This assay is a one-step immunoassay for the qualitative detection of HBsAg in human adult and pediatric serum and plasma using chemiluminescent microparticle immunoassay (CMIA) technology.

Sample, assay specific diluent, anti-HBs coated paramagnetic microparticles, and anti-HBs acridinium-labeled conjugate are combined to create a reaction mixture and incubated. The HBsAg present in the sample binds to the anti-HBs coated microparticles and to the anti-HBs acridinium-labeled conjugate. Following a wash cycle, ancillary wash buffer is added to the reaction mixture. Following another wash cycle, Pre-Trigger and Trigger Solutions are added.

The resulting chemiluminescent reaction is measured as relative light units (RLUs). There is a direct relationship between the amount of HBsAg in the sample and the RLUs detected by the system optics.

The presence or absence of HBsAg in the specimen is determined by comparing the chemiluminescent signal in the reaction to the cutoff signal determined from an active calibration. If the chemiluminescent signal in the reaction is greater than or equal to the cutoff signal, the specimen is considered reactive for HBsAg.

HBsAg Next Confirmatory
This assay consists of two single tests (HBsAgNx_C1, also referred to as C1 and HBsAgNx_C2, also referred to as C2) that are both one-step pre-treatment immunoassays for the confirmation of the presence of hepatitis B surface antigen (HBsAg) in human serum and plasma using chemiluminescent microparticle immunoassays (CMIA) technology with flexible assay protocols, referred to as Chemiflex.

C1:

Sample and Pre-Treatment 1 are combined and incubated. The HBsAg present in the sample is neutralized by the anti-HBs in Pre-Treatment 1.

An aliquot of the pretreated sample, anti-HBs coated paramagnetic microparticles, assay specific diluent, and anti-HBs acridinium-labeled conjugate are combined to create a reaction mixture and incubated. Any remaining non-neutralized HBsAg present in the

sample binds to the anti-HBs coated microparticles and to the anti-HBs acridinium-labeled conjugate. The neutralized HBsAg is blocked from forming a sandwich with acridinium-labeled anti-HBs conjugate and anti-HBs coated microparticles. After washing, ancillary wash buffer is added and the mixture is incubated. Following a wash cycle, Pre-Trigger and Trigger Solutions are added.

The resulting chemiluminescent reaction is measured as a relative light unit (RLU). There is a direct relationship between the amount of non-neutralized HBsAg in the sample and the RLU detected by the system optics.

C2:

Sample and Pre-Treatment 2 are combined and incubated. Pre-Treatment 2 does not contain anti-HBs and will not neutralize HBsAg present in the sample.

An aliquot of the pretreated sample, anti-HBs coated paramagnetic microparticles, assay specific diluent, and anti-HBs acridinium-labeled conjugate are combined to create a reaction mixture and incubated. HBsAg present in the sample binds to the anti-HBs coated microparticles and to the anti-HBs acridinium-labeled conjugate. After washing, ancillary wash buffer is added and the mixture is incubated. Following another wash cycle, Pre-Trigger and Trigger Solutions are added.

The resulting chemiluminescent reaction is measured as an relative light unit (RLU). There is a direct relationship between the amount of HBsAg in the sample and the RLU detected by the system optics.

If the signal for the non-neutralized sample (incubated with Pre-Treatment 2) result is greater than or equal to the cutoff of 0.70 S/CO and the RLU of the neutralized sample (incubated with Pre-Treatment 1) is reduced by at least 50% compared to the non-neutralized sample, the sample is considered confirmed positive for HBsAg.

Interpretation of Results

The ARCHITECT i System calculates results for the ARCHITECT HBsAg Next Qualitative assay using ratio of the sample RLU to the cutoff RLU (S/CO) for each specimen and control.

Cutoff RLU=(Calibrator 1 mean RLUx0.085)+(Calibrator 2 mean RLU x 0.25)

The cutoff RLU is stored for each reagent lot calibration.

S/CO=Sample RLU/Cutoff RLU The cutoff is 1.00 S/CO

The following tables show the initial and duplicate retest results interpretation.

Table 1 Results Interpretation for Initial Testing

S/CO	Instrument Interpretation	Retest Procedure
< 1.00	Nonreactive	No retest required.
≥ 1.00	Reactive	Retest in duplicate.

Table 2 Results Interpretation for Duplicate Retest Results

Instrument Interpretation	Specimen Classification
Both results nonreactive	Specimen considered negative for HBsAg.
One or both results reactive	Specimen considered repeatedly reactive; confirm using a neutralizing assay.*#

*Only the ARCHITECT HBsAg Next Confirmatory assay has been evaluated with the ARCHITECT HBsAg Next Qualitative assay.

The name(s) of the assays used to detect and confirm reactive results should be included in the results reported by the laboratory.

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Specimens repeatedly reactive were tested as follows with the confirmatory assay in the clinical study section described later in this Review Memo. The following table shows how the confirmatory assay results are interpreted.

Table 3:Results Interpreation for Confirmatory Testing

Dilution	HBsAg Qualitative C2 S/CO	% Neutralization*	Final Interpretation
Neat (undiluted)	< 0.70	Not applicable	Not confirmed
	< 10.00	< 50%	Not confirmed
	≥ 0.70	≥ 50%	Positive
	≥ 10.00	< 50%	Repeat test using a 1:500 dilution
1:500	< 0.70	Not applicable	Not confirmed
	≥ 0.70	≥ 50%	Confirmed Positive
	≥ 0.70	< 50%	Repeat test using a 1:20,000 dilution
1:20,000	< 0.70	Not applicable	Not confirmed
	≥ 0.70	≥ 50%	Confirmed Positive
	≥ 0.70	< 50%	Not confirmed

*If the % neutralization is < -15%, then the results should be considered invalid and the specimen should be retested. Perform the retest using the calculated assay (HBsAgNx_%N) and both constituent assays (HBsAgNx_C1 and HBsAgNx_C2).

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 invitro 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 expectations and lifestyle.

VII. MARKETING HISTORY

The ARCHITECT HBsAg NEXT Qualitative Reagent Kit, ARCHITECT HBsAg NEXT Confirmatory Reagent Kit, ARCHITECT HBsAg NEXT Qualitative Calibrators, ARCHITECT HBsAg NEXT Qualitative Controls, ARCHITECT HBsAg NEXT Confirmatory Manual Diluent has been marketed outside of the United States since February 2019 as indicated in the following table.

Table 4: Where ARCHITECT HBsAg Next Qualitative assay is Currently Marketed

Australia	Morocco
Belarus	Nigeria
Bosnia Herzegovina	North Macedonia
Canada	Pakistan
Columbia	Peru
Ecuador	Republic of Moldova
El Salvador	Saudi Arabia
Guatemala	Serbia
India	Singapore
Indonesia	Taiwan
Israel	Tanzania
Japan	Thailand
Kazakhstan	Turkey
Kenya	Ukraine
Malaysia	Vietnam
Montenegro	

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

IX. SUMMARY OF NONCLINICAL STUDIES

A. Laboratory Studies

1. Cut-off Study in International Standard Units

The purpose of this study was to evaluate analytical sensitivity when used to test the WHO Second International Standard for HBsAg, subtype adw2, genotype A, NIBSC code: 00/588. The standard was reconstituted with distilled water and diluted with recalcified normal human plasma to a target concentration of 1000 mIU/mL and labeled as "Intermediate." Additional dilutions were prepared by combining the Intermediate and recalcified normal human plasma to target concentrations of 0, 3, 5, 8, 10, 15, 20, and 40 mIU/mL. Each dilution was tested in a minimum of 4 replicates and each positive member was tested in a minimum of 2 replicates using one ARCHITECT i2000SR instrument, three reagent lots, three calibrator lots, and one control lot.

For each instrument and reagent lot combination, the mean s/co values were calculated for each dilution. Plots were generated using mean s/co values on y axis versus target concentration on x axis. A least squares linear regression analysis was performed by regressing mean s/co versus target concentration across dilutions. Slope and intercept of regression was calculated.

The analytical sensitivity is 6.14 mIU/mL and ranged from 4.62 to 6.14 mIU/mL (between lots).

2. Limit of Blank (LoB) and Limit of Detection (LoD)

The LoB and LoD studies were performed based on CLSI EP17-A2. One zero-analyte sample (normal human plasma) and two low-level samples with HBsAg concentrations of approximately 3 and 5 mIU/mL were pepared by diluting WHO Second International Standard for HBsAg, subtype adw2, genotype A, NIBSC code: 00/588 into normal human plasma. Testing was conducted over a minimum of three days. Testing was conducted on one ARCHITECT i2000SR with three reagent lots, three calibrator lots, and one control lot. The maximum observed LoB and LoD are shown in the following table:

Table 5: LoB and LoD

	mIU/mL
LoB[a]	1.07
LoD[b]	2.34

[a] The LoB represents the 95th percentile from n ≥ 60 replicates of zero-analyte samples.

[b] The LoD presented in the table is in alignment with the ARCHITECT HBsAg Next Qualitative assay on the ARCHITECT i2000SR System. The observed LoD on the ARCHITECT i System was 2.34 mIU/mL and represents the lowest concentration at which the analyte can be detected with 95% probability based on n ≥ 60 replicates of low analyte level samples.

3. Genotype Detection

A total of 109 HBsAg genotype panels (genotypes A through H) were obtained. Fifteen of the panels were dilutions prepared from the 1st WHO International Reference Panel for Hepatitis B Virus (HBV) Genotypes for HBsAg Assays PEI Code 6100/09 and 94 were HBsAg native based genotype panels as shown in the following table:

Table 6:Genotype Detection

Genotype	**N**
Genotype A	26
Genotype B	15
Genotype C	22
Genotype D	23
Genotype E	7
Genotype F	13
Genotype G	1
Genotype H	2
Total	109

Each sample was tested in 1 replicate with 1 of 3 lots of reagents and calibrators and 1 lot of controls on 1 ARCHITECT i2000SR instrument.

All samples were initial and repeat reactive and confirmed reactive in both the candidate and comparator assays. There were no discordant samples.

4. HBsAg Mutant Detection
   A panel consisting of 71 internally prepared recombinant mutant samples and two wild type controls, and a panel of 95 native mutant samples were obtained. Samples had been diluted with recalcified negative human plasma to an S/CO of approximately 2.0 in the ARCHITECT HBsAg Qualitative assay. All recombinant mutant samples were antigens with amino acid sequences representing native mutants of hepatitis B surface antigen. Across the recombinant and native panels, four out of the 166 mutant samples shared the same mutation pattern. One hundred fifty-one of the samples contained at least one substitution or insertion in the region spanning amino acids (aa) 120 – 145 within the 'a' determinant of the surface antigen. Forty-two of the samples had single substitutions, 32 had double substitutions, 86 had 3 to a maximum of 18 substitutions or insertions, and 6 had insertions following aa 122 or 123 of the surface antigen. Thirty-nine samples contained mutants Gln-129-His, Met-133-Leu, Asp-144-Ala, Gly-145-Arg, and Thr-123-Ala or insertion mutants 122NT, 122RA, P142L+G145R, P142S+G145R.

   All mutant specimens were evaluated with the ARCHITECT HBsAg Next Qualitative and ARCHITECT HBsAg Qualitative assays and their respective confirmatory assays. All specimens were initial and repeatedly reactive in both assays and were confirmed positive in the respective confirmatory assays. There was one native mutant specimen that could not be confirmed (48% neutralization) in the ARCHITECT HBsAg Qualitative Confirmatory assay but was confirmed in the ARCHITECT HBsAg Next Confirmatory assay.

   This following table shows the list of recombinant or native mutants tested and detected as reactive.

Table 7: HBsAg Mutations Evaluted: Recombinant and Native

Mutation Type	**Amino Acid Position Substitution**
Single	C137Y, C138W, C147S, C124R, Q129H, M133L, D144A, G145R, T123A, T123N, K141E, P120Q, G145K, T143L, T123S, F161L, C76Y, C121Y, C137A, G145E, C149Y, S154W, T126S, M133T, S136T, C139W, G145A, C147Y, T126I, S143L, Q129H, L127V, A128V, G145AG, L88P, T126S, T126NT, T118A, M133L, G145A, S143L, G130R
Double	T123N+C124R, P142L+G145R, P142S+G145R, T123A+G145R, C76Y+F83S, M133L+G145R, P108H+S113T, T123N+T143S, T126A+M133I, P127T+G145R, F134V+D144G, D144E+G145R, C147Y+C149Y, T127P+T131I, L77LQ+G145GR, Y100C+M133I, F134FL+E164EG, S140L+T189IT, Y100C+Q129QR, T123AT+E164EG, L127P+D144E, S143L+G145GR, G145A+S174N, N59S+Q129H, Q101H+I110L, T127P+S143L, S143L+P211H, G145A+T189I, Q101H+Q129H, S143L+V177A, P127L+Q129H, S143L+T189I
Three to eighteen	P120S+T125M+P127Y+S143L, C121Y+K122L+T123N+G130E+M133I+D144G+G145R, P120S+D144E+G145R+T189I, F134H+P142L+D144E+G145R, P120Q+N131K+G145R, M133I+Y134H+T143M, T143L+Y206G+S207R, T126I+F134H+P142L+G145R, T143L+V190A+Y200C+Y206R, L109I+G112K+S113A+P120T+F134S, I110R+K122Y+F134S+P142L+D144A, T114S+K122R+N131T+F134Y+T143S, I110M+T116N+S117T+T118S+T140S+T143L, T115N+P120L+M133I+F134H+D144V+S154P, T118V+M133I+F1`34N+P142S+T143L+G145R, P120T+S132F+F134N+P135A+D144G+I150T,

	T114S+S117T+T123S+N131T+M133I+F134R+I150T+A194V+Y200S+S207N+V209L+I213M, JPA, T125M+T126N+P127T, Q101R+G112K+.T118V+R122K+T126N+S136Y+S143L G112K+S114L+T115N+T118R+Q129P, R122K+P127S+G130E, Q101H+P111S+T118P+P120T, L110I+T118M+S154LS+R160KR, L77Q+L88P+P120PT+K122T+T126S, P120AP+G145AG+E164EG, Q101R+S154PS+K160N, E164G L91HL+I92IT+Q101H, F134FV+G145A+S167LS, Y100C+Q101PQ+P120PT Y100C+M103I+N131S+E164G+R169HR, Y100C+S113FS+T116IT+C121CGS+T123P+M133IM+F134FL+P135H, M103I+T126I+Q129H+E164G, T27KT+A45AT+I110IL+S113KT+S114PS+P120PT+T126I+L127P+S140LS+D144DE+G145GR+I150T+F158F L+A168AV+L175LS+V177AEPQ+V180AV Y72F+P120T+L127P+K160R N59S+Q129R+S136SY T57I+L127P+D144E+L216StopL T118M+D144A+I150T V47G+L49P+R122K+F134L+Y200F+I213L+L216stop S55F+Y100C+T123A+T126I+L127P+S143L+S174N+L176P+V177A+P178L+S193LS+P214L+V224AV L49P+Y72F+Q101R+I110L+D144AD+G145A+K160N+E164V+S174N+V177A+P178L+Q181R+I213T S34L+F41S+S117T+Q129P+N131K+S154P+S155Y+E164D+A166AG+V168A+S174N+V177A+Y200F+I213S +P217L+I226T s3n+F8L+G44E+A128V+L175S G18V+V96G+L127P+S143L+K160N+E164G+S167L+R169H+S174N+P178L+S210NS+P214H+L216FL Q101R+L127P+S140L+G145A+S154L+K160R+S174N+F219S+F220Y+V224A F8FL+T45NT+L49LR+P120S+T189IT+S193LS+M198MT+P203PQ+S207NS+P211PR+P217LP F8FL+S64FS+C69stopC+I110IL+T127P+S143L+T189IT F8L+P120S+T127P+P135LP+S204N+Y206C+F220C+V224A Q30K+S31N+T127P+G130R+T131N+M133T+I208T P142FLPS+G145KR+S174NS+A194V Q30K+L49P+N59S+L91H+Y100S+Q101R+I110L+T123V+T126I+L127P+M133L+K160N+L175S+P178L+P21 1L+I213M+I218L L94S+V96G+R122K+G145A+G159V I68T+S114P+L127P+A128V+S174N+S204G+V224A L127P+S143L+D144DE+K160N+E164V+L175S+V177A+P211L Q101QR+S143L+F219L M133IM+P142LP+S143L+D144E T27K+Y100C+Q129R+L175S+W199L V96AG+Y100C+T116I+G119R+P120L+F134L+P135H+S174N+S210DG S31N+Q101R+G145A+S154QR+K160KN+F220L L49R+Q101H+T126I+E164G R79H+L91HL+F93S+L98LR+Y100C+G102S+Q129L+F134S+P135H+W182stop T23I+L127I+M133I L49LR+G145A+S204RS+I226IT C76W+P120S+S132F E2EG+F8FL+Q101R+P127IT+G145A+F219S+F220L L49R+R79HR+P120T+M133IM D144E+V184I+T189I L21LS+R24KR+Q101QR+P120S+T189I+S204K+P217LP D144E+S204N+S207N F8P+T45NT+F83CF+Y100C+Q129R+Y134ADFSVY S143L+S204R+L209LV+L213IL+P214LP P70T+S143L+S193L T126IT+Y134NY+G145R

	G145A+T189I+F212Y G145A+S207N+I208T+P214L M103IM+S114AS+T131AT+S143L+L175LS+V184AV T57I+M103I+D144A+W172L+V177A+Y206C+S207R+P214Q+Y225F I92T+L109M+M133I+F134I+D144A+G145A+I208T+P217L F8L+T126S+M197T+S204N+N207R F83S+V96G+M103I+F134V+I150M+S174N+S204R+N207T S64FS+V96GV+K141KR+P142PS+G145R S31RS+Q101R+T131P+M133I+K141KT+G145A+K160N+E164G+Y206HY+F220Y+I226T G11AG+S53L+P62L+M103I+P105L+T113AT+P120K+T123ATP127PS+A128AV+M133I+W165R+S174N+F179Y+Q181R+V184G+G185E+S210N T118K+T140I+C149Y P135L+C139Y+D144A+G145R+S171Y+V180A F93C+M103I+G145R+S174N
Insertion after 122 or 123	122DT 122NT 122RA insertion 123NSTGPCTT 123RGA G145R/122DT Insertion

5. Within Assay Sample Carryover

A study was performed to evaluate the susceptibility of the ARCHITECT HBsAg Next Qualitative assay to within-assay sample carryover. Three replicates of wash buffer were tested to clear the system. A single replicate of an HBsAg high nonreactive (negative) sample was tested to serve as a sample that was not exposed to potential sample carryover (protected sample). This was followed by a single replicate of an HBsAg high reactive sample (HBsAg concentration ≥ 125,000 IU/mL), then by a single replicate of the negative sample to serve as a sample exposed to potential sample carryover (unprotected sample). The sequence of wash buffer, protected negative sample, high sample, and unprotected negative sample was repeated an additional 9 times for a total of 10 iterations.

One carryover run was performed using 1 lot each of ARCHITECT HBsAg Next Qualitative Reagents, Calibrators, and Controls on 1 ARCHITECT i2000SR instrument.

The difference between the protected sample and the unprotected sample was 0.04 S/CO (two-sided 95% CI [0.02, 0.06]), demonstrating that the ARCHITECT HBsAg Next Qualitative assay is not susceptible to within-assay sample carryover.

6. Endogenous Interfering Substances

A study was performed based on guidance from CLSI document EP07=A2. Each substance was tested at two analyte levels (approximately 0.8 S/CO and 1.20 S/CO). No significant interference was observed at the following concentrations.

Table 8: Endogenous Interfering Substances

Potentially Interfering Endogenous Substance	Interferent Level
Unconjugated Bilirubin	40 mg/dL
Conjugated Bilirubin	40 mg/dL
Hemoglobin	1000 mg/dL
Triglycerides	3000 mg/dL
Total Protein	15 g/dL

7. Exogenous Interfering Substances

A study was performed based on guidance from CLSI EP07-A2. Each substances was tested at two analyte levels (approximately 0.8 S/CO and 1.20 S/CO). Each sample was tested in a minimum of 10 replicates with one lot each of ARCHITECT HBsAg Next Qualitative reagents, calibrators, and controls on one ARCHITECT i2000SR instrument. Positive samples were tested with one lot of ARCHITECT HBsAg Next Confirmatory reagents and one lot of ARCHITECT HBsAg Next Qualitative calibrators, and control on one ARCHITECT i2000SR instrument. No significant interference was observed at the following drug compound concentrations.

Table 9: Exogenous Interfering Substances

Potentially Interfering Substance	Interferent Level
Acetaminophen	250 mg/L
Acetylcysteine	150 mg/L
Acetylsalicylic Acid	1000 mg/L
Adefovir	10 mg/L
Ampicillin-Na	1000 mg/L
Ascorbic Acid	300 mg/L
Biotin	4250 ng/mL
Ca-dobesilate	200 mg/L
Cefoxitin	2500 mg/L
Cyclosporine	5 mg/L
Doxycycline	50 mg/L
Entecavir	0.5 mg/L
Ibuprofen	500 mg/L
Lamivudin	300 mg/L

Potentially Interfering Substance	Interferent Level
Levodopa	20 mg/L
Methyldopa	20 mg/L
Metronidazole	200 mg/L
PEG interferon-alpha	180 ug/L
Phenylbutazone	400 mg/L
Rifampicin	60 mg/L
Sodium Heparin	10 U/mL
Telbivudine	600 mg/L
Tenofovir*	245 mg/L
Theophylline (1,3-dimethylxanthine)	100 mg/L

* Tenofovir concentration tested exceeds the Test Concentration listed in EP37 1st Edition.

8. Cross reactivity (Analytical Specificity)
   The ARCHITECT HBsAg Next Qualitative assay and confirmation by the ARCHITECT HBsAg Next Confirmatory assay were evaluated for potential interference using specimens from individuals with medical conditions unrelated to hepatitis B.

   The ARCHITECT HBsAg Next Qualitative and ARCHITECT HBsAg Qualitative assays and their respective confirmatory assays (for repeatedly reactive specimens) evaluated 288 specimens from 27 other disease states categories. Of the 288 specimens tested, 277 specimens were concordant nonreactive on both the ARCHITECT HBsAg Next Qualitative and ARCHITECT HBsAg Qualitative assays, while 10 of the 288 specimens were concordant repeatedly reactive and confirmed on both assays. One HIV-1 sample was repeatedly reactive on the ARCHITECT HBsAg Next Qualitative assay and confirmed positive by the ARCHITECT HBsAg Next Confirmatory assay and elevated nonreactive on the ARCHITECT HBsAg Qualitative assay. Results are shown in the following table.

Table 10: Cross Reactivity (Analytical Specificity)

Category	n	Comparator ARCHITECT HBsAg Qualitative Final Interpretation			
		Nonreactive		Repeatedly Reactive and Confirmed	
		ARCHITECT HBsAg Next Qualitative Final Interpretation		ARCHITECT HBsAg Next Qualitative Final Interpretation	
		Nonreactive	Repeatedly Reactive and Confirmed	Nonreactive	Repeatedly Reactive and Confirmed
HTLV-1/2	10	10	0	0	0
CMV	10	10	0	0	0
HCV	10	10	0	0	0
EBV	10	10	0	0	0
HIV-1	10	8	1	0	1
HIV-2	10	10	0	0	0
HAV	10	10	0	0	0
T.pallidum (Syphilis)	10	10	0	0	0
Rheumatoid Factor (RF)	10	10	0	0	0
Antinuclear Autoantibodies (ANA)	10	10	0	0	0
Anti-dsDNA autoantibodies	10	10	0	0	0
Pregnant females 1st trimester	10	10	0	0	0
Pregnant females 2nd trimester	10	10	0	0	0
Pregnant females 3rd trimester	20	20	0	0	0
Multiparous females	10	9	0	0	1
Immunoglobulin from monoclonal gammopathy for IgG	7	7	0	0	0
Immunoglobulin from multiple myeloma	10	8	0	0	2
Influenza vaccine recipients	20	20	0	0	0
Hemodialysis patients	10	9	0	0	1
Human anti-mouse antibody (HAMA)	20	20	0	0	0
Non-viral liver disease / alcoholic liver disease	10	10	0	0	0
Autoimmune hepatitis	10	10	0	0	0
Fatty liver disease	10	10	0	0	0
Hepatocellular carcinoma (HCC)*	10	5	0	0	5
Obstructive jaundice and smooth muscle antibody	6	6	0	0	0

positive (SMA)					
ANCA (neutrophil cytoplasmatic antibodies)	8	8	0	0	0
AMA (anti-mitochondrial antibodies) or histology	7	7	0	0	0
Total	288	277	1	0	10

*Of the 10 HCC samples, 5 were concordant nonreactive and 5 were concordant reactive. Chronic and/or persistent infection with hepatitis B and/or hepatitis C are known risk factors for hepatocellular cancer.

9. Matrix Equivalency/Tube Type Equivalency

A study was conducted to confirm that the claimed blood collection tube types are suitable for use with the ARCHITECT HBsAg Next Qualitative and ARCHITECT HBsAg Next Confirmatory assays. Sample sets from a minimum of 25 donors were obtained in the control tube type (plastic serum) and the blood collection tube types selected for evaluation. The blood collection tubes were supplemented with two HBsAg positive stocks to targets of 0.80 S/CO and 1.20 S/CO.

The samples from each sample set were tested in a minimum of 2 replicates using 1 lot each of ARCHITECT HBsAg Next Qualitative reagents, calibrators, and controls on 1 ARCHITECT i2000SR instrument. Additionally, the samples from each sample set spiked to a target of 1.20 S/CO were tested in 1 replicate using 1 lot of ARCHITECT HBsAg Next Confirmatory reagents, and 1 lot of ARCHITECT HBsAg Next Qualitative calibrators and controls on 1 ARCHITECT i2000SR instrument.

The results support the use of the following blood collection tube types with the ARCHITECT HBsAg Next Qualitative and ARCHITECT HBsAg Next Confirmatory assays:

- Serum, including serum separator
- Dipotassium EDTA
- Tripotassium EDTA
- Lithium heparin
- Lithium heparin separator
- Sodium heparin

The following results were observed.

Table 11: Matrix Equivency/Tube Type Equivalency

	Distribution of Differences for High Negative Samples			**Distribution of %Differences for Low Positive Samples**		
Evaluation Tube Type	**< 0.10 S/CO**	**≥ 0.10 S/CO to ≤ 0.20 S/CO**	**> 0.20 S/CO**	**< -20%**	**≥ -20% to ≤ -10%**	**> -10%**
Serum separator, plastic	100.00% (29/29)	0.0% (0/29)	0.0% (0/29)	0.0% (0/30)	0.0% (0/30)	100.0% (30/30)

Evaluation Tube Type	Distribution of Differences for High Negative Samples			Distribution of %Differences for Low Positive Samples		
	< 0.10 S/CO	**≥ 0.10 S/CO to ≤ 0.20 S/CO**	**> 0.20 S/CO**	**< -20%**	**≥ -20% to ≤ -10%**	**> -10%**
Dipotassium EDTA	100.00% (29/29)	0.0% (0/29)	0.0% (0/29)	0.0% (0/30)	3.3% (1/30)	96.7% (29/30)
Tripotassium EDTA	100.00% (29/29)	0.0% (0/29)	0.0% (0/29)	0.0% (0/30)	10.0% (3/30)	90.0% (27/30)
Lithium heparin	100.00% (29/29)	0.0% (0/29)	0.0% (0/29)	0.0% (0/30)	13.3% (4/30)	86.7% (26/30)
Sodium heparin	100.00% (29/29)	0.0% (0/29)	0.0% (0/29)	0.0% (0/30)	6.7% (2/30)	93.3% (28/30)
Lithium heparin plasma separator	100.00% (29/29)	0.0% (0/29)	0.0% (0/29)	0.0% (0/30)	3.3% (1/30)	96.7% (29/30)

10. Hook Effect

    A high dose hook study was performed to characterize the performance of the ARCHITECT HBsAg Next Qualitative assay when used to test a dilution series of specimens containing very high levels of HBsAg that have the theoretical potential to cause a high dose hook effect. The results for this study also apply to the ARCHITECT HBsAg Next Confirmatory assay (C2 assay protocol) because the assay specific diluent, microparticle, conjugate, and ancillary wash buffer reagents are identical between the 2 assays.

    The highest available HBsAg positive human specimen (concentration 150,125,000 mIU/mL) was used as positive stock for this study. Serial dilutions of the High Positive Sample were prepared using recalcified HBsAg negative human plasma. The samples were tested in a minimum of 3 replicates using 1 ARCHITECT i2000SR instrument using 1 lot each of ARCHITECT HBsAg Next Qualitative reagents, calibrators, and controls. The study demonstrates that although samples ≥6,325,000 mIU/mL show a decrease in signal, the ARCHITECT HBsAg Next Qualitative and the ARCHITECT HBsAg Next Confirmatory qualitative results are not impacted by high dose hook effect.

11. Within Laboratory Precision (20 day)

    A 20-day precision study was performed to evaluate the precision performance of the ARCHITECT HBsAg Next Qualitative assay based on guidance from the Clinical and Laboratory Standards Institute (CLSI) document EP05-A3.[25]
    Testing was conducted using 3 lots of the ARCHITECT HBsAg Next Qualitative reagent, 3 lots of the ARCHITECT HBsAg Next Qualitative Calibrators, and 3 lots of the ARCHITECT HBsAg Next Qualitative Controls and 2 ARCHITECT i2000SR instruments. Two controls and 3 human plasma panels were tested in replicates of 3 (to obtain a minimum of 2 replicates), twice per day on 20 days on 6 reagent lot/calibrator lot//instrument combinations, where a unique reagent lot and a unique calibrator lot is paired with 1 instrument.

Results are shown in the following table.

Table 12: Precision (20 Days)

Instrument	Reagent Lot	Sample	n	Mean (S/CO)	Within- Run (Repeatability)		Within-Laboratory[a]	
					SD	%CV	SD	%CV
i2000SR (1)	1	Negative Control	120	0.36	0.027	N/A	0.039	N/A
		Positive Control	120	3.15	0.065	2.1	0.076	2.4
		High Negative Panel	120	0.82	0.027	3.2	0.052	6.3
		Low Positive Panel	120	1.31	0.039	3.0	0.064	4.9
		Moderate Positive Panel	120	2.92	0.076	2.6	0.080	2.8
	2	Negative Control	119	0.19	0.023	N/A	0.035	N/A
		Positive Control	119	3.25	0.077	2.4	0.099	3.0
		High Negative Panel	119	0.72	0.027	3.7	0.049	6.8
		Low Positive Panel	119	1.28	0.037	2.9	0.058	4.5
		Moderate Positive Panel	119	3.11	0.072	2.3	0.087	2.8
	3	Negative Control	120	0.31	0.021	N/A	0.031	N/A
		Positive Control	119	3.21	0.090	2.8	0.101	3.1
		High Negative Panel	120	0.80	0.027	3.4	0.041	5.1
		Low Positive Panel	120	1.31	0.040	3.0	0.056	4.2
		Moderate Positive Panel	119	3.03	0.066	2.2	0.079	2.6
i2000SR (2)	1	Negative Control	120	0.35	0.032	N/A	0.042	N/A
		Positive Control	119	3.18	0.083	2.6	0.093	2.9
		High Negative Panel	119	0.80	0.044	5.5	0.051	6.4
		Low Positive Panel	116	1.26	0.042	3.4	0.051	4.1
		Moderate Positive Panel	118	2.92	0.075	2.6	0.085	2.9
	2	Negative Control	120	0.19	0.023	N/A	0.040	N/A
		Positive	120	3.23	0.138	4.3	0.145	4.5

Instrument	Reagent Lot	Sample	n	Mean (S/CO)	Within- Run (Repeatability)		Within-Laboratory[a]	
					SD	%CV	SD	%CV
		Control						
		High Negative Panel	120	0.68	0.026	3.8	0.034	5.0
		Low Positive Panel	119	1.20	0.038	3.2	0.041	3.4
		Moderate Positive Panel	118	3.04	0.087	2.8	0.103	3.4
	3	Negative Control	119	0.30	0.014	N/A	0.028	N/A
		Positive Control	120	3.13	0.083	2.7	0.095	3.0
		High Negative Panel	119	0.76	0.074	9.7	0.077	10.2
		Low Positive Panel	119	1.24	0.041	3.3	0.047	3.8
		Moderate Positive Panel[b]	118	2.89	0.121	4.2	0.129	4.4

N/A = Not applicable

[a] Includes within-run, between-run, and between-day variability.

[b] An outlying run was observed. A replacement run was performed and the results are shown in the preceding table. Without the replacement run, the within-run (repeatability) %CV was 130.3% and the within-laboratory precision %CV was 130.4%.

12. Seroconversion Sensitivity

A study was conducted to determine the seroconversion sensitivity of the ARCHITECT HBsAg Next Qualitative assay and confirmation by the ARCHITECT HBsAg Next Confirmatory assay. Thirty-two HBV seroconversion panels obtained from commercial vendors were tested on the ARCHITECT i System using the ARCHITECT HBsAg Next Qualitative and ARCHITECT HBsAg Next Confirmatory assays. The panel results were evaluated against the ARCHITECT HBsAg Qualitative assay and data are summarized in the table below.

HBsAg was first detected by the ARCHITECT HBsAg Next Qualitative assay and confirmed by the ARCHITECT HBsAg Next Confirmatory assay 2 to 43 days earlier than it was first detected by the ARCHITECT HBsAg Qualitative assay in 24 seroconversion panel sets and coincident with the first day detected by the ARCHITECT HBsAg Qualitative assay in 8 seroconversion panel sets.

In 25 of 32 panels (78%) the number of days to the first repeatedly reactive and confirmed result was less for the ARCHITECT HBsAg Next Qualitative assay compared to the ARCHITECT HBsAg Qualitative assay. Of 483 panel members tested, the ARCHITECT HBsAg Next Qualitative and ARCHITECT HBsAg Next Confirmatory assays detected 271 specimens as repeatedly reactive and confirmed positive. The ARCHITECT HBsAg Qualitative assay detected a total of 223 of the 483 specimens.

Table 13: Seroconversion

Panel ID	Days to HBsAg Repeatedly Reactive Result from Initial Draw Date		Difference in Days (ARCHITECT HBsAg Next Qualitative – Comparator ARCHITECT HBsAg Qualitative)[a]
	ARCHITECT HBsAg Next Qualitative	Comparator ARCHITECT HBsAg Qualitative Assay	
6271	0	7	-7
6272	51	94	-43
6273	14	14	0
6275	2	7	-5
6277	26	33	-7
6278	4	8	-4
6279	21	26	-5
6281	13	13	0
6282	12	14	-2
6284	46	50	-4
6285	38	40	-2
6286	29	29	0[b]
6290	7	14	-7
9074	66	70	-4
11000	0	26	-26
11001	44	44	0
11002	0	7	-7
11003	133	142	-9
11006	35	42	-7
11007	29	34	-5
11008	62	69	-7
11012	18	18	0
11013	239	244	-5
11014	37	51	-14
11017	34	40	-6
11026	36	39	-3
11029	32	35	-3
13867/3482	0	0	0
1807/3463	4	4	0
43527/3453	0	0	0
26022/14518	0	7	-7
0994/3457	0	4	-4

[a] Negative values indicate an earlier detection by the Investigational Method.

[b] For the ARCHITECT HBsAg Qualitative assay, the first repeat reactive bleed (bleed 4) did not confirm so was repeatedly reactive only. Therefore, the investigational assay detected this panel earlier as repeat reactive and confirmed for i2000SR.

13. Reproducibility (5-day)

A 5-day precision study was performed based on guidance form CLSI EP05-A3. Testing was conducted at 3 clinical sites using 3 lots each of ARCHITECT HBsAg Next Qualitative reagents, calibrators, and controls and one ARCHITECT i2000SR per site. Two controls and 3 pansls were assayed in replicates of 4 at 2 separate times of day for 5 days. The results are summarized in the following table:

Table 14: Reproducibility

			Within-Run		Between-Run		Between-Day		Within-Laboratory [a]			Between-Site		Between-Lot		Reproducibility[b]	
Sample	n	Mean S/CO	SD	%CV	SD	%CV	SD	%CV	SD	%CV	%CV Upper CL[c]	SD	%CV	SD	%CV	SD	%CV
Negative Control	359	0.32	0.030	N/A	0.005	N/A	0.000	N/A	0.030	N/A	N/A	0.011	N/A	0.098	N/A	0.103	N/A
Positive Control	360	3.18	0.081	2.5	0.021	0.6	0.008	0.3	0.084	2.6	2.8	0.030	0.9	0.033	1.0	0.096	3.0
High Negative Panel	360	0.80	0.026	3.2	0.016	2.0	0.000	0.0	0.030	3.8	4.1	0.022	2.7	0.062	7.8	0.074	9.2
Low Positive Panel	360	1.31	0.044	3.4	0.024	1.8	0.000	0.0	0.050	3.8	4.1	0.031	2.4	0.036	2.8	0.070	5.3
Moderate Positive Panel	359	3.07	0.083	2.7	0.056	1.8	0.022	0.7	0.102	3.3	3.6	0.055	1.8	0.101	3.3	0.156	5.1

% CV= percent coefficient of variation N/A = Not applicable

[a] Includes within-run, between-run, and between-day variability.

[b] Includes within-run, between-run, between-day, between-site, between-lot, and the site-lot interaction variability.

[c] One-sided upper 95% confidence limit for %CV with degrees of freedom calculated by Satterthwaite met

14. Sample Stability

Sample Stability

A study was conducted to evaluate the effect of sample storage under various conditions (room temperature storage, 2 to 8°C storage, and freeze/thaw) and time periods when testing serum and plasma specimens with the ARCHITECT HBsAg Next Qualitative and ARCHITECT HBsAg Next Confirmatory assays.
The data demonstrate that human serum (including serum collected in serum separator tubes) or plasma collected in tripotassium EDTA and lithium heparin plasma separator tubes may be used with the ARCHITECT HBsAg Next Qualitative and ARCHITECT HBsAg Next Confirmatory assays when:

- Stored at 2 to 8°C for up to 7 days
- Stored at room temperature for up to 3 days
- If testing will be delayed more than 7 days, remove serum or plasma from the clot, red blood cells, or separator gel and store at -20°C or colder.Do not exceed 3 freeze/thaw cycles

Sample Onboard Stability

The purpose of this study was to evaluate stability of samples when stored on ARCHITECT i2000SR System and tested with the candidate device. The results support a sample onboard stability claim of 3 hours.

15. Reagent Stability Studies

Real Time Stability

A stability study was performed to establish real time stability shelf life of the ARCHITECT HBsAg NEXT Qualitative Reagent Kit, ARCHITECT HBsAg NEXT Confirmatory Reagent Kit, ARCHITECT HBsAg NEXT Qualitative Calibrators, ARCHITECT HBsAg NEXT Qualitative Controls, ARCHITECT HBsAg NEXT Confirmatory Manual Diluent. Results support a real time stability claim of 11 months at 2-8ºC.

Reagent Onboard Drift

The purpose of this study was to evaluate the performance of the candidate device by determining if sample results were susceptible to drift when the candidate reagents were stored for a minimum of 30 days onboard ARCHITECT System while instrument in continuous running mode. The results showed that the sample results were not susceptible to drift when the candidate reagents were stored for a minimum of 30 days on board.

In addition, this study evaluated stability of a calibration stored on the ARCHITECT System. The results showed that the stored calibration is stable for 30 days.

16. Antimicrobial Effectiveness (AET)

An AET study was performed to establish the level of antimicrobial protection provided by the preservative formulation of the ARCHITECT HBsAg Next Qualitative Reagents, Calibrators, and Controls and the ARCHITECT HBsAg Next Confirmatory Reagents and Manual Diluent.
Note: The ARCHITECT HBsAg Next Confirmatory Manual Diluent (4P77P) will not be tested, since it has the same formulation as the ARCHITECT HBsAg Next Qualitative Negative Control (4P76L).
The on-test materials were inoculated at a concentration of 10^5 to 10^6 colony forming units per mL (CFU/mL) with each of the following microbial organisms:

Table 15: Antimocrobial Effectiveness (AET)

Organism	**Organism Type**
Candida albicans (*C. albicans*)	Fungal
Aspergillus brasiliensis (A. brasiliensis)	Fungal
Escherichia coli (E. coli)	Bacterial
Pseudomonas aeruginosa (P. aeruginosa)	Bacterial
Staphylococcus aureus (S. aureus)	Bacterial
Bacillus idriensis (B. idriensis)	Bacterial
Micrococcus luteus (M. luteus)	Bacterial
Pseudomonas fulva (P. fulva)	Bacterial
Corynebacterium mycetiodes (C. mycetiodes)	Bacterial

Control materials (uninoculated) were prepared by inoculating the material under evaluation with sterile saline. On Days 14 and 28, the uninoculated and inoculated materials were plated onto agar petri plates, incubated, and examined for growth. The number of colony forming units was counted.
Assay Specific Diluent (4P76X/4P77X) is bacteriostatic and fungistatic for the microorganisms tested. Calibrator 1 (4P76K), Calibrator 2 (4P76Q), and Positive Control (4P76M) are bacteriostatic and fungicidal. All other components are bactericidal and fungicidal.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of the ARCHITECT HBsAg NEXT Qualitative Reagent Kit, ARCHITECT HBsAg NEXT Confirmatory Reagent Kit, ARCHITECT HBsAg NEXT Qualitative Calibrators, ARCHITECT HBsAg NEXT Qualitative Controls, ARCHITECT HBsAg NEXT Confirmatory Manual Diluent 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 2018 and 2019 at three clinical testing sites in Texas, Indiana, and Florida. Specimens were collected from a total of 12 sites and 4 vendors. A total of 2790 specimens were tested with the ARCHITECT HBsAg Next Qualitative assay. Specimens were initially tested once and were testested in duplicate if initial results were reactive. Specimens that were repeatedly reactive were then confirmed with the ARCHITECT HBsAg Next Qual Confirmatory assay. The specimens were from the following categories:

- 1205 specimens from individuals at increased risk of HBV infection due to lifestyle, behavior, occupation, or known exposure event.
- 622 specimens from individuals with signs and symptoms of hepatitis infection
- 129 specimens from individuals diagnosed with acute or chronic HBV infection
- 706 specimens from pregnant females with both low and increased risk for hepatitis B
- 128 de-identified specimens from a pediatric population

B. Accountability of PMA Cohort

The clinical agreement study involved the testing of 2790 samples (prospective and supplemental) obtained for the different study cohorts described in Section C. below. 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). This testing was performed using FDA approved assays from 3 manufacturers, and testing was performed following the manufacturer's instructions.

HBV Classification

All samples were tested to determine the HBV classification with FDA approved assays for detecting HBV serological markers. The following table shows the different HBV Reference Markers and HBV Classification.

Table 16: HBV Classification

HBV Reference Markers				HBV Classification*
HBsAg	Anti-HBc IgM	Total Anti-HBc	Anti-HBs	
+	–	–	–	Early acute
+	I	+	–	Acute infection
+	I	–	–	Acute infection
+	+	+	–	Acute infection
+	–	+	–	Chronic infection
+	–	+	+	Chronic infection
+	–	–	+	Chronic infection
–	+	+	+	Recovering acute
–	+	+	–	Recovering acute/undetectable HBsAg
–	+	–	+	Recovering acute

HBV Reference Markers				HBV Classification*
HBsAg	Anti-HBc IgM	Total Anti-HBc	Anti-HBs	
–	+	–	–	Possible recovering acute, undetectable HBsAg
–	I	+	+	Distantly immune
–	I	+	–	Possible distantly immune, anti-HBs not detected
–	–	+	–	Distantly immune, anti-HBs not detected
–	–	+	+	Immune due to natural infection
–	–	–	+	Immune due to HBV vaccination
–	–	–	–	Susceptible

+ = Positive/Reactive; – = Negative; I = Indeterminate
*Classification presented is a modification of the National Center of Infectious Diseases (CDC) Interpretation of Viral Hepatitis B Panel testing, based on the results of 4 HBV serological markers.

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a HBsAg detection study performed in the US. Demographics for the different study cohorts are shown in the following tables where age is reported as median [Min to Max].

Individuals at Increased risk

Of the 2790 specimens tested in the ARCHITECT HBsAg Next Qualitative clinical study, 1205 specimens were from individuals with increased risk of HBV infection. All 1205 individuals were at risk of HBV infection due to lifestyle, behavior, occupation, or a known exposure event but reported no current signs or symptoms of hepatitis and are shown in the following table:

Table 17: Individuals at Increased Risk of HBV Infection

	Summary
Age	
Age	39.0 [17.0 to 72.0]
Age Range	
18 and Younger	12 / 1205 (1.0%)
19 to 30	359 / 1205 (29.8%)
31 to 40	276 / 1205 (22.9%)
41 to 50	351 / 1205 (29.1%)
51 to 60	176 / 1205 (14.6%)
61 to 70	29 / 1205 (2.4%)
71 to 80	2 / 1205 (0.2%)
Gender	
Female	431 / 1205 (35.8%)

Male	774 / 1205 (64.2%)
Race/Ethnicity	
Black or African American	741 / 1205 (61.5%)
White	229 / 1205 (19.0%)
Hispanic or Latino	152 / 1205 (12.6%)
Asian	8 / 1205 (0.7%)
American Indian or Alaska Native	1 / 1205 (0.1%)
Native Hawaiian or other Pacific Islander	1 / 1205 (0.1%)
Lebanese	1 / 1205 (0.1%)
Mixed Race	69 / 1205 (5.7%)
Other	2 / 1205 (0.2%)
Unknown	1 / 1205 (0.1%)

Individuals with Increased Risk of HBV Infection and Signs and Symptoms of Hepatitis Infection

Of the 2970 specimens tested and analyzed, 1827 specimens were from increased risk of HBV infection and with signs and symptoms of hepatitis infection and are shown in the following table.

Table 18: Individuals at Increased Risk of HBV Infection and with Signs and Symptoms of Hepatitis Infection

	Summary
Age	
Age	40.0 [17.0 to 84.0]
Age Range	
18 and Younger	19 / 1827 (1.0%)
19 to 30	516 / 1827 (28.2%)
31 to 40	386 / 1827 (21.1%)
41 to 50	502 / 1827 (27.5%)
51 to 60	330 / 1827 (18.1%)
61 to 70	62 / 1827 (3.4%)
71 to 80	10 / 1827 (0.5%)
81 to 90	2 / 1827 (0.1%)
Gender	
Female	727 / 1827 (39.8%)
Male	1100 / 1827 (60.2%)
Race/Ethnicity	
Black or African American	962 / 1827 (52.7%)
White	551 / 1827 (30.2%)

Hispanic or Latino	200 / 1827 (10.9%)
Asian	13 / 1827 (0.7%)
American Indian or Alaska Native	4 / 1827 (0.2%)
Native Hawaiian or other Pacific Islander	4 / 1827 (0.2%)
Lebanese	1 / 1827 (0.1%)
Mixed Race	86 / 1827 (4.7%)
Other	5 / 1827 (0.3%)
Unknown	1 / 1827 (0.1%)

Pregant Females

The pregnant female population (n = 706) consisted of the following race/ ethnic groups: 139 (19.7%) Black or African American, 167 (23.7%) White, 348 (49.3%) Hispanic or Latino, 16 (2.3%) Asian, 1 (0.1%) American Indian/Alaska Native, 1 (0.1%) Native Hawaiian or other Pacific Islander, 4 (0.6%) Mixed Race, 14 (2.0%) Other, and 16 (2.3%) Unknown and is shown in the following two tables.

Table 19: Pregant Female High Risk

	Summary
Age	
Age	25.0 [18.0 to 43.0]
Age Range	
18 to 31	151 / 182 (83.0%)
32 to 45	31 / 182 (17.0%)
Gender	
Female	182 / 182 (100.0%)
Race/Ethnicity	
Black or African American	45 / 182 (24.7%)
White	25 / 182 (13.7%)
Hispanic or Latino	97 / 182 (53.3%)
Asian	2 / 182 (1.1%)
Mixed Race	2 / 182 (1.1%)
Other	6 / 182 (3.3%)
Unknown	5 / 182 (2.7%)

Table 20: Pregnant Female Low Risk

	Summary
Age	
Age	28.0 [18.0 to 43.0]
Age Range	

18 to 31	363 / 524 (69.3%)
32 to 45	161 / 524 (30.7%)
Gender	
Female	524 / 524 (100.0%)
Race/Ethnicity	
Black or African American	94 / 524 (17.9%)
White	142 / 524 (27.1%)
Hispanic or Latino	251 / 524 (47.9%)
Asian	14 / 524 (2.7%)
American Indian or Alaska Native	1 / 524 (0.2%)
Native Hawaiian or other Pacific Islander	1 / 524 (0.2%)
Mixed Race	2 / 524 (0.4%)
Other	8 / 524 (1.5%)
Unknown	11 / 524 (2.1%)

Pediatric

A total of 128 specimens were from a pediatric population. Of these, 11 were excluded because they were from individuals less than 2 years of age. Results from a total of 117 specimens were included in the analysis. The distribution of ARCHITECT HBsAg Next Qualitative reactive and nonreactive results by age range and gender is show in the following table:

Table 21: Pediatric Population Overall

Age Range (Years)	Gender	ARCHITECT HBsAg Next Qualitative Result		Total
		RR (% of Total)	NR (%of Total)	
2 to 12	Female	1 (0.85)[a]	20 (17.09)	21
	Male	0 (0.00)	42 (35.90)	42
>12 to 21	Female	1 (0.85)[b]	35 (29.91)	36
	Male	0 (0.00)	18 (15.38)	18
Total		**2 (1.71)**	**115 (98.29)**	**117**

[a] The specimen was confirmed by ARCHITECT HBsAg Next Confirmatory. The corresponding comparator ARCHITECT HBsAg Qualitative result is nonreactive.

[b] The specimen was not confirmed by ARCHITECT HBsAg Next Confirmatory. The corresponding comparator ARCHITECT HBsAg Qualitative result is repeatedly reactive/not confirmed.

D. Safety and Effectiveness Results

1. Safety Results

With regard to safety, as an in vitro diagnostic test, the HBsAg Next Qualitative assay involves taking a sample of plasma and 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.

2. Effectiveness Results

The following table compares the ARCHITECT HBsAg Next Qualitative assay results with the HBsAg Qualitative and ARCHITECT HBsAg Qualitative Confirmatory assays final interpretation for each of the HBV classifications for the increased risk and signs and symptoms populations (n=1827) and the acute or chronic HBV infection population (n=129). The combined results are summarized in the following table.

Table 22 Performance for Individuals at Increased Risk and Signs and Symptoms, and Acute and Chronic Populations.

	Comparator ARCHITECT HBsAg Qualitative Final Interpretation			
	Confirmed Positive		**Negative/Not Confirmed**	
	ARCHITECT HBsAg Next Qualitative Result		**ARCHITECT HBsAg Next Qualitative Result**	
HBV Classification	**Repeatedly Reactive**	**Nonreactive**	**Repeatedly Reactive**	**Nonreactive**
	N	**N**	**N**	**N**
Early acute	26	0	0	0
Acute	38	0	0	0
Recovering acute / undetectable HBsAg	0	0	0	1
Recovering acute	0	0	0	8
Possible recovering acute / undetectable HBsAg	0	0	0	1
Chronic	68	0	0	0
Immune due to natural infection	0	0	0	165
Immune due to HBV vaccination	0	0	1[a]	553
Susceptible	0	0	1[b]	982
Uninterpretable	0	0	2	103
Total[c]	**132**	**0**	**4[d]**	**1813**

[a] Specimen was PCR positive, consistent with vaccine breakthrough or recent vaccination.
[b] Specimen was PCR positive, consistent with an early acute infection or an occult infection.
[c] Seven specimens were excluded due to no ARCHITECT HBsAg Qualitative Confirmatory results.
[d] The 4 specimens were confirmed reactive by the ARCHITECT HBsAg Next Confirmatory assay.

3. Subgroup Analyses

The study design enabled an assessment of assay performance by subgroup as depicted in the tables above which show subjects stratified by cohort.
The 2097 specimens were tested with the HBsAg Next Qualitative assay on the ARCHITECT i2000SR and an FDA approved reference assay to establish the clinical performance characteristics. The following tables compare the HBsAg Next Qualitative assay results with the results obtained on an FDA-approved HBsAg reference assay by HBV disease classification for the different cohorts tested.

Individuals at Increased Risk of HBV Infection

The percent agreement between the ARCHITECT HBsAg Next Qualitative assay results and the ARCHITECT HBsAg Qualitative assay final interpretation for the increased risk population by HBV classification (n = 1205) is summarized in the following table.

Table 23 Performance for Individuals at Increase Risk of HBV Infection

HBV Classification	Positive Percent Agreement	95% Confidence Interval	Negative Percent Agreement	95% Confidence Interval
Acute	100.00 (3/3)	(43.85, 100.00)	N/A[a]	N/A
Recovering acute	N/A	N/A	100.00 (5/5)	(56.55, 100.00)
Chronic	100.00 (6/6)	(60.97, 100.00)	N/A	N/A
Immune due to natural infection	N/A	N/A	100.00 (122/122)	(96.95, 100.00)
Immune due to HBV vaccination	N/A	N/A	99.73 (365/366)	(98.47, 99.95)
Susceptible	N/A	N/A	99.84 (635/636)	(99.11, 99.97)
Uninterpretable	N/A	N/A	98.51 (66/67)	(92.02, 99.74)
Total	**100.00 (9/9)**	**(70.09, 100.00)**	**99.75 (1193/1196)**	**(99.27, 99.91)**

[a] Not applicable

Individuals with Signs and Symptoms of HBV Infection

The percent agreement between the ARCHITECT HBsAg Next Qualitative assay results and the ARCHITECT HBsAg Qualitative assay final interpretation for the signs and symptoms population by HBV classification (n = 622) is summarized in the following table.

Table 24 Performance for Individuals with Signs and Symptoms of HBV Infection

HBV Classification	Positive Percent Agreement	95% Confidence Interval	Negative Percent Agreement	95% Confidence Interval
Recovering acute/ Undetectable HBsAg	N/A[a]	N/A	100.00 (1/1)	(20.65, 100.00)

HBV Classification	Positive Percent Agreement	95% Confidence Interval	Negative Percent Agreement	95% Confidence Interval
Recovering acute	N/A	N/A	100.00 (3/3)	(43.85, 100.00)
Possible recovering acute/ Undetectable HBsAg	N/A	N/A	100.00 (1/1)	(20.65, 100.00)
Chronic	100.00 (1/1)	(20.65, 100.00)	N/A	N/A
Immune due to natural infection	N/A	N/A	100.00 (43/43)	(91.80, 100.00)
Immune due to HBV vaccination	N/A	N/A	100.00 (188/188)	(98.00, 100.00)
Susceptible	N/A	N/A	100.00 (347/347)	(98.91, 100.00)
Uninterpretable	N/A	N/A	97.37 (37/38)	(86.51, 99.53)
Total	**100.00 (1/1)**	**(20.65, 100.00)**	**99.84 (620/621)**	**(99.09, 99.97)**

Combined Percent Agreement for Individuals at Increased Risk and Signs and Symptoms

The percent agreement between the ARCHITECT HBsAg Next Qualitative assay results and the ARCHITECT HBsAg Qualitative assay final interpretation for the increased risk and signs and symptoms populations by HBV classification (n = 1827) is summarized in the following table.

Table 25 Combined Percent Agreement for Individuals at Increased Risk and Signs and Symptoms

HBV Classification	Positive Percent Agreement	95% Confidence Interval	Negative Percent Agreement	95% Confidence Interval
Acute	100.00 (3/3)	(43.85, 100.00)	N/A	N/A
Recovering acute/ undetectable HBsAg	N/A	N/A	100.00 (1/1)	(20.65, 100.00)
Recovering acute	N/A	N/A	100.00 (8/8)	(67.56, 100.00)
Possible recovering acute / undetectable HBsAg	N/A	N/A	100.00 (1/1)	(20.65, 100.00)
Chronic	100.00 (7/7)	(64.57, 100.00)	N/A	N/A
Immune due to natural infection	N/A	N/A	100.00 (165/165)	(97.72, 100.00)
Immune due to HBV vaccination	N/A	N/A	99.82 (553/554)	(98.98, 99.97)
Susceptible	N/A	N/A	99.90 (982/983)	(99.43, 99.98)
Uninterpretable	N/A	N/A	98.10 (103/105)	(93.32, 99.48)
Total	**100.00 (10/10)**	**(72.25, 100.00)**	**99.78 (1813/1817)**	**(99.44, 99.91)**

Acute and Chronic HBV Infection

Of the 2790 specimens tested and analyzed, 129 specimens were from the acute and chronic HBV infection populations. The negative percent agreement and positive percent agreement results for preselected HBsAg positive individuals by specimen category are presented in the following table.

Table 26 Individuals with Acute and Chronic HBV Infection (preselected HBsAg Positive)

Specimen Category	Positive Percent Agreement (%)	95% Confidence Interval (%)	Negative Percent Agreement (%)	95% Confidence Interval (%)
Individuals with Acute HBV Infection	100.00 (55/55)	(93.47, 100.00)	N/A[a]	N/A
Individuals with Chronic HBV Infection	100.00 (74/74)	(95.07, 100.00)	N/A	N/A
Total	**100.00 (119/119)**	**(96.87, 100.00)**	**N/A**	**N/A**

[a] N/A = not applicable

Comparison of Results by HBV Classification

The ARCHITECT HBsAg Next Qualitative assay results were compared with the ARCHITECT HBsAg Qualitative and Confirmatory assays final interpretation for each of the HBV classifications for the increased risk of HBV infection and signs and symptoms of hepatitis infection populations (n = 1827) and the acute or chronic HBV infection populations (n = 129). The results are presented in the following table.

Table 27 Comparison of HBV Classification Results Between ARCHITECT HBsAg Next Qualitative Interpretation and ARCHITECT HBsAg Qualitative and Confirmatory Interpretation

HBV Classification	Comparator ARCHITECT HBsAg Qualitative Final Interpretation								Total	
	Confirmed Positive				Negative/Not Confirmed					
	ARCHITECT HBsAg Next Qualitative				ARCHITECT HBsAg Next Qualitative					
	RR		NR		RR		NR			
	N	%	N	%	N	%	N	%	N	%
Early Acute	26	19.70	0	NA	0	0.00	0	0.00	26	1.33
Acute	38	28.79	0	NA	0	0.00	0	0.00	38	1.95
Recovering Acute/Undetectable HBsAg	0	0.00	0	NA	0	0.00	1	0.06	1	0.05
Recovering Acute	0	0.00	0	NA	0	0.00	8	0.44	8	0.41
Possible Recovering Acute/Undetectable HBsAg	0	0.00	0	NA	0	0.00	1	0.06	1	0.05

HBV Classification	Comparator ARCHITECT HBsAg Qualitative Final Interpretation								Total	
	Confirmed Positive				Negative/Not Confirmed					
	ARCHITECT HBsAg Next Qualitative				ARCHITECT HBsAg Next Qualitative					
	RR		NR		RR		NR			
	N	%	N	%	N	%	N	%	N	%
Chronic	68	51.52	0	NA	0	0.00	0	0.00	68	3.49
Immune Due to Natural Infection	0	0.00	0	NA	0	0.00	165	9.10	165	8.47
Immune Due to HBV Vaccination	0	0.00	0	NA	1[a]	25.00	553	30.50	554	28.42
Susceptible	0	0.00	0	NA	1[b]	25.00	982	54.16	983	50.44
Uninterpretable	0	0.00	0	NA	2	50.00	103	5.68	105	5.39
Total*	**132**	**100.00**	**0**	**NA**	**4[c]**	**100.00**	**1813**	**100.00**	**1949**	**100.00**

* 7 Specimens were excluded due to no ARCHITECT HBsAg Qualitative Confirmatory results.

[a] Specimen was PCR positive, consistent with vaccine breakthrough or recent vaccination.

[b] Specimen was PCR positive, consistent with an early acute infection or an occult infection.

[c] The 4 specimens were confirmed reactive by the ARCHITECT HBsAg Next Confirmatory assay.

Pregnant Female Population

For the pregnant female population (n = 706), the negative percent agreement was 100.00% (706/706) with a 95% confidence interval of 99.46% to 100.00% and the overall agreement was 100.00% (706/706) with a 95% confidence interval of 99.46% to 100.00% for the ARCHITECT HBsAg Next Qualitative assay results versus the ARCHITECT HBsAg Qualitative assay results. The results are presented in the following tables.

Table 28 Reactive and Nonreactive Results from Pregnant Females

ARCHITECT HBsAg Next Qualitative	ARCHITECT HBsAg Qualitative	
	Reactive	Nonreactive
Reactive	0	0
Nonreactive	0	706

Table 29 Percent Agreement for Pregnant Females

Subjects	Negative Percent Agreement	95% Confidence Interval	Overall Percent Agreement	95% Confidence Interval
Pregnant Females – Increased Risk	100.00 (182/182)	(97.93 - 100.00)	100.00 (182/182)	(97.93 - 100.00)
Pregnant Females – Low Risk	100.00 (524/524)	(99.27 - 100.00)	100.00 (524/524)	(99.27 - 100.00)
Pregnant Females - Total	100.00 (706/706)	(99.46, 100.00)	100.00 (706/706)	(99.46, 100.00)

Specimen Equivalence in Pregnant and Non-Pregnant Individuals

A study was conducted to evaluate the results observed when samples from pregnant women were tested with the ARCHITECT HBsAg Next Qualitative

A total of 32 serum specimens from pregnant females (17 to 41 years) and 32 serum specimens from non-pregnant females of child-bearing age (20 to 41 years) were spiked with an HBsAg positive specimen to a target of 3.00 S/CO. The distribution by trimester was: 14 specimens from women in the 1st trimester, 11 in the 2nd trimester, and 7 in the 3rd trimester of pregnancy. Three replicates of the spiked specimens were tested with the ARCHITECT HBsAg Next Qualitative assay. The average recovery for the specimens from pregnant individuals was 93% and ranged from 81.0% to 101.4%. The results of the study suggest that specimens from pregnant individuals react in the same manner as specimens from non-pregnant individuals for HBsAg detection.

Table 30 Results of Specimen in Pregnant and Non-Pregnant Individuals

N	Test Adjusted S/CO	Control Adjusted S/CO	% Recovery
32	2.65	2.85	93.0

For all single female specimens, the % recovery of all individual specimens from pregnant individuals was within 80 to 120% of the reference population.

The results of the study suggest that specimens from pregnant individuals react in the same manner as specimens from non-pregnant individuals for HBsAg detection.

Pediatric Population

One hundred (128) specimens were from a pediatric population. The distribution of ARCHITECT HBsAg Next Qualitative reactive and nonreactive results by age range and gender is presented in the following table.

Table 31 Reactive and Nonreactive Results for Pediatric Population

Age Range (Years)	Gender	ARCHITECT HBsAg Next Qualitative Result		Total
		RR (% of Total)	NR (%of Total)	
2 to 12	Female	1 (0.85)[a]	20 (17.09)	21
	Male	0 (0.00)	42 (35.90)	42
>12 to 21	Female	1 (0.85)[b]	35 (29.91)	36
	Male	0 (0.00)	18 (15.38)	18
Total		**2 (1.71)**	**115 (98.29)**	**117**

[a] The specimen was confirmed by ARCHITECT HBsAg Next Confirmatory. The corresponding comparator ARCHITECT HBsAg Qualitative result is nonreactive.

[b] The specimen was not confirmed by ARCHITECT HBsAg Next Confirmatory. The corresponding comparator ARCHITECT HBsAg Qualitative result is repeatedly reactive/not confirmed.

Of the 2790 specimens in the clinical study, 128 specimens were from a pediatric population aged 0 to 21. There were 117 specimens (out of the 128) in the 2 to 21 year age range. For the 117 specimens, the negative percent agreement was 99.14% (115/116) with a 95% confidence interval of 95.28% to 99.85% and the positive percent agreement was 100.00% (1/1) with a 95% confidence interval of 20.65% to 100.00% for the ARCHITECT HBsAg Next Qualitative result versus the ARCHITECT HBsAg Qualitative final interpretation.

Pediatric versus Adult Specimen Comparison

A study was conducted to evaluate the results observed when pediatric samples were tested with the ARTCHITECT HBsAg Next Qualitative.

A total of 46 negative pediatric (2 years to 21 years) specimens (15 serum and 31 plasma) were used in the study and one adult reference plasma specimen. There were 14 (30%) specimens from individuals in the 2 to 12 years age range and 32 (70%) in the 13 to 21 years age range. The pediatric specimens and a single adult specimen were spiked with an HBsAg positive specimen to a target of 3.00 S/CO. Three replicates of the spiked specimens were tested with the ARCHITECT HBsAg Next Qualitative assay. Averaged results for each pediatric specimen were compared to results obtained from adult specimens. The average recovery for all pediatric specimens was 94% and ranged from 47.9% to 112.8%.

Table 32 %Recovery Summary

	N	Min[a]	Max	Mean	SD
%Recovery 1	46	47.9	112.8	93.8	9.8
%Recovery 2	46	48.6	113.2	93.8	9.6

%Recovery1 = first replicate vs mean

%Recovery2 = mean vs mean

[a] Specimen #45 from a 17-year-old individual obtained a recovery of 48%. The specimen was anti-HBs nonreactive at 0.27 mIU/mL. Additional testing of this sample to investigate the possible cause of the low recovery was not possible due to insufficient sample volume.

With exception of one specimen (#45), the % recovery of all individual pediatric specimens was within 80 to 120% of the reference base matrix.

The average recovery for pediatric specimens without sample #45 was 95%.

Table 33%Recovery Summary (Without Sample #45)

	N	Min	Max	Mean	SD
%Recovery 1	45	82.3	112.8	94.8	7.0
%Recovery 2	45	82.3	113.2	94.8	6.8

%Recovery1 = first replicate vs mean

%Recovery2 = mean vs mean

Averaged results for each pediatric specimen were compared to results obtained from adult specimens.

The results of the study suggest that pediatric specimens react in the same manner as adult specimens for HBsAg detection.

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

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 15 investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Microbiology Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The effectiveness of the ARCHITECT HBsAg Next Qualitative assay for the qualitative detection of hepatitis B surface antigen in human adult and pediatric (2 years to 21 years of age) serum, serum separator tube, and plasma (dipotassium EDTA, tripotassium EDTA, lithium heparin, lithium heparin separator, sodium heparin) samples 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 ARCHITECT HBsAg Next Qualitative assay when used according to the manufacturer's instructions can aid the physician in the diagnosis of HBV infection and 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 be recommended, as HBsAg is often the first test sent as part of the evaluation of hepatitis B infection.

1. Patient Perspective

   This submission either did not include specific information on patient perspectives or the information did not serve as part of the basis of the decision to approve or deny the PMA for this device.

In conclusion, given the available information above, the data support that for the claimed intended use the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The probable clinical benefits outweigh the potential risks for the proposed assay considering the performance of the device in the clinical 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.

XIII. CDRH DECISION

CDRH issued an approval order on August 20, 2022.

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

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.