SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Antibodies to Hepatitis B e antigen (Anti-HBe

Device Trade Name: Elecsys Anti-HBe, PreciControl Anti-HBe

Device Procode: LOM

Applicant's Name and Address: Roche Diagnostics
9115 Hague Road
Indianapolis, IN 46250

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P190005

Date of FDA Notice of Approval: February 3, 2021

II. INDICATIONS FOR USE

Elecsys Anti-HBe
Immunoassay for the in vitro qualitative detection of total antibodies to hepatitis B e antigen (anti-HBe) in human adult serum or plasma (potassium EDTA, lithium heparin, sodium citrate, sodium heparin) from individuals with symptoms of hepatitis or at risk for hepatitis B virus (HBV) infection. Assay results, in conjunction with other laboratory results and clinical information may be used as an aid in the diagnosis of hepatitis B virus (HBV) infection in patients with symptoms of hepatitis or who may be at risk for HBV infection. A reactive test is presumptive laboratory evidence of HBV seroconversion. Further HBV serological marker testing is required to define the specific disease state.

The **e**lectro**c**hemi**l**uminescence **i**mmuno**a**ssay "ECLIA" is intended for use on the cobas e 602 immunoassay analyzer.

PreciControl Anti-HBe
PreciControl Anti-HBe is used for quality control of the Elecsys Anti-HBe immunoassay on the cobas e 602 immunoassay analyzer. The performance of PreciControl Anti-HBe has not been established with any other anti-HBe assay.

III. CONTRAINDICATIONS

There are no known contraindications.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Elecsys Anti-HBe labeling.

V. DEVICE DESCRIPTION

The Elecsys Anti-HBe immunoassay is a qualitative test that employs the electrochemiluminescence "ECLIA" technology. The assay employs a two-incubation step assay using the competition principle test format and a total assay time of 18 minutes.

- 1st incubation: Anti-HBe in the sample (35 µL) binds to the added HBeAg.
- 2nd incubation: After addition of biotinylated antibodies and ruthenium complex-labeled antibodies specific for HBeAg, together with streptavidin-coated microparticles, the still-free binding sites on the HBe antigens become occupied. The entire complex is then bound to the solid phase via interaction of biotin and streptavidin.
- The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with ProCell M. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier.
- Results are determined automatically by the software by comparing the electrochemiluminescence signal obtained from the reaction product of the sample with the signal of the cutoff value previously obtained by calibration.

The Elecsys Anti-HBe consists of five components summarized below:

Table 1: Components of the Elecsys Anti-HBe

	Name	Description
Rackpack (bundle of three reagent bottles) labeled as A-HBE	M	Streptavidin-coated microparticles (transparent cap), 1 bottle 6.5 mL consists of streptavidin-coated microparticles 0.72 mg/mL; preservative.
	R1	HBeAg (gray cap), 1 bottle, 12 mL consists of HBeAg (E. coli, rDNA) > 7 ng/mL; HEPES) buffer 36 mmol/L, pH 7.4; preservative.
	R2	Anti-HBeAg-Ab~biotin; anti-HBeAg-Ab~Ru(bpy)$_3^{2+}$ (black cap), 1 bottle, 12 mL: Biotinylated monoclonal anti-HBe antibody (mouse) > 0.8 mg/L; monoclonal anti-HBe antibody (mouse) labeled with ruthenium

		complex > 0.2 mg/L; HEPES buffer 36 mmol/L, pH 7.4; preservative
	A-HBE Cal1	Negative calibrator 1 (white cap), 2 bottles of 1.0 mL each consists of negative human serum, preservative
	A-HBE Cal2	Positive calibrator 2 (black cap), 2 bottles of 1.0 mL each consists of Anti-HBe Positive human serum, preservative

The following results are reported:

Table 2: Interpretation of Results

Output Elecsys Anti-HBe (S/CO)	**Test Result**	**Interpretation**
> **1.00 S/CO***	Non-Reactive	Indicates sample is non-reactive for anti-HBe. A negative test result does not exclude the possibility of infection with hepatitis B virus.
≤ 1.00 S/CO	Reactive	Indicates sample is reactive for anti-HBe

s/co=signal/cutoff

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the detection of total antibodies to hepatitis B e antigen (anti-HBe). There are currently several FDA approved in vitro diagnostic tests commercially available for serological markers of hepatitis B virus (HBV) infection which, when used in conjunction with a patient's medical history, clinical examination and other laboratory 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 of HBV infection. The assay may be used as aid in determining acute infection. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The device has been marketed in the following countries (Table 3) and has not been withdrawn from any country for reasons relating to safety and effectiveness.

Table 3: Marketing History

Argentina	Ecuador	Mexico	Slovakia
Australia	Egypt	Middle East	Slovenia
Austria	Finland	Myanmar	South Africa
Baltics	France	Netherlands	Spain
Belgium	Germany	New Zealand	Sweden
Brazil	Greece	Norway	Switzerland
Canada	Hong Kong	Pakistan	Taiwan

Central America	Hungary	Peru	Thailand
Chile	India	Philippines	Turkey
China	Indonesia	Poland	United Kingdom
Colombia	Italy	Portugal	Uruguay
Croatia	Japan	Romania	Venezuela
Czech Republic	Korean Republic	Russian Federation	Vietnam
Denmark	Malaysia	Singapore	Slovakia

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 Elecsys Anti-HBe is intended for *in vitro* diagnostic use, and as a result, there is no direct adverse effect on the patient. Standard good laboratory practices are considered sufficient to minimize risks to the end user.

Failure of the product to perform as intended or human error in the use of the test may lead to a false result. Appropriate Warnings and Precautions for identified risks are contained in the labeling and assay Instructions for Use.

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

Risks of a false positive test includes improper patient management, including premature discontinuation of antiviral treatment should a clinician be falsely led to determine a patient has seroconverted. This risk is mitigated by the fact that this assay is usually repeated and is used as part of a panel. Repeatedly false positive results have the potential to lead to inappropriate treatment decisions, however anti-HBe is not used in isolation to determine seroconversion status. Because anti-HBe is sometimes included as part of a panel in clinical practice to diagnose hepatitis B but is more commonly utilized as part of a panel to determine chronicity of disease and immune-active versus chronic infection, the risk of a false positive will likely be somewhat mitigated as incongruous test results would lead a clinician to either retest the patient or further investigate the etiology of hepatitis.

Risk of a false negative test includes improper patient management, including continued treatment for hepatitis B with antiviral medication. 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 chance of an undiagnosed co-infection in a patient tested for hepatitis B is exceedingly unlikely. Anti-HBe is not used in this same manner as HBeAg to guide treatment decisions, and thus confers less clinical risk to this subpopulation than a false negative or false positive HBeAg test. Anti-HBe is not used in isolation to determine seroconversion status. Because anti-HBe is sometimes included as part of a panel in clinical practice to diagnose hepatitis B but is more commonly utilized as

part of a panel to determine chronicity of disease and immune-active v. chronic infection, the risk of a false negative will likely be mitigated as incongruous test results would lead a clinician to either retest the patient or further investigate the etiology of hepatitis

IX. SUMMARY OF NONCLINICAL STUDIES

A. Laboratory Studies

1. Cut-Off Determination
   The cut-off was established internally at Roche and verified by testing a total of 181 samples (84 positives and 97 negatives). A Receiver Operating Characteristics (ROC) analysis was performed on the results of the samples tested. The assay's cut-off was evaluated with the observed results to demonstrate that its selection represents the best level of specificity, without compromising sensitivity.

   The cut-off value of 1.0 is within the optimal range determined by the ROC curve to discriminate between negative and positive results.

2. Analytical Sensitivity/Dilution Study with Standard
   The WHO International Standard Anti-Hepatitis B virus e antigen (anti-HBe), code 129095/12, was diluted into HBV negative human serum by nine dilution steps to produce ten different concentrations (0, 0.02, 0.039, 0.078, 0.156, 0.313, 0.625, 1.25, 2.5, and 5 IU/mL). The samples were measured in duplicate with one reagent lot of Elecsys Anti-HBe to establish a standard curve. The sensitivity at the cut-off for the Elecsys Anti-HBe on the cobas e 602 analyzer is 0.127 IU/mL.

3. Sensitivity/Seroconversion Panels
   The seroconversion sensitivity of the Elecsys Anti-HBe has been demonstrated by testing 8 commercially seroconversion panels in comparison to a reference anti-HBe immunoassay in terms of number of days from initial draw to first positive sample, as well as the difference between the last negative results and the first positive results. The following table shows that the Elecsys Anti-HBe detected a positive result sooner by one or more blood draws than the comparator assay in 4 out of 8 panels.

Table 4: Seroconversion Performance of the Elecsys Anti-HBe

Panel ID	Bleed day of the last NR[a)] test		Bleed day of the first RX[b)] test		Difference in days[c)] to anti-HBe reactive
	Reference assay	Elecsys Anti-HBe assay	Reference assay	Elecsys Anti-HBe assay	
6281	54	41	N/A	43	>11
6510	56	14	70	28	42
9092	198	134	N/A	141	>57
9093	173	173	182	182	0
11024	54	54	N/A	N/A	N/A

Panel ID	Bleed day of the last NR[a] test		Bleed day of the first RX[b] test		Difference in days[c] to anti-HBe reactive
	Reference assay	Elecsys Anti-HBe assay	Reference assay	Elecsys Anti-HBe assay	
BMX11071	81	69	88	81	7
BMX11072	60	60	74	74	0
BMX11073	78	78	140	140	0

a) NR = non-reactive
b) RX = reactive
c) The dates of the first reactive test results were compared between the Elecsys Anti-HBe assay and the Reference assay

4. Analytical Specificity (Cross-Reactivity)
A study was conducted to evaluate the Elecsys Anti-HBe for potential cross-reactivity in specimens from individuals with various medical conditions. The specificity of 190 samples with 23 sub-categories of potentially interfering diseases or medical conditions was evaluated with the Elecsys Anti-HBe assay on the cobas e 602 immunoassay analyzer and the reference assay.

Of the 190 samples, there were 6 samples that showed cross-reactivity. The results of each potential cross reactant are shown in table below.

Table 5: Cross-Reactivity Results

Reactivity of the Elecsys Anti-HBe assay				
Category	Sub-category	RX[h]	NR[i]	Total
Immune disorders	ANA	0	12	12
	RF	0	12	12
Infections / disorders	T. pallidum	0	11	11
	Toxoplasmosis	0	11	11
Infectious Viral agents	CMV	0	10	10
	EBV	1	11	12
	HAV	0	12	12
	HCV	2	10	12
	HIV 1/2	0	10	10
	HSV	0	12	12
	Parvo B19	1	11	12
	Rubella	0	12	12
	VZV	0	12	12
Non-viral	Liver cancer	2	8	10

Reactivity of the Elecsys Anti-HBe assay				
Category	Sub-category	RX[h)]	NR[i)]	Total
liver disease	Chronic alcoholic liver disease	0	7	7
	Various cirrhosis	0	5	5
	Alcoholic fatty liver	0	4	4
	Alcoholic liver disease	0	4	4
	Abdominal pain / pelvic mass	0	4	4
	Unspecified jaundice	0	2	2
	Liver abscess or lesion	0	2	2
	Fatty infiltrate of liver	0	1	1
	Chronic passive congestion of liver	0	1	1
Total		6	184	190

5. Endogenous Interference
   To evaluate the effect of elevated levels of hemoglobin, bilirubin, intralipid, biotin, and total protein on the Elecsys Anti-HBe assay, one negative, one high negative, one low positive, and one positive anti-HBe serum samples were spiked with potential interferents. Each interferent was evaluated at 11 concentrations. All samples were tested in duplicate. Interferences were tested up to the listed concentration and no impact on results was observed.

Table 6: Interfering Substances

Compound	Concentration tested
Bilirubin	≤ 66 mg/dL
Hemoglobin	≤ 2000 mg/dL
Intralipid	≤ 2000 mg/dL
Albumin	≤ 7 g/dL

6. Endogenous Interference-Biotin
   Because this test employs strept-avidin technology and may be subject to potential interference with biotin, more extensive interference testing with biotin was performed. The following tables show the level of interference that was observed.

Table 7: Bias for Samples Containing Various Concentrations of Biotin

Sample (COI)[a]			Biotin concentration (ng/mL)				
			96	112	128	144	160
negative	1.56		-1.8	-5.2	-8.2	-12.5	-17.1

Sample (COI)[a]			Biotin concentration (ng/mL)				
			96	112	128	144	160
high negative	1.14	relative deviation (%)	-6.2	-6.9	-12.2	-14.3*	-19.8*
low positive	0.892	absolute deviation	-0.025	-0.052	-0.069	-0.108	-0.154
positive	0.371		-0.019	-0.032	-0.043	-0.058	-0.075

Sample (COI)			Biotin concentration (ng/mL)			
			200	300	600	1200
negative	1.56	relative deviation (%)	-46.2*	-74.1*	-89.3*	-95.8*
high negative	1.14		-45.5*	-73.7*	-88.4*	-93.1*
low positive	0.892	absolute deviation	-0.361	-0.604	-0.730	-0.765
positive	0.371		-0.151	-0.226	-0.263	-0.273

[a]COI=cutoff index

*false positive

Specimens with biotin concentrations up to 112 ng/mL demonstrated ≤ 10 % bias in results. Biotin concentrations greater than 112 ng/mL lead to higher negative bias and in consequence can lead to false negative Elecsys Anti-HBe results in samples near the medical decision value. Pharmacokinetic studies have shown that serum concentrations of biotin can reach up to 355 ng/mL within the first hour after biotin ingestion for subjects consuming supplements of 20 mg biotin per day and up to 1160 ng/mL for subjects after a single dose of 300 mg biotin.

7. Drug Interference

A drug interference study was performed with 16 common therapeutic drugs. Each drug was spiked into one negative, one high negative, one low positive, and one positive sample. Each sample was tested in triplicate. Each drug was found to be non-interfering at the following claimed concentrations.

Table 8: Drug Interference

Compound	Concentration (mg/L)
Acetyl cysteine	150
Ampicillin-Na	1000
Ascorbic acid	300
Cefoxitin	2500
Heparin	5000 U/L
Levodopa	20

Compound	Concentration (mg/L)
Methyldopa+ 1.5	20
Metronidazole	200
Doxycycline	50
Acetylsalicylic acid	1000
Rifampicin	60
Cyclosporine	5
Phenylbutazone	400
Acetaminophen	200
Ibuprofen	500
Theophylline	100

6. Human Anti-Mouse Antibody Effect (HAMA) Study
   Two samples (one anti-HBe negative sample, one native anti-HBe negative samples with positive anti-HBe sample) were spiked with Human anti-mouse antibodies in ten concentration levels with a maximum concentration of 60 ug/mL The samples were measured in duplicate. The percent recovery for the negative samples ranged from 98-102% while the standard deviation for the positive samples ranged from 0-0.019 s/co. Results met the acceptance criteria. No interference for Elecsys Anti-HBe was observed with 60 ug/mL HAMA titer.

7. Sample Equivalence/Matrix Equivalency
   Studies were conducted to evaluate the suitability of the following seven sample types: serum/gel separation tubes, sodium heparin plasma, sodium citrate plasma, lithium heparin plasma, K_2-EDTA plasma, K_3-EDTA plasma and plasma tubes containing separation gel, to be used with the Elecsys Anti-HBe assay.
   Samples were collected into matched serum and plasma collection tubes and assayed in single determinations. The study was conducted using negative, high negative, low positive, and positive samples for anti-HBe. The studies support the use of serum/gel separation tubes, and the following plasma types: lithium heparin, K_2-EDTA, K_3-EDTA, sodium heparin, sodium citrate, and plasma tubes containing separating gel.

8. Carry-Over Study
   The use of disposable tips for sample pipetting on the cobas e 602 immunoassay analyzer should eliminate the risk of sample carryover. A study was performed by testing six anti-HBe positive samples with Elecsys Anti-HBe in triplicate and a high signal generating sample in an Elecsys assay (Toxo IgG immunoassay) in alternating patterns. The percent recovery ranged from 103% to 110%.

9. Stability Studies

Sample Stability

Studies were performed to determine the storage stability of patient serum and plasma samples at storage temperatures of 2-8°C, room temperature (RT), and -20°C. A multiple freeze/thaw study was also performed.

Serum and plasma samples tested contained anti-HBs analyte levels of negative, high negative, low positive, and positive.

- 2-8°C study- samples were tested unstressed (T=0) and again after 1, 5, 7, 11, and 14 days at 2-8°C in triplicate.
- Room temperature study (RT)- samples were tested immediately after preparation and again after 1, 2, 3, and 7 days of storage at RT.
- -20°C Study-samples were tested unstressed (t=0) and stored at -20°C 1, 2, and 3 months.
- Freeze/thaw study-samples were tested unstressed (T=0) and after 6 freeze thaw cycles in triplicate.

Table 9: Sample Stability Claims in Serum and Plasma

Sample Matrix	Number of Freeze and Thaw Cycles	Storage at 2-8°C	Storage at -20°C	Storage at Room Temperature
Serum and Plasma	6	14 days	3 months	14 days

Reagent Stability-Real-Time (Shelf-Life)

Studies were performed to establish the shelf-life for the Elecsys Anti-HBe. A negative, high negative, low positive, and positive sample were tested with three lots of Elecsys Anti-HBe were stored at the recommended storage temperature of 2-8°C throughout the study. Performance was assessed against clinically relevant acceptance criteria. Study demonstrated reagents are stable and continue to meet acceptance criteria for 24 months after date of manufacture.

Reagent Stability- after First Opening

This study was performed to determine the time period over which the Elecsys Anti-HBe can be kept at 2-8°C once opened. One test kit was opened and the cobas e 602 analyzer calibrated. A negative, high negative, low positive, and positive serum sample and two Elecsys PreciControl Anti-HBe were tested with the opened reagent unstressed (T=0) and after 8 and 9 weeks at 2-8°C. Study demonstrated that reagents are stable for 8 weeks when stored at 2-8°C after first opening.

Reagent Stability-Reagent On-Board

This study was performed to determine the time period for which the Elecsys Anti-HBe reagents can be stored on the analyzer once opened. The reagent packs were stored on-board for 8 and 9 weeks at 20-25°C. Unstressed reagent packs were opened and the analyzer was calibrated. A negative, high negative, low positive, and positive serum sample and two Elecsys PreciControl Anti-HBe were tested with the unstressed reagent

packs (stored at 2-8°C) and with the reagent packs which were stressed on-board for 8 and 9 weeks. For each time point, the calibration occurred seven days prior. Study demonstrated that reagents are stable for 8 weeks when stored on-board the cobas e 602 analyzer.

Reagent Stability-Temperature Stress

Thi study was conducted to determine the effect of elevated temperature stress on the Elecsys Anti-HBe reagents during transportation. The reagent kit was stressed for one week at 35°C. A negative, high negative, low positive, and positive serum samples and both PreciControls were measured in duplicate with the stressed reagent kits and compared to the results from the unstressed kit. Study demonstrated that reagents are stable for one week at 35°C.

Lot Calibration Stability

An unstressed rackpack of Elecsys Anti-HBe reagent was calibrated on the cobas e 602 analyzer. A negative, high negative, low positive, and positive serum sample and PreciControls were tested in duplicate (T=0). After 28 and 35 days, reagent of the same lot was run again using the initial calibration. Study supports a claim for lot calibration of 28 days.

On-Board Calibration Stability

An Elecsys Anti-HBe reagent pack was tested unstressed (stored at 2-8°C) and after 7 and 14 days of storage on-board the cobas e 602 at 20-25°C, using the initial calibration of day 0 to demonstrate the stability of the initial calibration and the stability of the control measurements. Study supports a claim for on-board calibration stability of 7 days.

Calibrator Stability-After First Opening

This study was performed to determine the time period in which the Elecsys Anti-HBe calibrators can be kept at 2-8oC once opened. A new reagent pack was opened and the cobas e 602 calibrated. The opened calibrators were then tested again in duplicate after 13 weeks stored at 2-8oC. Study supports calibrator stability for 8 weeks at 2-8°C after first opening.

Calibrator Stability-On-Board

According to product specification, calibrators 1 and 2 may be used only once. Unless the entire volume is necessary for calibration on the analyzer, aliquots of the ready-for-use calibrators may be transferred into empty snap-cap bottles (CalSet vials), should be left on the analyzer only during calibration, and should be discarded after use on the cobas e 602 analyzer. This study was performed to assess stability of the calibrators on-board the cobas e 602 analyzer at 20-25°C. A pair of Elecsys Anti-HBe calibrators were opened and stored at 20-25°C to simulate on-board stress. After 7 hours of incubation at 20-25°C, the calibrators were tested in duplicate with a pair of unstressed calibrators. Study supports calibrator on-board stability of 6 hours.

PreciControl Stability-Real Time Shelf-Life

Shelf life was determined by testing one production lot in duplicate of PreciControl Anti-HBe stored at 2-8°C. Study supports PreciControl shelf life stability of 22 months at 2-8°C.

PreciControl Stability-After First Opening

Stability studies were performed to determine the time period over which the PreciControl Anti-HBe can be kept at 2-8°C once opened. A new PreciControl kit pack was opened, tested in duplicate on day 0 (unstressed reference) on the cobas e 602 analyzer, and then tested again in duplicate after 8 and 9 weeks of storage at 2-8°C. Study supports PreciControl Anti-HBe stored for 8 weeks at 2-8°C after first opening.

PreciControl Stability-On Board

Stability studies were performed to determine the time period over which PreciControl Anti-HBe can be kept on-board at 20-25oC once opened. A new PreciControl kit was opened and measured on the cobas e 602 analyzer in duplicate (unstressed reference). After stored open at 32oC for 7 hours, the control kit was run again on the cobas e 602 analyzer. Opened PreciControl Anti-HBe can be stored up to 6 hours on-board the cobas e 602 analyzer.

PreciControl Stability-Temperature Stress

This study was conducted to determine the effect of elevated temperature stress on the PreciControl Anti-HBe during transport. One kit was stored at the recommended storage of 2-8°C and a second kit was stressed for one week at 35°C. PreciControl Anti-HBe are stable for 1 week at 35°C.

10. Within Laboratory Precision

A six member precision panel consisten of four human serum (HS) pools (one negative, one high negative, one low positive, and one positive) and two PreciControls (PC1 and PC2) were tested in duplicate, on one cobas e 602 analyzer, at one site, with one reagent lot, in two runs per day for 12 days. Calibration was performed on day 1 and day 7 spanning at least two calibration cycles. Repeatability (within-run) and within-laboratory precision were calculated according to EP5-A3. Results are shown in the following table.

Table 10: Within Laboratory Precision

		Repeatability[a)]		**Intermediate precision[b)]**	
Sample	Mean COI	SD COI	CV %	SD COI	CV %
HS[c)], negative	1.50	0.016	1.0	0.030	2.0
HS, high negative	1.10	0.012	1.1	0.025	2.3
HS, low positive	0.799	0.008	1.0	0.020	2.5
HS, positive	0.023	0.001	2.8	0.002	7.0
PC[d)] A-HBe 1	1.49	0.027	1.8	0.034	2.3

		Repeatability[a)]		Intermediate precision[b)]	
Sample	Mean COI	SD COI	CV %	SD COI	CV %
PC A-HBe 2	0.660	0.008	1.2	0.021	3.1

a) Repeatability = within-run precision

b) Intermediate precision = within-laboratory precision

c) HS = Human serum

d) PC = PreciControl

11. Reproducibility

The study was performed at three sites with three reagent lots with PreciControl Anti-HBe and sample concentrations shown in the table below in three replicates per run, two runs per day, for five days, on three cobas e 602 analyzers in a modified protocol CLSI EP05-A3. The results are shown in the following table.

Table 11: Reproducibility

		Repeatability		Between-run		Between-day	
Sample	Mean COI	SD COI	CV %	SD COI	CV %	SD COI	CV %
HSP[a)] 01	0.576	0.009	1.5	0.012	2.2	0.015	2.6
HSP 02	0.783	0.012	1.6	0.013	1.6	0.021	2.7
HSP 03	0.885	0.013	1.5	0.011	1.3	0.024	2.7
HSP 04	1.05	0.017	1.6	0.014	1.3	0.030	2.9
HSP 05	1.08	0.019	1.8	0.012	1.1	0.029	2.7
HSP 06	1.22	0.020	1.7	0.013	1.1	0.033	2.8
PC A-HBe 1	1.53	0.029	1.9	0.018	1.2	0.031	2.1
PC A-HBe 2	0.643	0.012	1.8	0.012	1.9	0.013	2.1

a) HSP = human serum pool

	Between-lot		Between-site		Reproducibility	
Sample	**SD COI**	**CV %**	**SD COI**	**CV %**	**SD COI**	**CV %**
HSP 01	0.019	3.2	0.024	4.1	0.037	6.4
HSP 02	0.025	3.2	0.025	3.2	0.045	5.7
HSP 03	0.025	2.9	0.023	2.6	0.045	5.1
HSP 04	0.027	2.6	0.034	3.2	0.057	5.5
HSP 05	0.034	3.2	0.022	2.0	0.055	5.1
HSP 06	0.046	3.8	0.026	2.1	0.067	5.5
PC A-HBe 1	0.025	1.6	0.013	0.83	0.054	3.5
PC A-HBe 2	0.012	1.8	0.015	2.4	0.029	4.5

12. Antimicrobial Effectiveness Testing

The purpose of this study was to prove the effectiveness of the added preservatives in the reagents. One lot each of reagent was tested with a panel of microorganisms. All reagents were plated on appropriate media prior to inoculation. Non-inoculated reagent (reference) was incubated in parallel with inoculated reagents and palted at each time. After inoculation, the reagents were incubated for 14 and 28. To pass United States Pharmacopoeia) USP criteria, the bacterial concentration is to be reduced to < 0.1 % of the original inoculum by day 14 and remain at or below this level until day 28. Yeast and molds are to remain at or below the original inoculum during the 28-day period. USP criteria suggest that a suitable inoculum should be between 1×10^5 and 1×10^6 organisms per mL. All reagents met the USP requirements for antimicrobial effectiveness testing.

B. Animal Studies

Not Applicable

C. Additional Studies

Not Applicable

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness for the detection of antibodies to hepatitis B e antigen with the Elecsys Anti-HBe 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-site clinical study was conducted to evaluate the clinical performance of the Elecsys Anti-HBe on samples that would routinely be tested for hepatitis and samples that were selected from individuals that were diagnosed with acute or chronic Hepatitis B infection.

The clinical agreement study involved the testing of 1800 samples (1500 adult specimens were prospectively collected from individuals at increased risk and 300 supplemenal cohort specimens). The 1500 specimens were collected from seven collection sites located in Los Angeles, CA (32.0%), San Antonio, TX (24.9%), Baltimore, MD (17.9%), Miami, FL (7.9%), City of Industry, CA (6.9%), Darby, PA (6.8%), and Minneapolis, MN (3.6%). The 300 supplemental specimens were obtained from three external vendors. Testing of the specimens was performed at three clinical sites located in South Bend, IN, Iowa City, IA, and San Diego, CA.

B. Accountability of PMA Cohort

The clinical agreement study involved the testing of 1800 samples (1500 prospectively collected and 300 supplemental) on six (6) FDA approved reference assays, each detecting a unique serological marker (HBsAg, HBeAg, Anti-HBs, Anti-HBc, Anti-HBc

IgM, and Anti-HBe) in order to determine the HBV classification for each of the samples tested.

The following table shows the different HBV specimen classifications.

Table 12: Serological Classification by FDA-Approved HBV Panel

	HBsAg	HBeAg	Anti-HBc IgM	Anti-HBc	Anti-HBe	Anti-HBs
Acute	(+)	(+)	(+)	(+)	(-), (+)	(-)
Acute	(+)	(+)	(-), (+)	(-)	(-)	(-)
Acute	(+)	(-)	(-)	(-)	(-)	(-)
Acute	(+)	(+)	(eq)	(+)	(-), (+)	(-)
Acute	(+)	(-)	(+)	(+)	(-)	(-)
Acute	(+)	(-)	(eq)	(+)	(+)	(-)
Acute (late)	(+)	(-)	(+)	(+)	(+)	(-), (+)
Chronic	(+)	(+)	(+)	(+)	(+)	(+)
Chronic	(+)	(-)	(-)	(+)	(+)	(-), (+)
Chronic	(+)	(-)	(-)	(+)	(eq)	(-)
Chronic	(+)	(-)	(-)	(+)	(-)	(-), (+)
Chronic	(+)	(+)	(+)	(+)	(-)	(+)
Chronic	(+)	(+)	(-)	(+)	(-)	(-), (+)
Chronic	(+)	(+)	(-)	(+)	(+)	(-)
Early recovery	(-)	(-)	(-)	(+)	(-), (+)	(-)
Early recovery	(-)	(-)	(+)	(+)	(-)	(-), (+)
Early recovery	(-)	(-)	(+)	(+)	(+)	(-), (+)
Recovery	(-)	(-)	(-)	(-),(+)	(+)	(+)
Recovery	(-)	(-)	(-)	(+)	(+)	(eq)
Recovered or immune due to natural infection	(-)	(-)	(-)	(+)	(-)	(+), (eq)
HBV vaccine response	(-)	(-)	(-)	(-)	(-)	(+)
HBV vaccination response	(-)	(-)	(-)	(-)	(-)	(eq)
Not previously infected	(-)	(-)	(-)	(-)	(-)	(-)
Not interpretable	(-)	(+)	(-)	(+)	(-)	(+)
Not interpretable	(-)	(-)	(-)	(-)	(+)	(-)

	HBsAg	HBeAg	Anti-HBc IgM	Anti-HBc	Anti-HBe	Anti-HBs
Not interpretable	(-)	(+)	(-)	(+)	(+)	(-)
Not interpretable	(-)	(+)	(-)	(-)	(-)	(-), (eq), (+)

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for an Anti-HBe detection study performed in the US. The following tables show the demographics for the adult at increased risk (AIR) and supplemental study cohorts.

Table 13: Demogrpahics of Clinical Population by Gender

Cohort	Gender	N	% of cohort total
Adult AIR	Female	686	45.7
	Male	814	54.3
	Unknown	0	0.0
	Subtotal	1500	100
Supplemental	Female	117	39.0
	Male	182	60.7
	Unknown	1	0.3
	Subtotal	300	100
Total		1800	

Table 14: Demograhpics of Clinical Population by Ethnicity

Cohort	Ethnicity	N	% of cohort total
Adult AIR	Hispanic or Latino	421	28.1
	Not Hispanic or Latino	1073	71.5
	Unknown	6	0.4
	Subtotal	1500	100
Supplemental	Hispanic or Latino	2	0.7
	Not Hispanic or Latino	0	0.0
	Unknown	298	99.3
	Subtotal	300	100
Total		1800	

Table 15: Demographics of Clinical Population by Race

Cohort	Race	N	% of cohort total
Adult AIR	AIAN*	17	1.1
	Asian	9	0.6
	Black or African American	735	49.0
	Caucasian / White	709	47.3
	More than one race	21	1.4
	Nhopi	4	0.3
	Other	1	0.1
	Unknown	4	0.3
	Subtotal	1500	100
Supplemental	AIAN	0	0.0
	Asian	166	55.3
	Black or African American	114	38.0
	Caucasian / White	15	5.0
	More than one race	0	0.0
	Nhopi	0	0.0
	Other	0	0.0
	Unknown	5	1.7
	Subtotal	300	100
Total		1800	

*AIAN-American Indian and Alaskan Native

Table 16: Demograhpics of Clinical Population by Age

Cohort	Age group (years)	N	% of cohort total
Adult AIR	2-11	0	0.0
	12-21	0	0.0
	22-29	176	11.7
	30-39	253	16.9
	40-49	435	29.0
	50-59	481	32.1
	60-69	140	9.3
	70-79	12	0.8

Cohort	Age group (years)	N	% of cohort total
	≥ 80	3	0.2
	Unknown	0	0.0
	Subtotal	1500	100
Supplemental	2-11	0	0.0
	12-21	0	0.0
	22-29	73	24.3
	30-39	80	26.7
	40-49	70	23.3
	50-59	50	16.7
	60-69	26	8.7
	70-79	1	0.3
	≥ 80	0	0.0
	Unknown	0	0.0
	Subtotal	300	100
Total		1800	

D. Safety and Effectiveness Results

1. Safety Results

   With regard to safety, as an in vitro diagnostic test, the Elecsys Anti-HBe test 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 are drawn.

   There were no adverse effects that occurred in the PMA clinical study.

2. Effectiveness Results

   The analysis of effectiveness was based on 1800 evaluable patients. Key effectiveness outcomes are presented in the tables below.

   Specimens were tested using the Elecsys Anti-HBe assay on the cobas e 602 immunoassay analyzer and a FDA-approved reference assay to establish the clinical performance characteristics. The following tables compare the Elecsys Anti-HBe results and performance with the results and performance obtained on

an FDA-approved anti-HBe reference assay by HBV disease classification for the adult at increased risk cohort.

Table 17: Results comparing Elecsys Anti-HBe to the FDA-Approved Reference Assay by HBV Classification for Adults at Increased Risk Cohort

HBV classification	FDA-approved reference assay				Total
	Reactive		Non-reactive		
	Elecsys Anti-HBe		Elecsys Anti-HBe		
	RX[1)]	NR[2)]	RX	NR	
	n	n	n	n	
Acute	0	0	0	7	7
Chronic	25	0	0	7	32
Early recovery	40	2	16	139	197
Not previously infected	0	0	1	554	555
Recovered	0	0	47	195	242
Recovery	129	3	0	0	132
Vaccination	0	0	0	335	335
Total	194	5	64	1237	1500

1) RX = reactive

2) NR = non-reactive

Table 18: Percent Agreement between Elecsys Anti-HBe and FDA-Approved Reference Assay by HBV Classification for Adults at Increased Risk Cohort

	PPA[3)]		NPA[4)]	
HBV classification	% (n/N)	95 % Exact CI[5)]	% (n/N)	95 % Exact CI
Acute	N/A (0/0)	N/A	100 (7/7)	59.0 to 100
Chronic	100 (25/25)	86.3 to 100	100 (7/7)	59.0 to 100
Early recovery	95.2 (40/42)	83.8 to 99.4	89.7 (139/155)	83.8 to 94.0
Not previously infected	N/A (0/0)	N/A	99.8 (554/555)	99.0 to 100
Recovered	N/A (0/0)	N/A	80.6 (195/242)	75.0 to 85.4
Recovery	97.7 (129/132)	93.5 to 99.5	N/A (0/0)	N/A
Vaccination	N/A (0/0)	N/A	100 (335/335)	98.9 to 100

	PPA[3)]		NPA[4)]	
HBV classification	% (n/N)	95 % Exact CI[5)]	% (n/N)	95 % Exact CI
Total	97.5 (194/199)	94.2 to 99.2	95.1 (1237/1301)	93.8 to 96.2

3) PPA = positive percent agreement
4) NPA = negative percent agreement
5) CI = confidence interval

Table 19: Results comparing Elecsys Anti-HBe to the FDA-Approved Reference Assay by HBV Classification for Supplemental Cohort

HBV classification	FDA-approved reference assay				Total
	Reactive		Non-reactive		
	Elecsys Anti-HBe		Elecsys Anti-HBe		
	RX	NR	RX	NR	
	n	n	n	n	
Acute	7	0	97	24	128
Chronic	45	0	10	117	172
Total	52	0	107	141	300

Table 20: Percent Agreement between Elecsys Anti-HBe and FDA-Approved Reference Assay by HBV Classification for Supplemental Cohort

	PPA		NPA	
HBV classification	% (n/N)	95 % Exact CI	% (n/N)	95 % Exact CI
Acute	100 (7/7)	59.0 to 100	19.8 (24/121)	13.1 to 28.1
Chronic	100 (45/45)	92.1 to 100	92.1 (117/127)	86.0 to 96.2
Total	100 (52/52)	93.2 to 100	56.9 (141/248)	50.4 to 63.1

In order to demonstrate the presence or absence of anti-HBe antibody activity, an internal confirmatory assay was developed. The confirmatory principle used HBeAg covalently coupled to sepharose to bind to anti-HBe antibodies in the sample. Depletion of Anti-HBe antibodies in the sample distinguished a confirmed reactive or positive result from a false-positive or unconfirmed reactive result. After testing was completed at the three external sites, samples were transferred to Roche for storage. An internal study was then conducted testing all Elecsys Anti-HBe reactive samples (N=421) and approximately 1/3 of the concordant non-reactive samples (N=476). The concordant non-reactive samples were randomly selected for testing from the remaining samples with enough sample volume to complete testing.

The following algorithm was employed to obtain a composite method result for the samples evaluated with the confirmatory test.

Table 21: Composite Method Algorithm

Confirmatory assay result	FDA-approved Reference assay result	Composite result interpretation
Confirmed non-reactive	Non-reactive	Non-reactive
Confirmed non-reactive	Reactive	Reactive
Confirmed positive	Non-reactive	Reactive
Confirmed positive	Reactive	Reactive

False positive confirmatory assay results were considered non-reactive for the purposes of this analysis. Because only a subset of the clinical samples were tested by the confirmatory assay, a verification bias analysis was employed to impute the results for those samples that were not tested by confirmatory assay. The following results were obtained for the adult cohort and supplemental cohort.

Table 22: Results Comparing the Elecsys Anti-HBe with Composite Method Algorithm For the Adult at Increased Risk Cohort

HBV Classification	Composite Comparator				Total	PPA (95% CI, Wilson Score)	NPA (95% CI, Wilson Score)
	Reactive		Non-reactive				
	Elecsys Anti-HBe		Elecsys Anti-HBe				
	Reactive	Non-reactive	Reactive	Non-reactive			
Acute				7	7		100% (7/7)
Chronic	25			7	32	100% (25/25)	100% (7/7)
Early Recovery	56	10	0	131	197	84.8% (56/66)	100% (131/131)
Not previously infected				554	554		100% (554/554)
Recovered	1		1	155	157	100% (1/1)	99.4% (155/156)
Recovery	174	43			217	80.2% (174/217)	
Vaccination				335	335		100% (335/335)
Not Interpretable	1				1		
Total	257	53	1	1189	1500	82.9% (257/310)	99.9% (1189/1190)

Table 23: Results Comparing the Elecsys Anti-HBe with Composite Method Algorithm For the Supplemental Cohort

HBV Classification	Composite Comparator				Total	PPA (95% CI, Wilson Score)	NPA (95% CI, Wilson Score)
	Reactive		Non-reactive				
	Elecsys Anti-HBe		Elecsys Anti-HBe				
	Reactive	Non-reactive	Reactive	Non- reactive			
Acute	103	2	2	21	128	98.1% (103/105)	91.3% (21/23)
Chronic	54	4	1	113	172	93.1% (54/58)	99.1% (113/114)
Total	157	6	3	134	300	96.3% (157/163)	97.8% (134/137)

The following section provides further analysis comparing the results of the FDA approved reference assay and the Elecsys Anti-HBe to the Roche Confirmatory assay.

Table 24: Results Comparing the FDA Approved Reference Assay Versus Confirmatory Assay

FDA-approved reference assay	Confirmatory Reactive	Confirmatory Non-reactive	Total
Positive	197	2	199
Negative	211	1090	1301
Total	40	1092	1500

Table 25: Results Comparing the Elecsys Anti-HBe Versus Confirmatory Assay

Elecsys Anti-HBe	Confirmatory Reactive	Confirmatory Non-reactive	Total
Positive	255	3	258
Negative	50	1192	1242
Total	305	1195	1500

Adults at Increased Risk

A summary of performance, including percent agreements, of the Elecsys Ant-HBe and the FDA-approved reference assay compared to Confirmatory approach for the adult at increased risk cohort are presented in the table below.

Table 26: Summary of Performance of Elecsys Anti-HBe and the FDA-Approved Assay Compared to the Confirmatory Assay for Adults at Increased Risk

	Positive Percent Agreement	95% CI	Negative Percent Agreement	95% CI
Elecsys Anti-HBe	83.6 %	79.0 – 87.3 %	99.7 %	99.3 – 99.9 %
FDA-approved reference assay	48.3 %	43.5 – 53.1 %	99.8 %	99.3 – 99.9 %

Supplemental Cohort

A summary of performance, including percent agreements, of the Elecsys Ant-HBe and the FDA-approved reference assay compared to Confirmatory approach for the supplemental cohort are presented in the table below.

Table 27: Summary of Results of Elecsys Anti-HBe and the FDA-Approved assay Compared to the Confirmatory Assay for Supplemental Cohort

FDA-approved reference assay	Confirmatory Confirmed Reactive	Confirmatory Confirmed Non-reactive	Total
Positive	50	2	52
Negative	143	105	248
Total	193	107	300

Table 28: Summary of Performance of Elecsys Anti-HBe and the FDA-Approved assay Compared to the Confirmatory Assay for Supplemental Cohort

Elecsys Anti-HBe	Confirmatory Confirmed Reactive	Confirmatory Confirmed Non-reactive	Total
Positive	144	15	159
Negative	7	134	141
Total	151	149	300

Table 29: Summary of Performance of Elecsys Anti-HBe and the FDA-Approved assay Compared to the Confirmatory Assay for Supplemental Cohort

	Positive Percent Agreement	95% CI	Negative Percent Agreement	95% CI
Elecsys Anti-HBe	95.4 %	90.7 – 97.7 %	89.9 %	84.1 – 93.8 %
FDA-approved reference assay	25.9 %	20.2 – 32.5 %	98.1 %	93.4 – 99.5 %

Overall (Combined AIR and Supplemental Cohort) Results

The overall analysis of the study results completed between the FDA approved assay and the Confirmatory approach are summarized in the following table.

Table 30: Summary of Results of Elecsys Anti-HBe and the FDA-Approved assay Compared to the Confirmatory Assay Overall

FDA-approved reference assay	Confirmatory Confirmed Reactive	Confirmatory Confirmed Non-reactive	Total
Positive	247	4	251
Negative	415	1134	1549
Total	662	1138	1800

Table 31: Summary of Performance of Elecsys Anti-HBe and the FDA-Approved assay Compared to the Confirmatory Assay Overall

Elecsys Anti-HBe	Confirmatory Confirmed Reactive	Confirmatory Confirmed Non-reactive	Total
Positive	399	18	417
Negative	57	1326	1383
Total	456	1344	1800

Table 32: Summary of Performance of Elecsys Anti-HBe and the FDA-Approved assay Compared to the Confirmatory Assay Overall

	Positive Percent Agreement	95% CI	Negative Percent Agreement	95% CI
Elecsys Anti-HBe	87.5 %	84.1 – 90.2 %	98.7 %	97.9 – 99.2 %
FDA-approved reference assay	37.3 %	33.7 – 41.1 %	99.6 %	99.1 – 99.9 %

3. Subgroup Analyses
   The study design enabled an assessment of assay performance by subgroup as depicted in the tables in Section X.D.2 above which show subjects stratified by HBV classification.

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 11 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 Elecsys Anti-HBe for the qualitative detection of antibodies to hepatitis B e antigen in human serum and plasma (potassium EDTA, lithium heparin, sodium citrate, 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 with symptoms of hepatitis. 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 Elecsys Anti-HBe when used according to the manufacturer's instructions can aid the physician in the diagnosis of HBV infection.

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 as part of a hepatitis B panel, the appropriate determination of HBV seroconversion as part of disease management and treatment. Treatment for appropriate patients can mitigate the sequelae of hepatitis B infection and may result in improved morbidity and mortality in these patients. Known sequelae of hepatitis B infection include continued symptoms, increases in all-cause mortality, liver disease-related complications and death, hepato-cellular carcinoma rates, and need for liver transplantation. Additionally, management and appropriate treatment for hepatitis B infection can potentially decrease transmission and disease burden in the general population and particularly in populations at high risk for hepatitis B infection. While the performance of the device in the clinical study suggests that patients will benefit from the assay, low prevalence of certain HBV classifications is a source of potential uncertainty when analyzing the samples. The wide confidence intervals for those subgroups is expected due to the biology of hepatitis B infection and is acceptable

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 includes improper patient management, including premature discontinuation of antiviral treatment should a clinician be falsely led to determine a patient has seroconverted. This risk is mitigated by the fact that this assay is usually repeated and is used as part of a panel. Repeatedly false positive results have the potential to lead to inappropriate treatment decisions, however anti-HBe is not used in isolation to determine seroconversion status. Because anti-HBe is sometimes included as part of a panel in clinical practice to diagnose hepatitis B but is more commonly utilized as part of a panel to determine chronicity of disease and immune-active v. chronic infection, the risk of a false positive will likely be somewhat mitigated as incongruous test results would lead a clinician to either retest the patient or further investigate the etiology of hepatitis.

Risk of a false negative test includes improper patient management, including continued treatment for hepatitis B with antiviral medication. 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 chance of an undiagnosed co-infection in a patient tested for hepatitis B is exceedingly unlikely. Anti-HBe is not used in this same manner as HBeAg to guide treatment decisions, and thus confers less clinical risk to this subpopulation than a false negative or false positive HBeAg test. Anti-HBe is not used in isolation to determine seroconversion status. Because anti-HBe is sometimes included as part of a panel in clinical practice to diagnose hepatitis B but is more commonly utilized as part of a panel to determine chronicity of disease and immune-active v. chronic infection, the risk of a false negative will likely be mitigated as incongruous test results would lead a clinician to either retest the patient or further investigate the etiology of hepatitis.

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 and 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 uncommom 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 concjunction with other laboratory results and clinical information.

XIII. CDRH DECISION

CDRH issued an approval order on February 3, 2021.

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.