Table 21: Bland Altman Plot (Relative Difference)

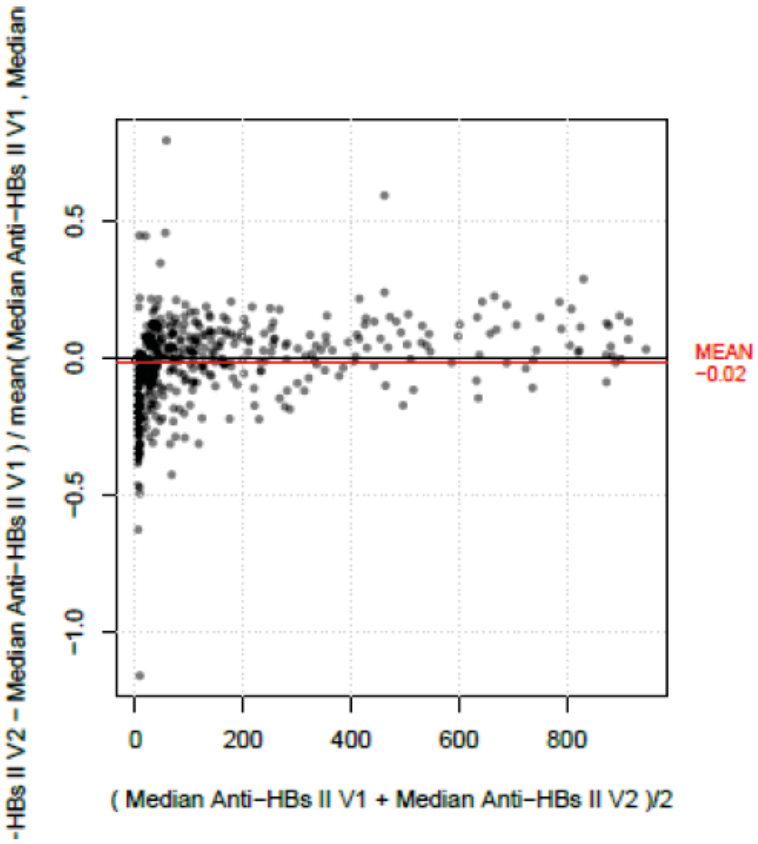

Table 22: Agreement Rates and Two-Sided 95% Confidence Intervals (CI)

Updated Elecsys Anti-HBs II*	**Current Elecsys Anti-HBs II***		
	Non-reactive	**Reactive**	**Total**
Non-reactive	180	7	187
Reactive	0	354	354
Total	180	361	541
Negative Percent Agreement	100% (180/180) 95% CI: 97.91-100%		
Positive Percent Agreement	98.06% (354/361) 95% CI: 96.05-99.06%		

*The median results of the three (3) lots were used to determine non-reactive and reactive status and are presented here.

Method Comparison between current and updated Elecsys Anti-HBs II assays on the cobas e 601 analyzer show equivalent results where there was no statistically significant systematic different between the two (2) systems and > 95% of the sample results fall within allowable total difference (ATD) zones.

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 surface antigen with the current Elecsys Anti-HBs II 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 to characterize the performance of the Elecsys Anti-HBs II assay on the **cobas e** 601 analyzer against the reference assay, Elecsys Anti-HBs, with individuals from definedpopulations. Performance of the Elecsys Anti-HBs II assay was assessed by testing a total of 4047 samples from adult, pediatric and pregnant subjects at increased risk, and vaccination subjects, at three (3) different study sites. All subjects were tested using FDA-approved reference methods. The 4047 subjects were comprised of 2067 adult subjects at increased risk (45.6 % female and 54.4 % male), 128 pediatric subjects (53.1 % female and 46.9 % male), 218 pregnant at increased risk subjects, and 70 vaccination subjects (45.7 % female and 54.3 % male), along with 692 supplemental samples (18.5 % female and 81.4 % male), 588 pregnant at low risk subjects and 284 specificity samples (57.0 % female and 27.5 % male), and were tested with the Elecsys Anti-HBs II assay and the Elecsys Anti-HBs assay. The supplemental cohort was used to provide an adequate number for both acute and chronic individuals. The three (3) sites tested the at-risk and supplemental specimens with a full panel of anti-HBc IgM, anti-HBc, HBsAg, HBeAg, anti-HBe, and anti-HBs (reference) for serological characterization. The study included the following races: Caucasian, African-American/Black, Asian, American Indian/Alaskan Native, and Hawaiian Native/Pacific Islander.

B. Accountability of PMA Cohort

The clinical agreement study involved the testing of 2759 samples Adult at increased risk (2067 prospectively collected and 692 supplemental) for the adult at increased risk (AIR) 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 23: Serological Classification by FDA-Approved HBV Panel

Serological classification by FDA-approved HBV panel						
	HBsAg	**HBeAg**	**Anti-HBc IgM**	**Anti-HBc**	**Anti-HBe**	**Anti-HBs**
Acute	(+)	(+)	(+)	(+)	(-), (+)	(-)
Acute	(+)	(+)	(-), (+)	(-)	(-)	(-)

Serological classification by FDA-approved HBV panel						
	HBsAg	**HBeAg**	**Anti-HBc IgM**	**Anti-HBc**	**Anti-HBe**	**Anti-HBs**
Acute	(+)	(-)	(-)	(-)	(-)	(-)
Acute	(+)	(+)	eq	(+)	(-), (+)	(-)
Acute	(+)	(-)	(+)	(+)	(-)	(-)
Acute	(+)	(-)	eq	(+)	(+)	(-)
Acute (late)	(+)	(-)	(+)	(+)	(+)	(-), (+)
Chronic	(+)	(+)	(+)	(+)	(+)	(+)
Chronic	(+)	(-)	(-)	(+)	(+)	(-), (+)
Chronic	(+)	(-)	(-)	(+)	eq	(-)
Chronic	(+)	(-)	(-)	(+)	(-)	(-), (+)
Chronic	(+)	(+)	(+)	(+)	(-)	(+)
Chronic	(+)	(+)	(-)	(+)	(-)	(-), (+)
Chronic	(+)	(+)	(-)	(+)	(+)	(-)
Early recovery	(-)	(-)	(-)	(+)	(-), eq, (+)	(-)
Early recovery	(-)	(-)	(+)	(+)	(-)	(-), (+)
Early recovery	(-)	(-)	(+)	(+)	(+)	(-), (+)
Recovery	(-)	(-)	(-)	(-), (+)	(+)	(+)
Recovery	(-)	(-)	(-)	(+)	(+)	eq
Recovery	(-)	(-)	(-)	(+)	eq	(+)
Recovered or immune due to natural infection	(-)	(-)	(-)	(+)	(-)	(+), eq
HBV vaccine response	(-)	(-)	(-)	(-)	(-)	(+)
HBV vaccine response (?)	(-)	(-)	(-)	(-)	(-)	eq
Not previously infected	(-)	(-)	(-)	(-)	(-)	(-)

Serological classification by FDA-approved HBV panel						
	HBsAg	**HBeAg**	**Anti-HBc IgM**	**Anti-HBc**	**Anti-HBe**	**Anti-HBs**
Not interpretable	(-)	(+)	(-)	(+)	(-)	(+)
Not interpretable	(-)	(-)	(-)	(-)	(+)	(-)
Not interpretable	(-)	(+)	(-)	(+)	(+)	(-)
Not interpretable	(-)	(+)	(-)	(-)	(-)	(-), eq, (+)

The following table shows the total numbers of the HBV Serological Classification for adult at increased risk prospective and retrospective cohorts.

Table 24: Adult AIR Prospective and Retrospective Cohorts by HBV Serological Classification

HBV Classification	Adult AIR Prospective	Adult AIR Retrospective	Total
Acute	7	75	82
Chronic	32	318	350
Early Recovery	198	16	214
Recovery	131	199	330
Recovered	248	83	331
Vaccination	497	0	497
Not previously infected	944	1	945
Not Interpretable	10	0	10
Total	2067	692	2759

The clinical study also included the following number of evaluable patients for each cohort: 71 evaluable patients for pre- and post- vaccination, 128 evaluable patients for pediatrics, and 806 evaluable patients (119 at increased risk, 16 ex-US, and 243 low risk).

C. **Study Population Demographics and Baseline Parameters**

The demographics of the study population are typical for an anti-HBs II detection study performed in the US. The following tables show the demographics for the different study cohorts.

Table 25: Demographics by Sex for Each Study Cohort

Sex	Adult AIR		Pediatric AIR		Pregnant AIR		Vaccination	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Female	943	45.62	68	53.13	218	100.00	32	45.71
Male	1124	54.38	60	46.88	na	na	38	54.29
Total	2067	100.00	128	100.00	218	100.00	70	100.00

Sex	Supplemental		Pregnant at Low Risk		Specificity		Total	
	n	%	n	%	n	%	n	%
Female	128	18.50	588	100.00	162	57.04	2139	52.85
Male	563	81.36	Na*	na	78	27.46	1863	46.03
Unknown	1	0.14	na	na	44	15.49	45	1.11
Total	692	100.00	588	100.00	284	100.00	4047	100.00

*na-not applicable

Table 26: Demographics by Ethinicity for Each Study Cohort

Ethnicity	Adult AIR		Pediatric AIR		Pregnant AIR		Vaccination	
	n	%	n	%	n	%	n	%
Hispanic / Latino	536	25.93	70	54.69	171	78.44	5	7.14
Not Hisp. / Latino	1524	73.73	57	44.53	31	9.63	65	92.86
unknown	7	0.34	1	0.78	16	7.34	0	0.00
Total	2067	100.00	128	100.00	218	100.00	70	100.00

Ethnicity	Supplemental		Pregnant At Low Risk		Specificity		Total	
	n	%	n	%	n	%	n	%
Hispanic / Latino	7	1.01	0	0.00	9	3.17	798	19.72
Not Hisp. / Latino	30	4.34	0	0.00	0	0.00	1707	42.18
unknown	655	94.65	588	100.00	275	96.83	1542	38.10
Total	692	100.00	588	100.00	284	100.00	4047	100.00

Table 27: Demograhpics by Race for Each Study Cohort

Race	Adult AIR		Pediatric AIR		Pregnant AIR		Vaccination	
	n	%	n	%	n	%	n	%
AIAN[a]	22	1.06	0	0.00	1	0.46	0	0.00
Asian	15	0.73	4	3.13	3	1.38	0	0.00
African Am./Black	1025	49.59	32	25.00	31	14.22	6	8.57
Caucasian/White	949	45.91	86	67.19	176	80.73	63	90.00
NHOPI[b]	4	0.19	1	0.78	1	0.46	0	0.00
Other	44	2.13	4	3.12	4	1.83	1	1.43
Unknown	8	0.39	1	0.78	2	0.92	0	0.00
Total	2067	100.00	128	100.00	218	100.00	70	100.00

Race	Supplemental		Pregnant At Low Risk		Specificity		Total	
	n	%	n	%	n	%	n	%
AIAN	3	0.43	2	0.34	0	0.00	28	0.69
Asian	88	12.72	10	1.70	4	1.41	124	3.06

African Am./Black	440	63.58	317	53.91	44	15.49	1895	46.82
Caucasian/White	82	11.85	150	25.51	105	36.97	1611	39.81
NHOPI	0	0.00	0	0.00	0	0.00	6	0.15
Other	8	1.16	105	17.86	16	5.63	182	4.50
Unknown	71	10.26	4	0.68	115	40.49	201	4.97
Total	692	100.00	588	100.00	284	100.00	4047	100.00

[a]AIAN-American Indian/Alaska Native
[b]NHOPI-Hawaiian Native/Pacific Islander

Table 28: Demograhpics by Age for Each Study Cohort

Age	Adult AIR		Pediatric AIR		Pregnant AIR		Vaccination	
	n	%	n	%	n	%	n	%
2 to 21	0	0.00	128	100.00	65	29.82	0	0.00
22 to 29	258	12.48	0	0.00	95	43.58	1	1.43
30 to 39	369	17.85	0	0.00	48	22.02	4	5.71
40 to 49	591	28.59	0	0.00	10	4.59	9	12.86
50 to 59	641	31.01	0	0.00	0	0.00	20	28.57
60 to 69	187	9.05	0	0.00	0	0.00	26	37.14
70 to 79	18	0.87	0	0.00	0	0.00	8	11.43
≥ 80	3	0.15	0	0.00	0	0.00	2	2.86
Total	2067	100.0	128	100.0	218	100.0	70	100.0
Age range	22 to 84 years		2 to 21 years		17 to 44 years		22 to 81 years	
Median range	46 years		19 years		25 years		61 years	

Age	Supplemental		Pregnant At Low Risk		Specificity		Total	
	n	%	n	%	n	%	n	%
2 to 21	4	0.58	174	29.59	29	10.21	400	9.88
22 to 29	130	18.79	288	48.98	37	13.03	809	19.99
30 to 39	154	22.25	119	20.24	36	12.68	730	18.04
40 to 49	209	30.20	7	1.19	46	16.20	872	21.55
50 to 59	163	23.55	0	0.00	31	10.92	855	21.13
60 to 69	26	3.76	0	0.00	27	9.51	266	6.57
70 to 79	6	0.87	0	0.00	15	5.28	47	1.16
≥ 80	0	0.00	0	0.00	9	3.17	14	0.35
unknown	0	0.00	0	0.00	54	19.01	54	1.33
Total	692	100.00	588	100.00	284	100.00	4047	100.00
Age range	21 to 78 years		15 to 41 years		5 to 89 years		2 to 89 years	
Median age	43 years		24.5 years		43 years		41 years	

D. Safety and Effectiveness Results

1. Safety Results

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

There was one death reported in the vaccination cohort which was determined to be unrelated to the vaccination in the PMA clinical study.

2. Effectiveness Results

The 4047 subjects were comprised of 2067 adult subjects at increased risk (45.6 % female and 54.4 % male), 128 pediatric subjects (53.1 % female and 46.9 % male), 218 pregnant at increased risk subjects, and 70 vaccination subjects (45.7 % female and 54.3 % male), along with 692 supplemental samples (18.5 % female and 81.4 % male), 588 pregnant at low risk subjects and 284 specificity samples (57.0 % female and 27.5 % male), and were tested with the Elecsys Anti-HBs II assay and the Elecsys Anti-HBs assay. The supplemental cohort was used to provide an adequate number for both acute and chronic individuals. The three (3) sites tested the at-risk and supplemental specimens with a full panel of anti-HBc IgM, anti-HBc, HBsAg, HBeAg, anti-HBe, and anti-HBs (reference) for serological characterization. The study included the following races: Caucasian, African-American/Black, Asian, American Indian/Alaskan Native, and Hawaiian Native/Pacific Islander. Key effectiveness outcomes are presented in the tables below.

Specimens were tested using the Elecsys Anti-HBs II on the cobas e 601 immunoassay analyzer and a FDA-approved reference assay to establish the clinical performance characteristics. The following tables compare the Elecsys Anti-HBs II results with the results obtained on an FDA-approved anti-HBs reference assay by HBV disease classification for the different cohorts tested.

Adult At Increased Risk (AIR)

A total of 2067 adults at increased risk were tested on the Elecsys Anti-HBs II and FDA approved reference assay, and the positive and negative percent agreement calculated as shown in the tables below.

Table 29: Results For Adult AIR Cohort by HBV Classification

HBV Classification	Elecsys Anti-HBs						Total
	positive		indeterminate		negative		
	Elecsys Anti-HBs II						
	RX[a]	NR[b]	RX	NR	RX	NR	
Acute	0	0	0	0	0	7	7
Chronic	1	0	0	0	0	31	32
Early Recovery	5	0	0	0	26	167	198
Recovery	130	0	1	0	0	0	131
Recovered	239	3	4	2	0	0	248
HBV Vaccination	49	5	1	0	0	0	497
Not Previously Infected	0	0	0	0	10	934	944
Not Interpretable	2	1	0	1	0	6	10
Total	868	9	6	3	36	1145	2067

[a]RX- reactive
[b]NR-non-reactive

Table 30: Results for Prospective Adult AIR Cohort by HBV Classification

	Elecsys Anti-HBs						
	positive		indeterminate		negative		
	Elecsys Anti-HBs II		Elecsys Anti-HBs II		Elecsys Anti-HBs II		
HBV classification	**RX**	**NR**	**RX**	**NR**	**RX**	**NR**	**Total**
Acute	0	0	0	0	0	7	7
Chronic	1	0	0	0	0	31	32
Early recovery	5	0	0	0	26	167	198
Recovery	130	0	1	0	0	0	131
Recovered	239	3	4	2	0	0	248
HBV vaccination	491	5	1	0	0	0	497
Not previously infected	0	0	0	0	10	934	944
Not interpretable	2	1	0	1	0	6	10
Total	1868	9	6	3	36	1145	2067

Table 31: Performance for Prospective Adult AIR Cohort by HBV Classification

HBV classification				
	positive percent agreement		negative percent agreement	
	% (ratio)	95 % Exact CI	% (ratio)	95 % Exact CI
Acute	n/a (0/0)	n/a (0/0)	100 (7/7)	59.0 to 100
Chronic	100 (1/1)	2.50 to 100	100 (31/31)	88.8 to 100
Early recovery	100 (5/5)	47.8 to 100	86.5 (167/193)	80.9 to 91.0
Recovery	100 (130/130)	97.2 to 100	0.00 (0/1)	0.00 to 97.5
Recovered	98.0 (239/244)	95.3 to 99.3	0.00 (0/4)	0.00 to 60.2
HBV vaccination	99.0 (491/496)	97.7 to 99.7	0.00 (0/1)	0.00 to 97.5
Not previously infected	n/a (0/0)	n/a (0/0)	98.9 934/944)	98.1 to 99.5
Not interpretable	50.0 (2/4)	6.76 to 93.2	100 (6/6)	54.1 to 100
Total	98.6 (868/880)	97.6 to 99.3	96.5 (1145/1187)	5.3 to 97.4

Additional Samples were sourced from vendors (retrospective) to enrich the different HBV classifications. The following tables show the results and performance.

Table 32: Results for Retrospective Adult AIR Cohort by HBV Classification

HBV Classification	Elecsys Anti-HBs Immunoassay						Total
	positive		indeterminate		negative		
	Elecsys Anti-HBs II						
	RX	NR	RX	NR	RX	NR	
Acute	3	0	0	0	2	70	75
Chronic	7	4	0	0	2	305	318
Early Recovery	0	0	0	0	5	11	16
Recovery	197	0	1	1	0	0	199
Recovered	80	0	3	0	0	0	83
Not Previously Infected	0	0	0	0	0	1	1
Total	287	4	4	1	9	387	692

Table 33: Performance for Retrospective Adult AIR Supplemental Cohort by HBV Classification

HBV Classification	Positive Percent Agreement, PPA (%)	95% Exact Confidence Interval	Negative Percent Agreement, NPA (%)	95% Exact Confidence Interval
Acute	100.00 (3/3)	29.24 to 100.00	97.22 (70/72)	90.32 to 99.66
Chronic	63.64 (7/11)	30.79 to 89.07	99.35 (305/307)	97.67 to 99.92
Early Recovery	na (0/0)	na	68.75 (11/16)	41.34 to 88.98
Recovery	99.49 (197/198)	97.22 to 99.99	0.00 (0/1)	0.00 to 97.50
Recovered	100.00 (80/80)	95.49 to 100.00	0.00 (0/3)	0.00 to 70.76
Not Previously Infected	na (0/0)	na	100.00 (1/1)	2.50 to 100.00
Total	98.29 (287/292)	96.05 to 99.44	96.75 (387/400)	94.51 to 98.26

Table 34: Combined Results for Prospective and Retrospective Adult AIR Subjects

	Elecsys Anti-HBs						
	positive		indetermine		negative		
	Elecsys Anti-HBs II		Elecsys Anti-HBs II		Elecsys Anti-HBs II		
HBV classification	**RX**	**NR**	**RX**	**NR**	**RX**	**NR**	**Total**
Acute	3	0	0	0	2	77	82
Chronic	8	4	0	0	2	336	350
Early recovery	5	0	0	0	31	178	214
Not interpretable	2	1	1	1	0	6	10
Not previously infected	0	0	0	0	10	935	945
Recovered	319	3	2	2	0	0	331
Recovery	327	0	1	1	0	0	330
Vaccination	491	5	0	0	0	0	497
Total	1155	13	4	4	45	1532	2759

Table 35: Combined Performance for Prospective and Retrospective Adult AIR Subjects

HBV classification				
	Positive percent agreement		Negative percent agreement	
	% (ratio)	95 % Exact CI	% (ratio)	95 % Exact CI
Acute	100 (3/3)	29.2 to 100	97.5 (77/79)	91.2 99.7
Chronic	66.7 (8/12)	34.9 to 90.1	99.4 (336/338)	97.9 to 99.9

HBV classification				
	Positive percent agreement		Negative percent agreement	
	% (ratio)	95 % Exact CI	% (ratio)	95 % Exact CI
Early recovery	100 (5/5)	47.8 to 100	85.2 (178/209)	79.6 to 89.7
Recovery	99.7 (327/328)	98.3 to 100	0.00 (0/2)	0.00 to 84.2
Recovered	98.5 (319/324)	96.4 to 99.5	0.00 (0/7)	0.00 to 41.0
Not previously infected	98.5 (319/324)	n/a	98.9 (935/945)	98.1 to 99.5
Vaccination	n/a (0/0)	97.7 to 99.7	0.00 (0/1)	0.00 to 97.5
Not interpretable	50.0 (2/4)	6.76 to 93.2	100 (6/6)	54.1 to 100
Total	98.6 (1155/1172)	97.7 to 99.2	96.5 (1532/1587)	5.5 to 97.4

Vaccination

Pre- and post-vaccination samples were collected from a minimum of 71 subjects who were incoculated with one of three (3) US-approved hepatitis B vaccines. Testing of the pre-vaccination samples found all 71 samples to be negative for anti-HBs, but one subject was anti-HBc positive and was therefore excluded. All 17 nonresponder specimens were negative/non-reactive in another FDA-approved anti-HBs assay. The following table shows the results.

Table 36: Performance for Vaccination Cohort

	Elecsys Anti-HBs								
	Pre-vaccination			Post-vaccination			Total		
Elecsys Anti-HBs II	**Pos**	**Ind**	**Neg**	**Pos**	**Ind**	**Neg**	**Pos**	**Ind**	**Neg**
Reactive	0	0	0	52	0	0	52	0	0
Non-reactive	0	0	70	1	0	17	1	0	87
Total	0	0	70	53	0	17	53	0	87
PPA[a]	(0/0)			98.1 (52/53)			98.1 (52/53)		
95 % CI[b]	n/a			89.9 to 100.0			89.9 to 100.0		
NPA[c]	100 (70/70)			100 (17/17)			100 (87/87)		
95 % CI	94.9 to 100			80.5 to 100			95.9 to 100		

[a]PPA-positive percent agreement
[b]CI-confidence interval
[c]NPA-negative percent agreement

Pediatric

The pediatric increased-risk for hepatitis subgroup was acquired from the US-prospective sample collection to demonstrate the clinical performance of the Elecsys Anti-HBs II assay in subjects from 2 years through and including 21 years of age. A total of 128 samples were collected. The following table shows the results.

Table 37: Performance for Pediatric Cohort

	Elecsys Anti-HBs Immunoassay			
Elecsys Anti-HBs II	**positive**	**indeterminate**	**negative**	**Total**
Positive (pos)	55	1	1	57
Negative (neg)	3	0	68	71
Total	58	1	69	128
PPA	94.8 (55/58)			
95% CI	85.6 to 98.9			
NPA	97.1 (68/70)			
95% CI	90.0 to 99.7			

In addition, there were 59 specimens from pregnant young women that met the age criteria for pediatric subjects at increased risk for hepatitis obtained in the prospective collection. Thirty-four (34) of these specimens were concordantly negative between the Elecsys Anti-HBs II assay and the Elecsys Anti-HBs assay, while 23 were concordantly positive. There was 1 positive and 1 negative in the test assay that was indeterminate with the reference assay. The NPA for this pregnant pediatric sub-group was 97.1% (34/35) with confidence limits of 85.1 to 99.9%. The PPA was 95.8% (23/24) with confidence limits of 78.9 to 99.9%.

Pregnant

Pregnant subjects with increased risk for hepatitis (n=218) and with low risk for hepatitis (remnant samples n=588) were tested and analyzed. The results are shown in the following table.

Table 38: Performance for Pregnant Cohort

	Elecsys Anti-HBs		
Elecsys Anti-HBs II	**positive**	**indeterminate**	**negative**
Reactive	420	4	8
Non-reactive	3	3	368
Total	423	7	376
PPA	98.6 (420/426)		
95 % CI	97.0 to 99.5		

	Elecsys Anti-HBs		
Elecsys Anti-HBs II	**positive**	**indeterminate**	**negative**
NPA	96.8 (368/380)		
95 % CI	94.6 to 98.4		

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.

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-HBs II for the quantitative detection of antibodies to hepatitis B surface antigen in human serum and plasma (potassium EDTA) 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 and as an aid in determination of susceptibility to HBV infection for individuals prior to or following HBV vaccination. 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-HBs II when used according to the manufacturer's instructions can aid the physician in the diagnosis of HBV infection and as an aid in determination of susceptibility to HBV infection for individuals prior to or following HBV vaccination.

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.

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 device.

Risks of false positive results when the device is 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 include improper patient management, including 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 coinfected but undiagnosed with other viruses that are treated with the same antiviral medication, such as HIV, can lead to viral resistance, however the chance of an undiagnosed co-infection in a patient treated forhepatitis B is unlikely.

Risks of false positive results when the device is used as an aid in the determination of susceptibility to HBV infection in individuals prior to or following HBV

vaccination or where vaccination status is unknown includes leading a provider to falsely believe that a patient has been vaccinated in the past and/or has current immunity when the patient, in fact, does not. This could lead to a missed opportunity to vaccinate a patient in whom Hepatitis B vaccination is indicated. Vaccination 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, hepatocellular carcinoma rates, and need for liver transplantation. Vaccination 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.

Risks of false negative results when the device is 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 include potentially missing and not treating a patient who has hepatitis B infection. Missing and not treating a patient with hepatitis B infection whose clinical picture warrants antiviral treatment could result in the known sequelae of HBV infection and may result in high morbidity and mortality in these patients. Additionally, missing a diagnosis of hepatitis B infection will not allow for clinicians to potentially decrease transmission and disease burden in the general population, particularly in populations at high risk for hepatitis B infection.

Risks of false negative results when the device is used as an aid in the determination of susceptibility to HBV infection in individuals prior to or following HBV vaccination or where vaccination status is unknown include unnecessary repeated vaccination for hepatitis B. Although vaccination has risks such as local reactions, and serious adverse events due to Hepatitis B vaccination are rare, administration of extra doses of single-antigen hepatitis Bvaccine is not generally harmful. In fact, it is common practice to administer higher dose vaccinations in an accelerated schedule for patients undergoing organ transplantation, for example.

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 susceptibility to HBV infection for individuals prior to or following HBV vaccination.

XIII. CDRH DECISION

CDRH issued an approval order on February 23, 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.