U.S. FOOD & DRUG ADMINISTRATION

510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION

DECISION SUMMARY

ASSAY AND INSTRUMENT

I Background Information:

A 510(k) Number

K260046

B Applicant

Roche Diagnostics

C Proprietary and Established Names

Elecsys Anti-HBc II

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
SEI	II	21 CFR 866.3173 Hepatitis B virus antibody assays	MI- Microbiology

II Submission/Device Overview:

A Purpose for Submission:

To obtain clearance for the Elecsys Anti-HBc II assay's addition of pediatric (2 through 21 years of age) population to the indications for use.

B Measurand:

Total antibodies to hepatitis B core antigen (anti-HBc)

C Type of Test:

Qualitative electrochemiluminescence immunoassay (ECLIA)

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

Immunoassay for the in vitro qualitative determination of total antibodies to hepatitis B core antigen (anti-HBc) in human serum and plasma (lithium heparin, sodium citrate, potassium EDTA) from adult and pediatric (2 through 21 years of age) patients with the symptoms of hepatitis or who may be at risk for hepatitis B virus (HBV) infection. The detection of total anti-HBc is indicative of a laboratory diagnosis for HBV infection. Further HBV serological marker testing is required to define the specific disease state. The immunoassay's performance has not been established for the monitoring of HBV disease or therapy.

The electrochemiluminescence immunoassay "ECLIA" is intended for use on cobas e immunoassay analyzers.

C Special Conditions for Use Statement(s):

Rx – For Prescription Use Only

D Special Instrument Requirements:

For use with the cobas e immunoassay analyzers

IV Device/System Characteristics:

A Device Description:

Elecsys Anti-HBc II is a qualitative, serological, competitive assay with a total test time of 27 minutes. The assay is based on competition principle with a pretreatment step. First, the sample is incubated with a reducing agent. During the second incubation, HBcAg is added to form a complex with the anti-HBc antibodies. In the third incubation, biotinylated antibodies specific for HBcAg, along with ruthenium complex-labeled antibodies, are added to occupy the remaining binding sites on the HBcAg. The addition of streptavidin-coated microparticles bridges the entire complex to the solid phase, allowing the detection of the anti-HBc antibody-HBcAg complex via electrochemiluminescence.

The microparticles are magnetically captured on the surface of an electrode and the bound complex is washed. Application of a voltage to the electrode induces chemiluminescence, which is measured by a photomultiplier. Results are determined automatically by the Elecsys software by comparing the electrochemiluminescence signal obtained from the sample with the signal of the cut-off value previously obtained by Anti-HBc calibration.

PreciControl Anti-HBc II contains ready-for-use control serum based on human serum. The controls are used for monitoring the accuracy of the Elecsys Anti-HBc II immunoassay. The controls, 1 (negative) and 2 (positive) contain IgG and IgM Anti-HBc antibodies in human serum. These controls are packaged and sold separately from the Anti-HBc II immunoassay.

B Principle of Operation:

Competition principle. Total duration of assay: 27 minutes.

- First incubation: Pretreatment of 40 µL of sample with reducing agent
- Second incubation: After addition of HBcAg, a complex is formed with anti HBc antibodies in the sample.

- Third incubation: After addition of biotinylated antibodies and ruthenium complex, labeled antibodies specific for HBcAg, together with streptavidin-coated microparticles, the still free binding sites on the HBc antigens become occupied. The entire complex becomes 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.

a) Tris(2,2'-bipyridyl) ruthenium (II)-complex (Ru(bpy))

Interpretation of results

Initial Elecsys Anti-HBc II assay result			
COI	**Result**	**Interpretation of results**	**Retest procedure**
> 1.1	Non-reactive[A)]	No antibodies to HBc were detected	No retest required
1.1 ≥ COI > 0.9	Border	Borderline zone (undetermined)	Retest in duplicate with the Elecsys Anti-HBc II assay
≤ 0.9	Reactive	Antibodies to HBc detected	Follow CDC recommendations for supplemental testing

A) Please note: A non-reactive anti-HBc result can indicate that the patient is either susceptible to HBV infection due to no past exposure or is immune to HBV infection due to vaccination.

Final Elecsys Anti-HBc II assay result			
Initial result (COI)	**Result after retest (COI)**	**Final results**	**Interpretation of results**
> 1.1	No retest required	Non-reactive [A)]	Antibodies to HBc were not detected; does not exclude the possibility of exposure to HBV
1.1 ≥ COI > 0.9	If 2 of the 3 results have a COI > 1.0	Non-reactive	Antibodies to HBc were not detected; does not exclude the possibility of exposure to HBV
	If 2 of the 3 results have a COI ≤ 1.0	Reactive	Presumptive evidence of antibodies to HBc. Follow CDC recommendations for supplemental testing.
≤ 0.9	No retest required	Reactive	Presumptive evidence of antibodies to HBc. Follow CDC recommendations for supplemental testing.

[A)] Please note: A non-reactive anti-HBc result can indicate that the patient is either susceptible to HBV infection due to no past exposure or is immune to HBV infection due to vaccination.

C Instrument Description Information:

1. Instrument Name:

   cobas e immunoassay analyzer.

2. Specimen Identification:

   Automated specimen identification using barcode scanning by the instrument.

3. Specimen Sampling and Handling:

   Specimen sampling and handling is fully automated on the instrument.

4. Calibration:

   Elecsys Anti-HBc II reagent components contain calibrators AHBC2 Cal1 and AHBC2 Cal2.

   - AHBC 2 Cal1(negative): 1 bottle of 1.0 mL human serum; preservative
   - AHBC 2 Cal2 (positive): 1 bottle of 1.0 mL, Anti HBc (human) > 8 WHO IU/mL in human serum; preservative

5. Quality Control:

   The Elecsys Anti-HBc II assay uses PreciControl Anti-HBc II for quality control.

   - PC A-HBCII 1 (negative): Each bottle contains 1.3 mL of human serum, negative for anti-HBc; buffered and preserved with 0.4% Bronidox L.
   - PC A-HBCII 2 (positive): Each bottle contains 1.3 mL of control serum Anti- HBC antibodies (human) approximately 1 IU/mL (WHO units) in human serum; buffered with HEPES and preserved with 0.4% Bronidox L.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Abbott ARCHITECT CORE

B Predicate 510(k) Number(s):

P080023

C Comparison with Predicate(s):

Device & Predicate Device(s):	**K260046**	**P080023**
Device Trade Name	Elecsys Anti-HBc II	Abbott ARCHITECT CORE
General Device		

Characteristic Similarities		
Regulation Number	21 CFR 866.3173	Same
Regulation Name	Hepatitis B virus antibody assays	Same
Regulatory Class	Class II	Class III
Product Code	SEI	Same
Intended Use	Immunoassay for the in vitro qualitative determination of total antibodies to hepatitis B core antigen (anti HBc) in human adult and pediatric (2 through 21 years of age) serum and plasma (lithium heparin, sodium citrate, potassium EDTA) in patients with the symptoms of hepatitis or who may be at risk for hepatitis B virus (HBV) infection. The detection of total anti HBc is indicative of a laboratory diagnosis for HBV infection. Further HBV serological marker testing is required to define the specific disease state. The immunoassay's performance has not been established for the monitoring of HBV disease or therapy. The electrochemiluminescence immunoassay "ECLIA" is intended for use on the cobas e immunoassay analyzers.	The ARCHITECT CORE assay is a chemiluminescent microparticle immunoassay (CMIA) for the qualitative detection of IgG and IgM antibodies to hepatitis B core antigen (anti-HBc) in human adult and pediatric serum and plasma (dipotassium EDTA, lithium heparin, sodium heparin) and neonatal serum. It is intended as an aid in the diagnosis of acute, chronic, or resolved hepatitis B virus (HBV) infection in conjunction with other laboratory results and clinical information.
Analyte Measured	Total anti-HBc antibodies	Same
General Device Characteristic Differences		
Test Principle	Competition principle	Two-step immunoassay
Sample Type/Matrix	Serum and plasma (lithium heparin, sodium citrate, potassium EDTA)	Serum and plasma (dipotassium EDTA, lithium heparin, sodium heparin)

Calibrator	AHBC2 Cal1 AHBC2 Cal2	ARCHITECT CORE Calibrators
Controls	PreciControl Anti-HBc II	ARCHITECT CORE Controls
Instrument Platform	cobas e immunoassay analyzers	ARCHITECT i System

VI Standards/Guidance Documents Referenced:

CLSI EP05-A3: Clinical Laboratory Standards Institute. Evaluation of the Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition. CLSI Guideline EP05-A3, CLSI: Wayne, PA, 2014.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:
   See P100031.

2. Linearity:
   Not applicable.

3. Analytical Specificity/Interference:
   See P100031.

4. Detection Limit and Assay Reportable Range:
   Not applicable.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):
   See P100031.

6. Assay Cut-Off:
   See P100031.

B Comparison Studies:

1. Method Comparison with Predicate Device:

   Not Applicable. See Clinical Studies below.

2. Matrix Comparison:
See P100031.

C Clinical Studies:

1. Clinical Sensitivity:
Not Applicable.

2. Clinical Specificity:
Not Applicable.

3. Clinical Cut-Off:
Not Applicable.

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

Performance of Anti-HBc II on cobas e801 was evaluated against comparator/s by testing 119 prospectively collected serum specimens from pediatric participants aged 2 through 21 years, at risk for hepatitis B.

Table 1. Prospective pediatric study results for Elecsys Anti-HBc II

Elecsys Anti-HBc II	Comparator Reactive [n]	Comparator Nonreactive [n]
Reactive	0	0
Nonreactive	0	119
Total	0	119

Table 2. Percent agreements with confidence intervals (CI)

Age range (years)	PPA		NPA	
	% (n/N)	95% CI	% (n/N)	95% CI
2-11	NA (0/0)	NA	100(38/38)	90.6-100
12-21	NA (0/0)	NA	100(81/81)	95.4-100
Total	NA	NA	100(119/119)	96.9-100

Because no positive specimens were identified in the comparison study, a spiking study was conducted to evaluate the performance of the Elecsys Anti-HBc II assay in adult and pediatric samples. Thirty negative pediatric samples, with ages ranging from 2 through 21 years, were spiked with Anti-HBc human positive serum and compared to samples from a single pool of non-reactive adult serum (≥22 years of age) that were spiked with the same volume of positive sample. The absolute differences between the 30 pediatric (spiked) and

adult (spiked) samples ranged from 0.00103 to 0.0266 COI, with a mean absolute difference of 0.0107 COI. The results met the ≤ 0.20 COI acceptance criteria, supporting that the assay is suitable for the pediatric population.

D Expected Values/Reference Range:

See P100031

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.