510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT

I Background Information:

A 510(k) Number

K260049

B Applicant

Roche Diagnostics

C Proprietary and Established Names

Elecsys Anti-HBc IgM

D Regulatory Information

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

II Submission/Device Overview:

A Purpose for Submission:

Addition of pediatric (2 through 21 years of age) population to the indications for use.

B Measurand:

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

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 IgM antibodies to hepatitis B core antigen (anti-HBc IgM) in human serum and plasma (potassium EDTA, lithium heparin, sodium heparin, sodium citrate) from adult and pediatric (2 through 21 years of age) patients with symptoms of hepatitis or who may be at risk for hepatitis B (HBV) infection. The presence of anti-HBc IgM, in conjunction with other laboratory results and clinical information, is indicative of acute or recent hepatitis B virus (HBV) infection. 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.

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:
The Elecsys Anti-HBc IgM immunoassay is a qualitative, serologic, µ-capture assay. The sample is incubated with biotinylated monoclonal h-IgM-specific antibodies and then with HBcAg labeled with ruthenium. Streptavidin-coated microparticles are subsequently added to capture the immune complexes. The biotinylated antibodies and ruthenium-labeled antigen form a sandwich complex with the anti-HBc IgM antibodies present in the sample. This complex then binds to the solid phase through the interaction between biotin and streptavidin. The microparticles are magnetically captured on the surface of an electrode and unbound substances are removed in a washing step. Application of a voltage to the electrode induces chemiluminescence, which is measured by a photomultiplier. Results are determined automatically by comparing the signal obtained from the sample with the signal of the cut-off value previously obtained by anti-HBc IgM calibration. Results are expressed as cutoff indices (COIs).

The Elecsys Anti-HBc IgM is intended to be used with the following calibrators and controls:

- AHBCIGM Cal1 and AHBCIGM Cal2
- PreciControl Anti-HBc IgM

B Principle of Operation:
The Elecsys Anti-HBc IgM immunoassay employs electrochemiluminescence technology and is a qualitative serological, µ-capture assay. Total duration of the assay is 18 minutes.

- 1st incubation: Pretreatment of 6 µL of sample (automatically prediluted 1:400 with Diluent Universal) with anti Fdγ reagent to block specific IgG.

- 2nd incubation: Biotinylated monoclonal h IgM specific antibodies, HBcAg labeled with a ruthenium complex[a)] and streptavidin-coated microparticles are added to the pretreated sample. Anti HBc IgM antibodies present in the sample react with the ruthenium labeled HBcAg and the biotinylated anti h IgM to form a sandwich complex which 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 II 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 IgM assay results			
COI	**Result**	**Interpretation of results**	**Retest procedure**
< 0.9	Non-reactive[A)]	No IgM antibodies to HBc were detected	No retest required
0.9 ≤ COI < 1.1	Border	Borderline zone (undetermined)	Retest in duplicate with the Elecsys Anti-HBc IgM assay
≥ 1.1	Reactive	IgM antibodies to HBc detected	Presumptive evidence of IgM antibodies to HBc. Follow CDC recommendations for ancillary testing. No retest required.

[A)] Please note: A negative anti-HBc IgM result can indicate that the patient is either susceptible to HBV infection due to no past exposure, is chronically infected with HBV, or is immune to HBV infection due to a resolved past infection or vaccination.

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

[A)] Please note: A negative anti-HBc IgM result can indicate that the patient is either susceptible to HBV infection due to no past exposure, is chronically infected with HBV, or is immune to HBV infection due to a resolved past infection or 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 IgM reagent components contain calibrators AHBCIGM Cal1 and AHBCIGM Cal2.

5. Quality Control:
   The Elecsys Anti-HBc IgM assay uses PreciControl Anti-HBc IgM for quality control. The controls 1(negative) and 2(positive), contain human serum in the negative and positive concentration ranges for anti-HBc IgM.

V Substantial Equivalence Information:

A Predicate Device Name(s):
Abbott ARCHITECT CORE-M assay

B Predicate 510(k) Number(s):
P060035

C Comparison with Predicate(s):

Device & Predicate Device(s):	K260049	P060035
Device Trade Name	Elecsys Anti-HBc IgM	Abbott ARCHITECT CORE-M
General Device Characteristic Similarities		
Regulation No./Product Code	21 CFR 866.3173/SEI	Same
Regulation Name	Hepatitis B virus Antibody assays	Same
Device Class	Class II	Class III
Intended Use/Indications For Use	Immunoassay for the in vitro qualitative determination of IgM antibodies to hepatitis B core antigen (anti HBc	The ARCHITECT CORE-M assay is a chemiluminescent microparticle immunoassay (CMIA)

	IgM) in human serum and plasma (potassium EDTA, lithium heparin, sodium heparin, sodium citrate) from adult and pediatric (2 through 21 years of age) patients with symptoms of hepatitis or who may be at risk for hepatitis B (HBV) infection. The presence of anti HBc IgM, in conjunction with other laboratory results and clinical information, is indicative of acute or recent hepatitis B virus (HBV) infection. 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.	used for the qualitative detection of IgM antibody to hepatitis B core antigen (IgM anti-HBc) in human adult and pediatric serum or plasma (dipotassium EDTA, lithium heparin, and sodium heparin) and neonatal serum on the ARCHITECT i System. The ARCHITECT CORE-M assay is to be used as an aid in the diagnosis of acute or recent hepatitis B virus (HBV) infection in conjunction with other laboratory results and clinical information.
Analyte Measured	Anti-HBc IgM	Same
Test Principle	μ Capture test principle	Two-step immunoassay
General Device Characteristic Differences		
Sample Type/Matrix	Serum and plasma (potassium EDTA, lithium heparin, sodium heparin, sodium citrate)	Serum or plasma (dipotassium EDTA, lithium heparin, and sodium heparin)
Calibrator	AHBCIGM Cal1 AHBCIGM Cal2	ARCHITECT CORE-M Calibrators
Controls	PreciControl Anti-HBc IgM	ARCHITECT CORE-M 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 P110022.

2. Linearity:
   Not applicable.

3. Analytical Specificity/Interference:
   See P110022.

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

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):
   See P110022.

6. Assay Cut-Off:
   See P110022.

B Comparison Studies:

1. Method Comparison with Predicate Device:
   Not applicable. See Clinical Studies below.

2. Matrix Comparison:
   See P110022.

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 characteristics of the Elecsys Anti-HBc IgM assay in pediatric population were established with prospective and spiking studies.

For the prospective study, serum samples were collected from 119 Pediatric participants (age 2 through 21 years) who presented with signs and symptoms of hepatitis or who may be at risk for HBV infection. The age distribution of the study was as follows: 31.9% (n=38) of study participants were 2-11 years old and 68.1% (n=81) were 12-21 years old. These samples were tested using the Elecsys Anti-HBc IgM assay and the results were used to calculate the percent agreement and confidence interval relative to the comparator device (Table 1-2).

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

Elecsys Anti-HBc IgM	Comparator		
	Reactive	Grayzone	Nonreactive
Reactive	0	0	0
Nonreactive	0	0	119
Total	0	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 positives specimens were identified in the prospective study, a spiking study was conducted to evaluate the performance of the Elecsys Anti-HBc IgM assay using 30 pediatric (age 2 through 21 years) and 30 adult (>22 years of age) serum samples spiked with anti-HBc IgM positive samples. Percent difference between the index values of pediatric (spiked) and adult (spiked) samples were calculated. The percent difference between the pediatric and adult samples was ≤±12%.

D Expected Values/Reference Range:
See P110022.

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.