510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K260048

B Applicant

Roche Diagnostics

C Proprietary and Established Names

Elecsys Anti-HAV IgM

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
SEI	Class II	21 CFR 866.3310 Hepatitis A virus (HAV) serology assay	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:

Addition of pediatric patients (2 through 21 years of age) to the intended use population.

B Measurand:

IgM antibodies to hepatitis A virus

C Type of Test:

Qualitative electrochemiluminescence immunoassay (ECLIA)

Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
www.fda.gov

III Intended Use/Indications for Use:

A Intended Use(s):

Immunoassay for the in vitro qualitative detection of IgM antibodies to hepatitis A virus (anti-HAV IgM) in human serum and plasma (potassium EDTA, lithium heparin, sodium heparin, sodium citrate) from adult and pediatric (2 to 21 years of age) patients with signs and symptoms of hepatitis or persons who may be at risk for hepatitis A infection. The assay is intended for use as an aid in the laboratory diagnosis of an acute or recently acquired hepatitis A virus (HAV) infection. Assay results, in conjunction with other laboratory results and clinical information, may be used to provide presumptive evidence of infection with HAV.

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

B Indication(s) for Use:

See Intended Use

C Special Conditions for Use Statement(s):

Rx – For Prescription Use Only

D Special Instrument Requirements:

For use with e cobas immunoassay analyzers.

IV Device/System Characteristics:

A Device Description:

The Elecsys Anti-HAV IgM immunoassay utilizes a µ-capture test concept based on a monoclonal h-IgM directed biotinylated antibody, cell culture derived Hepatitis A Virus and a ruthenylated monoclonal antibody directed to HAV. Capture of formed immune complexes from the reaction mixture is based on biotin binding to streptavidin-coated magnetic microparticles which are collected on a measuring cell electrode. Signal generation is triggered by the application of a voltage to the electrode (electrochemiluminescence technology). Results are determined automatically by comparing the signal obtained from the reaction product of the sample with the signal of the cutoff value previously obtained by calibration. The Elecsys Anti-HAV IgM test kit includes 2 Anti-HAV IgM calibrators, one consisting of human serum negative for anti-HAV IgM and one positive calibrator consisting of Anti-HAV IgM in human serum. PreciControl Anti-HAV IgM is also available and is packaged and sold separately.
The Elecsys PreciControl Anti-HAV IgM contains control serum based on human serum in the negative and positive concentration ranges. The controls are used for monitoring the accuracy of Elecsys Anti-HAV IgM immunoassays.

B Principle of Operation:

The Elecsys Anti-HAV 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 10 uL of the automatically 1:400 diluted sample (using Diluent Universal) with anti-Fdy reagent to block specific IgG in the presence of monoclonal anti-HAV antibodies labeled with ruthenium complex.[a)]

2nd incubation: After addition of biotinylated monoclonal h-IgM-specific antibodies, HAV antigen, and streptavidin-coated microparticles, the anti-HAV IgM antibodies present in the sample form a sandwich complex with the HAV antigen and the ruthenium-labeled anti-HAV antibody 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/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 ($Ru(bpy)_3^{2+}$)

Interpretation of results

The cutoff for the Elecsys Anti-HAV IgM assay was initially established by measuring a total of 1004 samples including 575 negative from post acute, dialysis, hospitalized, routine samples with request for anti-HAV IgM testing, samples from blood donors and 429 positive samples from seroconverters < 90 days (commercial sources), HAV follow-ups after infection < 90 days and samples suspected for HAV obtained from several European sites. The distribution of positive, equivocal and negative results was compared with the AxSym HAVAB-M 2.0 assay and the cutoffs were set as noted below. The result of a sample is given in the form of a cutoff index (signal sample/cutoff).
Results obtained with the Elecsys Anti-HAV IgM assay can be interpreted as follows:

Non-reactive	< 0.90 COI
Border	0.90 ≤ COI < 1.10
Reactive	COI ≥ 1.10

Samples with a COI < 0.90 are considered non-reactive in the Elecsys Anti-HAV IgM assay and no further testing is necessary. Samples with a COI ≥ 1.10 are considered reactive in the Elecsys Anti-HAV IgM assay. Samples with a COI between 0.90 and < 1.10 are considered border (borderline). The sample should be retested in duplicate.

- If 2 of the 3 results have a COI < 0.90, the result is interpreted as non-reactive, and no further testing is necessary.
- If 2 of the 3 results have a COI between 0.90 and < 1.10, the result is interpreted as borderline. It is recommended that a specimen be drawn in 2 weeks and retested.
- If 2 of the 3 results have a COI ≥ 1.10, the result is interpreted as reactive.

V Substantial Equivalence Information:

A Predicate Device Name(s):
Access anti-HAV IgM

B Predicate 510(k) Number(s):
K251995

C Comparison with Predicate(s):

Device & Predicate Device(s):	**K260048**	**K251995**
Device Trade Name	Elecsys Anti-HAV IgM	Access anti-HAV IgM
General Device Characteristic Similarities		
Regulation Number	21 CFR 866.3310	Same
Regulation Name	Hepatitis A virus (HAV) serological assays	Same
Regulatory Class	II	Same
Product Code	LOL	Same
Intended Use	Immunoassay for the in vitro qualitative detection of IgM antibodies to hepatitis A virus (anti-HAV IgM) in human serum and plasma (potassium EDTA, lithium heparin, sodium heparin, sodium citrate) from adult and pediatric (2 to 21 years of age) patients with signs and symptoms of hepatitis or persons who may be at risk for hepatitis A infection. The assay is intended for use as an aid in the laboratory diagnosis of an acute or recently acquired hepatitis A virus (HAV) infection. Assay results, in conjunction with other laboratory results and clinical information, may be used to provide presumptive	The Access anti-HAV IgM assay is a paramagnetic particle, chemiluminescent immunoassay for the in vitro qualitative detection of IgM antibodies to hepatitis A virus (anti-HAV IgM) in human pediatric (2 through 21 years) and adult serum and serum separator tubes or plasma [lithium heparin, lithium heparin separator tubes, dipotassium (K2) EDTA, and tripotassium (K3) EDTA] using the DxI 9000 Access Immunoassay Analyzer. The Access anti-HAV IgM assay results may be used as an aid in the laboratory diagnosis of acute or recent hepatitis A virus (HAV) infection in individuals with signs and symptoms of hepatitis A

	evidence of infection with HAV. The **e**lectro**c**hemi**l**uminescence **i**mmuno**a**ssay "ECLIA" is intended for use on **cobas e** immunoassay analyzers.	virus, when used in conjunction with other serological and clinical information. This assay is not intended for use for screening donors of blood or blood products or human cells, tissues, or cellular or tissue-based products (HCT/Ps).
Test principle	μ Capture test principle	Two-step sandwich immunoassay
Analyte measured	Anti-HAV IgM	Same
General Device Characteristic Differences		
Sample type/matrix	Human serum and plasma (potassium EDTA, lithium heparin, sodium heparin, sodium citrate)	Serum and Plasma [Lithium Heparin, Lithium Heparin separator tube, dipotassium (K2) EDTA, and tripotassium (K3) EDTA]
Instrument platform	**cobas e** immunoassay analyzers	DxI 9000 Access Immunoassay Analyzer
Calibrator	AHAVIGM Cal1 AHAVIGM Cal2	Access anti-HAV IgM Calibrator
Controls	PreciControl Anti-HAV IgM	Access anti-HAV IgM

VI Standards/Guidance Documents Referenced:

Hepatitis A Virus Serological Assays - Class II Special Controls Guidance for Industry and FDA Staff

EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:
   See K093955

2. Linearity:

Not applicable.

3. Analytical Specificity/Interference:
   See K093955

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

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):
   See K093955

6. Assay Cut-Off:
   See K093955

B Comparison Studies:

1. Method Comparison with Predicate Device:

Clinical performance in pediatric subjects
The performance of the Elecsys Anti-HAV IgM assay on the **cobas** e 801 immunoassay analyzer and an FDA-approved Anti-HAV IgM reference assay was performed on 123 pediatric subjects for hepatitis from US subjects.

	Reference Anti-HAV IgM assay final interpretation		
Anti-HAV IgM	**Reactive**	**Grayzone**	**Non-reactive**
Reactive	0	0	0
Borderline	0	0	0
Non-reactive	0	0	123
Total	0	0	123

Percent agreement in pediatric subject population	
Positive percent agreement	NA (0/0)
95 % confidence interval	NA
Negative percent agreement	100 (123/123)
95 % confidence interval	97.0 to 100

Due to the low prevalence of HAV in the pediatric population, a comparative study comparing 30 spiked pediatric samples against one adult sample pool was performed with Elecsys Anti-HAV IgM. 30 pediatric samples that were anti-HAV IgM antibody negative and one adult anti-HAV IgM-negative sample pool were spiked with analyte from a high positive sample to the level of 2-4 times the cutoff to assess performance.
The percent difference between all 30 pediatric samples the adult samples met the acceptance criteria which was ≤ 20% supporting that the assay is suitable for the pediatric population.

2. Matrix Comparison:
   See K093955

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):
   See K093955 and below

D Expected Values/Reference Range:
See K093955

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.