510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K220924

B Applicant

Roche Diagnostics

C Proprietary and Established Names

Elecsys HSV-2 IgG (08948887160)

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
MYF	Class II	21 CFR 866.3305 - Herpes Simplex Virus Serological Assays	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:

Market clearance for a previously cleared assay to detect antibodies to Herpes Simplex HSV-2 IgG in human serum and plasma that has been modified to:

- remove analyzers which are no longer manufactured or supported by Roche (Modular Analytics E170 instrumentation)
- increase biotin tolerance
- reduce streptavidin interference.

B Measurand:

Antibodies to Herpes Simplex HSV-2 IgG

C Type of Test:

A qualitative sandwich electrochemiluminescence immunoassay “ECLIA”

III Intended Use/Indications for Use:

A Intended Use(s):

Immunoassay for the in vitro qualitative determination of IgG class antibodies to HSV-2 in human serum and lithium-heparin plasma, K2-EDTA plasma, and K3-EDTA plasma. The test is intended for sexually active individuals and expectant mothers as an aid in the presumptive diagnosis of HSV-2 infection. The test results may not determine the state of active lesions or associated disease manifestations, particularly for primary infection. The predictive value of positive or negative results depends on the population's prevalence and the pretest likelihood of HSV-2.
The electrochemiluminescence immunoassay "ECLIA" is intended for use on **cobas e** immunoassay analyzers.

This test is not FDA-cleared for screening blood or plasma donors.

The performance of this assay has not been established for use in a pediatric population, neonates, or immunocompromised patients or for use at point-of-care facilities.

B Indication(s) for Use:

Same as Intended Use

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

For use with the **cobas e** 411.

IV Device/System Characteristics:

A Device Description:

The Elecsys HSV-2 IgG immunoassay makes use of a sandwich test principle using biotinylated recombinant HSV-2-specific antigens and HSV-2-specific recombinant antigens labeled with a ruthenium complex. The Elecsys HSV-2 IgG immunoassay is intended for the qualitative determination of IgG class antibodies to HSV-2 in human serum and plasma to aid in the presumptive diagnosis of HSV-2 infection. It is intended for use on the **cobas e** immunoassay analyzers.
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.

Results Interpretation.

The cutoff for the Elecsys HSV-2 IgG assay was initially established by measuring a total of 267 serum samples from two cohorts: sexually active adults and pregnant women. The distribution of positive and negative results was compared with the predicate assay, an FDA-cleared immunoblot. The cutoff was set as noted below. The result of a sample is given either as reactive or non-reactive as well as in the form of a cutoff index (signal sample/cutoff). Results obtained with the HSV-2 IgG assay are interpreted as follows:

Non-reactive:	< 1.0 COI
Reactive:	≥ 1.0 COI

Samples with a cutoff index < 1.0 are non-reactive in the HSV-2 IgG assay. These samples are considered negative for HSV-2 IgG-specific antibodies and do not need further testing.
Samples with a cutoff index ≥ 1.0 are considered reactive in the Elecsys HSV-2 IgG assay.
The HSV-2 IgG results for a given specimen, as determined by assays from different manufacturers, can vary due to differences in reagents and assay methods.
If control results are out of their specified range, no patient results should be reported.

B Principle of Operation:

Sandwich principle. Total duration of assay: 18 minutes.

- 1st incubation: 20 µL of sample, biotinylated recombinant HSV-2-specific antigens, and HSV-2-specific recombinant antigens labeled with a ruthenium complex (Tris(2,2'-bipyridyl)ruthenium(II)-complex ($Ru(bpy)_3^{2+}$) form a sandwich complex.
- 2nd incubation: After addition of streptavidin-coated microparticles, the 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. 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.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Elecsys Hsv-2 Igg Immunoassay

B Predicate 510(k) Number(s):

K121895

C Comparison with Predicate(s):

Table 1. Similarities and Differences between Elecsys HSV-2 IgG (current assay) and Elecsys HSV-2 IgG (updated assay).

Device & Predicate Device(s):	**Elecsys HSV-2 IgG K220924**	**Elecsys HSV-2 IgG K121895**
General Device Characteristic Similarities		
Intended Use/Indications For Use	Immunoassay for the in vitro qualitative determination of IgG class antibodies to HSV-2 in human serum and lithium-heparin plasma, K_2-EDTA plasma, and K_3-EDTA plasma. The test is intended for sexually active individuals and expectant mothers as an aid in the presumptive diagnosis of HSV-2 infection. The test results may not determine the state of active lesions or associated disease manifestations, particularly for primary infection. The predictive value of positive or negative results depends on the population's prevalence and the pretest likelihood of HSV-2. The electrochemiluminescence immunoassay "ECLIA" is intended for use on **cobas e** immunoassay analyzers. This test is not FDA-cleared for screening blood or plasma donors. The performance of this assay has not been established for use in a pediatric population, neonates, immunocompromised patients, or for use at point-of-care facilities.	Immunoassay for the in vitro qualitative determination of IgG class antibodies to HSV-2 in human serum and lithium-heparin plasma, K2-EDTA plasma, and K3-EDTA plasma. The test is intended for sexually active individuals and expectant mothers as an aid in the presumptive diagnosis of HSV-2 infection. The predictive value of positive or negative results depends on the population's prevalence and the pretest likelihood of HSV-2. The electrochemiluminescence immunoassay "ECLIA" is intended for use on Elecsys and **cobas e** immunoassay analyzers. This test is not FDA-cleared for screening blood or plasma donors. The performance of this assay has not been established for use in a pediatric population, neonates, or immunocompromised patients or for use at point-of-care facilities.
Technology	Same	ECLIA
Test format	Same	Sandwich
Test type	Same	qualitative
Application time	Same	18 min
Buffer Composition R2	Same	2-morpholino-ethane sulfonic acid
	Same	Stabilizer: Bovine serum albumin
	Same	Preservatives

		N-Methylisothiazolone Oxy-PYRION
Reporting of values	Same	COI and result message (non-reactive) < 1.0 COI = non-reactive ≥ 1.0 COI = reactive
Calibrators	Same	HSV-2 Cal1 / HSV-2 Cal2
Control material	Same	PreciControl HSV
Antigens/Antibodies used in R2	Same	Ruthenium-complex labeled antigen (recombinant, *E. coli*)
General Device Characteristic Differences		
Antigens/Antibodies used in R2	Anti-Biotin antibody specific for free, unconjugated biotin ("scavenger antibody") in R2	None
Streptavidin interference reducing agent	SA Mutein Poly	None
Biotin tolerance	≤ 1200 ng/mL	< 70 ng/mL
SA interference elimination	Yes, optimized	No
Instrument Platform	**cobas e** 411	**cobas e** 411, e 601, e 602, Modular Analytics e170

VI Standards/Guidance Documents Referenced:

CLSI EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – 3rd Edition.

CLSI EP07 3rd Edition: Interference Testing in Clinical Chemistry.

CLSI EP09c 3rd Edition: Measurement Procedure Comparison and Bias Estimation Using Patient Samples.

Elecsys HSV-2 IgG, product code MYF, follows Special Control "Class II Special Controls Guidance Document: Herpes Simplex Virus Types 1 and 2 Serological Assays" issued August 9, 2011.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

   a. Repeatability and intermediate precision studies.

Precision was determined on the **cobas e** 411 analyzer using Elecsys reagents and controls in a protocol (EP05-A3) of the CLSI (Clinical and Laboratory Standards Institute). Results were generated from 5 human serum samples (covering a range of negative, near cut-off, and positive values), and 2 controls assayed in 2 runs per day in duplicate each for 21 days (n = 84). The following results were obtained:

Table 2. Repeatibility and Intermediate precision.

cobas e 411 analyzer					
		Repeatability		**Intermediate precision**	
Sample	**Mean COI[a)]**	**SD[b)] COI**	**CV %**	**SD COI**	**CV %**
HS[c)] 1	0.098	0.001	1.3	0.002	1.6
HS 2	1.15	0.015	1.3	0.024	2.1
HS 3	12.0	0.138	1.2	0.223	1.9
HS 4	49.4	0.970	2.0	1.19	2.4
HS 5	0.861	0.011	1.3	0.020	2.3
PC[d)] HSV_1	0.287	0.003	0.9	0.005	1.8
PC HSV_2	7.72	0.075	1.0	0.169	2.2

a) COI = cutoff index

b) SD = standard deviation

c) HS = human serum

d) PC = PreciControl

b. Reproducibility study.

See K121895.

2. Linearity:

Not applicable; this is a qualitative assay.

3. Analytical Specificity/Interference:

Potential interference of the analyte in the presence of biotin using the updated Elecsys HSV-2 IgG assay was determined by testing three serum samples (negative, near cut-off, positive) on the **cobas e** 411 immunoassay analyzer. One aliquot of each sample was spiked with the interfering substance (biotin) and another aliquot was spiked with the same volume of the respective solvent (dilution pool). The interfering pool was then incrementally diluted into the

dilution pool. The recovery for each sample was calculated by comparison to the analyte concentration of the respective dilution pools.
The results of the study support the following statement in the assay labeling:

"Serum samples that contain biotin at a concentration of 1200 ng/mL demonstrate less than or equal to 10 % negative bias in COI values".

For complete endogenous substances interference study results see K121895.

4. Assay Reportable Range:

   See K121895.

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

   Reagent and Calibration Stability Studies.

   a. On-board Reagent Stability:

   The claimed on-board reagent stability study of 28-days reported in K121895 was confirmed for the updated Elecsys HSV-2 IgG assay.

   b. Lot Calibration Stability:

   The claimed lot calibration stability of 12 weeks reported in K121895 was confirmed for the updated Elecsys HSV-2 IgG assay.

6. Detection Limit:

   See K121895.

7. Assay Cut-Off:

   See K121895.

B Comparison Studies:

1. Method Comparison with Predicate Device:

   A method comparison study was conducted to confirm the updated assay shows equivalent performance compared to the originally cleared assay (K121895). The results obtained from 206 samples distributed across the span of the reportable range were measured internally with one reagent lot of the current assay and three different reagent lots of the updated assay in single determination. The study showed 100% agreement of the qualitative results and regression analysis of the COI values demonstrated acceptable concordance between the assays. The results of the original method comparison study are found in K121895.

2. Matrix Comparison:

See K121895.

C Clinical Studies:

1. Clinical Sensitivity:

   See K121895

2. Clinical Specificity:

   See K121895

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

   Not Applicable

D Clinical Cut-Off:

See K121895

E Expected Values/Reference Range:

See K121895

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.