

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY**

A. 510(k) Number:

K072617

B. Purpose for Submission:

New device

C. Measurand:

Rubella IgG antibodies

D. Type of Test:

Chemiluminescent immunoassay

E. Applicant:

Roche Diagnostics

F. Proprietary and Established Names:

Elecsys Rubella IgG immunoassay
Elecsys Rubella IgG PreciControl

G. Regulatory Information:

1. Regulation section: 21 CFR 866.3510, ELISA, Rubella
21 CFR 862.1660, Quality control material
2. Classification: Class: II
3. Product code: LFX, JJX
4. Panel: 83 Microbiology

H. Intended Use:

1. Intended Use(s):

The Elecsys Rubella IgG immunoassay is for the in vitro quantitative determination of IgG antibodies to rubella virus in human serum and Li-heparin, K3-EDTA and sodium citrate plasma. This assay may be used as an aid in the

assessment of immune status to rubella in individuals including women of childbearing age. The electrochemi-luminescence immunoassay “ECLIA” is intended for use on Elecsys and **cobas e** immunoassay analyzers.

PreciControl Rubella IgG: Elecsys PreciControl Rubella IgG is used for quality control of the Elecsys Rubella IgG immunoassay on the Elecsys and **cobas e** immunoassay analyzers.

2. Indication(s) for use:

Same as intended use

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

Instrument comparison: A total of 390 samples were tested on both the Elecsys 2010 analyzer and the MODULAR ANALYTICS E170 analyzer. Samples had anti-Rubella IgG values ranging from 0 - 500 IU/mL. The positive agreement was 197/197 or 100% (95% CI: 98.14% - 100%). The negative agreement was 192/ 193 or 99.5% (95% CI 97.15% - 99.99%)

I. Device Description:

Samples are incubated with biotinylated monoclonal anti-human IgG antibody, RLP (Rubella-like particles) and a ruthenylated monoclonal anti-Rubella antibody fragment. In addition a biotinylated Rubella virus-specific recombinant antigen E1 (*E. coli*) and E1 labeled with ruthenium complex Tris(2,2'-bipyridyl)ruthenium(II)-complex react with anti-Rubella IgG from the sample to form a sandwich complex. A second incubation is performed with the addition of streptavidin-coated microparticles. 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 via a calibration curve which is instrument-specifically generated by 2-point calibration and a master curve provided via the reagent barcode.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Zeus, Rubella IgG ELISA Test

2. Predicate 510(k) number(s):

K984180

1. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	The Elecsys Rubella IgG immunoassay is for the in vitro quantitative determination of IgG antibodies to rubella virus in human serum and Li-heparin, K3-EDTA and sodium citrate plasma. This assay may be used as an aid in the assessment of immune status to rubella in individuals including women of childbearing age. The electrochemi-luminescence immunoassay “ECLIA” is intended for use on Elecsys and cobas e immunoassay analyzers.	The Zeus Scientific, Inc. Laboratories Rubella IgG ELISA Test System is designed for the qualitative and/or quantitative detection of IgG antibodies to rubella virus in human serum. The test system is intended to be used to evaluate single sera for immune status or paired sera to demonstrate seroconversion, and is for in vitro diagnostic use.
Method	Qualitative and quantitative	Qualitative and quantitative
Differences		
Item	Device	Predicate
Specimen Type	Human serum and plasma	Human serum
Type of assay	Chemiluminescence	ELISA

K. Standard/Guidance Document Referenced (if applicable):

- a. CLSI I/LA6-A-Detection and Quantitation of Rubella IgG Antibody
- b. CLSI EP-17A - Limit of Blank (LoB) and Limit of Detection (LoD)
- c. CLSI EP5-A - Evaluation of Precision Performance

L. Test Principle:

Chemiluminescent immunoassay

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Reproducibility was determined at three different sites using Elecsys reagents, human sera, and controls in a modified protocol of the CLSI EP5-A document: 6 times daily for 10 days (n = 60). Total precision varied from 2-13% for positive samples. The following results were obtained:

MODULAR ANALYTICS E170 and cobas e 601 analyzers						
Sample	N	Mean IU/mL	Within-run precision		Total precision	
			SD IU/mL	CV %	SD IU/mL	CV %
PC ^b Rubella IgG 1	60	3.83	0.090	2.34	0.199	5.19
PC Rubella IgG 2	60	66.0	1.65	2.49	2.21	3.35
Serum pool 1	60	3.79	0.091	2.41	0.215	5.68
Serum pool 2	60	20.4	0.335	1.64	0.589	2.89
Serum pool 3	60	79.6	1.35	1.69	1.65	2.08
Serum pool 4	60	321	6.73	2.10	7.66	2.39
Li-heparin plasma pool 1	60	6.14	0.122	1.98	0.249	4.05
Li-heparin plasma pool 2	59	50.7	1.01	1.98	1.33	2.63
K ₃ -EDTA plasma pool 1	60	2.38	0.071	2.99	0.186	7.84
K ₃ -EDTA plasma pool 2	60	20.2	0.413	2.05	0.598	2.96

^b PC = PreciControl

MODULAR ANALYTICS E170 and cobas e 601 analyzers						
Sample	N	Mean IU/mL	Within-run precision		Total precision	
			SD IU/mL	CV %	SD IU/mL	CV %
PC Rubella IgG 1	60	3.66	0.075	2.04	0.118	3.21
PC Rubella IgG 2	60	64.1	0.770	1.20	2.30	3.58
Serum pool 1	60	3.52	0.110	3.11	0.146	4.13
Serum pool 2	60	20.0	0.351	1.75	0.527	2.64
Serum pool 3	60	76.6	1.37	1.79	2.76	3.61
Serum pool 4	60	303	5.29	1.74	12.0	3.95
Li-heparin plasma pool 1	60	5.80	0.335	5.78	0.378	6.52
Li-heparin plasma pool 2	60	47.8	2.49	5.21	2.93	6.13
K ₃ -EDTA plasma pool 1	60	2.21	0.059	2.67	0.076	3.42
K ₃ -EDTA plasma pool 2	60	19.6	0.372	1.90	0.615	3.15

Elecsys 2010 and **cobas e 411** analyzers

Sample	N	Mean IU/mL	Within-run precision		Total precision	
			SD IU/mL	CV %	SD IU/mL	CV %
PC Rubella IgG 1	60	4.10	0.176	4.29	0.319	7.77
PC Rubella IgG 2	60	69.7	4.73	6.79	5.36	7.69
Serum pool 1	60	3.87	0.399	10.3	0.428	11.1
Serum pool 2	59	17.7	0.989	5.58	2.34	13.4
Serum pool 3	60	61.7	4.96	8.04	5.54	8.98
Serum pool 4	59	312	25.6	8.21	29.8	9.54
Li-heparin plasma pool 1	60	6.53	0.418	6.40	0.569	8.71
Li-heparin plasma pool 2	57	48.9	2.13	4.34	3.07	6.28
K ₃ -EDTA plasma pool 1	59	2.44	0.356	14.6	0.423	17.4
K ₃ -EDTA plasma pool 2	59	15.3	0.723	4.73	1.14	7.49

b. Linearity/assay reportable range:

0.21-500 IU/mL

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Calibrators traceable to NIBSC 1st International Standard for anti-Rubella Immunoglobulin, human, formerly referred to as the proposed 3rd WHO Reference Standard Preparation

d. Detection limit:

Limit of Detection: < 0.21 IU/mL

e. Analytical specificity:

The specificity of the Elecsys Rubella IgG assay was evaluated by testing a total of 60 specimens representing a variety of disease states (ANA, CMV, EBV, FTA, HBV, HCV, HIV 1/2, HSV, Mumps, Parv B19, RH, and VZV).

The testing results are summarized in the table below.

Cross-reactant	N	IgG Elecsys/ reference Neg/Neg	IgG Elecsys/ reference Pos/Neg	IgG Elecsys/ reference Neg/Pos	IgG Elecsys/ reference Pos/Pos
ANA	3	0	0	0	3
CMV¹	4	1	0	0	2
EBV	1	0	0	0	1
FTA	5	1	0	0	4
HBV	6	0	0	2	4
HCV	5	0	0	0	5
HIV 1/2	9	1	0	0	8
HSV	8	0	0	0	8
Mumps	3	0	0	0	3
Parv B19	4	0	0	0	4
RH	7	0	0	0	7
VZV	5	0	0	0	5
Subtotal	60	3	0	2	54
Total	60	59			

¹One CMV sample was repeatedly equivocal by the reference method and was excluded from the calculations.

f. Assay cut-off:

The CLSI subcommittee on Rubella Serology recommended 10 IU/mL as the cutoff level.

2. Comparison studies:

a. Method comparison with predicate device:

US clinical study: 500 samples were obtained from a US reference laboratory; representing subjects for whom anti-Rubella testing had been ordered per clinical routine. All samples were frozen sera which had been banked consecutively from the routine collective. This group consisted predominantly of women of childbearing age; and contained 94% females and 6% males, ranging in age from 1 to 82.

		Reference Rubella IgG Assay			
Elecsys Rubella IgG		Positive	Negative	Equivocal	Total
	Positive	466	9	0	475
	Negative	9	16	0	25
	Total	475	25	0	500

Agreement classification	Numerator/ Denominator	Percent agreement (%)	95% confidence interval
Negative agreement	16/25	64.0	42.5 - 82.0
Positive agreement	466/475	98.1	96.4 - 99.1

Testing of Banked Samples: 345 additional banked samples were tested. 295 samples which had tested negative with a Hemagglutination Inhibition (HI) assay were selected from the banked routine collective of a laboratory in Germany. An additional 50 positive samples were selected from the archived routine collective of a US reference laboratory. All samples were frozen sera. 332 were from females (179 of whom were pregnant) and 14 were from males; ages ranged from 5-61.

		Reference Rubella IgG Assay			
Elecsys Rubella IgG		Positive	Negative	Equivocal*	Total
	Positive	168	3	2	173
	Negative	31	140	1	172
	Total	199	143	3	345

Agreement classification	Numerator/ Denominator	Percent agreement (%)	95% confidence interval
Negative agreement	140/145	96.6	92.1 - 98.9
Positive agreement	168/ 200	84.0	78.2 – 88.8

*The repeatedly equivocal result was counted as a discrepant against the Elecsys

Samples collected during a rubella outbreak: Samples were collected from 71 pregnant women during a rubella outbreak in Italy.

		Reference Rubella IgG Assay			
Elecsys Rubella IgG		Positive	Negative	Equivocal	Total
	Positive	50	0	0	50
	Negative	8	10	3	21
	Total	58	10	0	71

Agreement classification*	Numerator/Denominator	Percent agreement (%)	95% confidence interval
Negative agreement	10/10	100	69.1-100
Positive agreement	50/58	86.2	74.6-93.9

*The equivocal result, which could not be repeated due to insufficient quantity, was counted as a discrepant against the Elecsys

Pregnant women study: Serum samples were collected from 150 pregnant women in the US and tested on the Elecsys and the reference assay. The Elecsys Rubella IgG showed 100 % agreement (95% CI: 97.57- 100%), with 150/150 positive tests.

Vaccination follow-up: Commercially available vaccination follow-up panels comprising 152 samples from 13 subjects were also tested. The final specimen from each panel yielded 100 % agreement (95% CI: 75.29% -100%) between the methods, with 13/13 positive test results.

Evaluation of low positive samples: 84 serum samples that gave low positive results (10-20 IU/mL) on the reference assay were tested with Elecsys Rubella IgG assay. The positive agreement was 80/84 or 95.2 % (95 % CI: 88.25-98.69 %).

Evaluation of CDC reference panel: A panel of 100 serum specimens was obtained through the US Centers for Disease Control and Prevention (CDC) and tested for Rubella IgG on the Elecsys 2010 analyzer. The sera panel consists of 100 specimens, 50 pairs of sera titrated by HI. There are 9 negative sera resulting in 18 negative specimens and 41 positive sera resulting in 82 positive specimens. As evaluated by the CDC, the Elecsys 2010 analyzer showed 100% agreement, with 82/82 positive tests on 82 positive sera and 18/18 negative tests on 18 negative sera.

CDC Standard: The low titer (21.0 IU/mL) anti-rubella human reference serum from CDC was tested neat and diluted 1:2 as described in the CLSI document I/LA6-A. The mean result of the neat standard was 38.8 IU/mL. The mean result of the two fold diluted standard was 15.4 IU/mL.

b. Matrix comparison:

Serum and plasma comparison: Results for the comparison between serum and 3 plasma matrices. Plasma matrix, number of specimens showing recovery to serum within various ranges

	< 10%	10% - 20%	> 20%
Li-heparin	32	0	0
K3-EDTA	37	1	0
Sodium citrate	19	10	0

3. Clinical studies:

a. *Clinical Sensitivity:*

Not applicable

b. *Clinical specificity:*

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

The CLSI subcommittee on Rubella Serology recommended 10 IU/mL as the cutoff level to determine the immunity from infection.

5. Expected values/Reference range:

Not applicable

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

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