

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

- A. 510(k) Number:** k092322
- B. Purpose for Submission:** Clearance of new device
- C. Measurand:** Rubella-specific IgM in human serum and plasma
- D. Type of Test:** Electrochemiluminescence immunoassay (ECLIA)
- E. Applicant:** Roche Diagnostics
- F. Proprietary and Established Names:** Elecsys Rubella IgM immunoassay
Elecsys PreciControl Rubella IgM

G. Regulatory Information:

1. Regulation section: 21 CFR §866.3510, Rubella virus serological reagents
21 CFR §862.1660, Quality control material
2. Classification: Class II
3. Product code: LFX (Enzyme Linked Immunoabsorbent Assay, Rubella)
JJX (Quality control material, assayed and unassayed)
4. Panel: Virology (81)

H. Intended Use:

1. Intended use(s):

The Elecsys Rubella IgM immunoassay is for the in vitro qualitative determination of IgM 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 presumptive diagnosis of an acute or recent rubella infection, including women of childbearing age.

The electrochemiluminescence immunoassay “ECLIA” is intended for use on Elecsys and **cobas e** immunoassay analyzers.

The Elecsys PreciControl Rubella IgM is used for quality control of the Elecsys Rubella IgM immunoassay on the Elecsys and **cobas e** immunoassay analyzers. NOTE: This assay has not been cleared/approved by the FDA for blood/plasma donor screening.

2. Indication(s) for use:

The Elecsys Rubella IgM assay may be used as an aid in the presumptive diagnosis of an acute or recent rubella infection, including in women of childbearing age.

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

Previously cleared with: K961481 (Elecsys 2010 and E170); K060373 (cobas e601). Inclusion of the **cobas e** analyzers in the labeling has been accepted previously for K072617 and K073501 after review by FDA on Dec. 10, 2008.

I. Device Description:

Samples are incubated with biotinylated monoclonal anti-human IgM-specific antibodies and rubella-specific recombinant antigens, forming a complex with the anti-rubella IgM antibodies present in the sample. The addition of ruthenium-labeled rubella specific antibodies and streptavidin-coated microparticles forms a sandwich complex via biotin-streptavidin interaction. The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode, and unbound substances are then removed with ProCell. Voltage application to the electrode induces chemiluminescent emission, which is then measured by a photomultiplier. Results are determined via a calibration curve generated by 2-point calibration and a master curve provided via the reagent barcode.

J. Substantial Equivalence Information:

1. Predicate device name(s): K984180, Zeus Scientific Rubella IgM ELISA Test System.

Additional predicates for a two out of three consensus (routine and supplemental positive cohorts): Abbott Labs. AxSYM Rubella IgM Antibody Assay (K954318) and DPC Immulite IgM (K012077)

2. Comparison with main predicate:

Similarities		
Item	Device	Main Predicate
Intended Use	The Elecsys Rubella IgM immunoassay is for the in vitro qualitative determination of IgM antibodies to rubella virus in human serum and Li-heparin, K ₃ -	The Zeus Scientific, Inc. Laboratories Rubella IgM ELISA Test System is designed for the qualitative detection of IgM antibodies to rubella virus in

Similarities		
Item	Device	Main Predicate
	EDTA and sodium citrate plasma. This assay may be used as an aid in the presumptive diagnosis of an acute or recent rubella infection, particularly in women of childbearing age. The electrochemiluminescence immunoassay “ECLIA” is intended for use on Elecsys and cobas e immunoassay analyzers.	human serum. The test system is intended to be used to evaluate serological evidence of acute or recent infection with rubella virus and is for <i>in vitro</i> diagnostic use.
Indications for Use	Aid in the presumptive diagnosis of an acute or recent rubella infection, particularly in women of childbearing age.	Intended to be used to evaluate serological evidence of acute or recent infection with rubella virus.
Unit of Measure	COI (S/CO)	COI (S/CO)
Calibrator	Included in kit	Included in kit
Differences		
Item	Device	Predicate
Sample Type	Human serum, lithium heparin plasma, potassium EDTA plasma, and sodium citrate plasma.	Serum.
Assay Technique	Electrochemiluminescent immunoassay	ELISA
Instrument Platform	Automated. Roche Elecsys 2010 and Modular Analytics E170 (Elecsys module) and cobas e immunoassay analyzers.	No automated instrument platform. ELISA equipment/microwell plate reader needed. No specific model required.
Cut-off	Neg: <0.8 Pos: ≥ 1.0 (S/CO)	Neg: ≤ 0.9 Pos: ≥ 1.10 (S/CO)
Equivocal Zone	0.8 to 1.0 (S/CO)	0.91 to 1.09 (S/CO)
Calibrator levels	Two	One
Calibration frequency	Once per reagent lot and <ul style="list-style-type: none"> - After 1 month when using same reagent lot - After 7 days when using same reagent kit - As required per QC findings or pertinent regulations 	Each time the assay is run.
Controls	PreciControl Rubella IgM (sold separately)	Positive and negative control included in kit.

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

CLSI EP5-A2, “Evaluation of Precision Performance of Quantitative Measurement Methods”

CLSI EP17-A, “Protocols for Determination of Limits of Detection”

L. Test Principle:

The Elecsys Rubella IgM Immunoassay is a two-step sandwich immunoassay with

streptavidin microparticles and electrochemiluminescence detection. The Rubella IgM is composed of a biotin-labeled monoclonal antibody against human IgM, a Rubella-like particle and a ruthenium-labeled anti-Rubella antibody. A relationship exists between the concentration of the IgM antibody targets present in a patient sample and the level of signal count detected by the system. The IgM assay is a qualitative test based on a cut-off formula dependent on the negative and positive calibrators. Cut-off index (COI) is based on the ratio of assay signal to cut-off signal (also abbreviated s/co). COI values equal to or greater than 1.0 are considered positive for the presence of anti-Rubella IgM antibody. Results are determined using a 2 point calibration. The test system contains the human serum-based calibrators intended for use with the system. The Elecsys Precicontrol Rubella IgM contains two levels of human serum. The positive control contains native, inactivated Rubella IgM antibodies.

The Elecsys PreciControl Rubella IgM contains two levels of human serum. The positive control contains native, inactivated Rubella IgM antibodies.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Reproducibility was determined at three different external sites (Site A, B, and C) using Elecsys reagents, human sera, and controls in a modified protocol (EP5-A2) of the CLSI (Clinical and Laboratory Standards Institute): 6 times daily for 10 days (n = 60). Precision was determined at one internal site (Site D), where the samples were run 20 times for repeatability and tested twice a day for 10 days (n=100) for intermediate precision. Note that the site C intermediate precision %CV values (using the Elecsys 2010 and cobas e 411 analyzer) are significantly higher than those from sites A and B (using the Modular Analytics E170 and cobas e 601). The following results were obtained:

Site A						
MODULAR ANALYTICS E170 and cobas e 601 analyzers						
			Repeatability ^b		Intermediate precision ^c	
Sample	N	Mean S/CO	SD S/CO	CV %	SD S/CO	CV %
PC _d Rubella IgM 1	59	0.24	0.006	2.70	0.009	3.89
PC Rubella IgM 2	59	1.77	0.085	4.83	0.098	5.57
Serum Pool 1	58	0.23	0.003	1.43	0.006	2.86
Serum Pool 2	58	1.87	0.041	2.18	0.056	3.00
Serum Pool 3	58	6.21	0.125	2.01	0.208	3.35

Li-Heparin Plasma Pool 1	60	0.24	0.005	2.08	0.007	3.03
Li-Heparin Plasma Pool 2	58	1.86	0.036	1.91	0.056	3.01
K3-EDTA Plasma Pool 1	60	0.26	0.004	1.57	0.007	2.79
K3-EDTA Plasma Pool 2	59	1.84	0.039	2.14	0.056	3.04

b) repeatability = within-run precision c) intermediate precision = total precision (includes inter-assay precision) d) PC = PreciControl

Site B						
MODULAR ANALYTICS E170 and cobas e 601 analyzers						
			Repeatability		Intermediate precision	
Sample	N	Mean S/CO	SD S/CO	CV %	SD S/CO	CV %
PC Rubella IgM 1	60	0.23	0.004	1.75	0.005	2.04
PC Rubella IgM 2	60	1.68	0.041	2.46	0.047	2.77
Serum Pool 1	60	0.22	0.003	1.54	0.004	1.72
Serum Pool 2	60	1.88	0.036	1.94	0.047	2.49
Serum Pool 3	60	6.47	0.122	1.89	0.178	2.75
Li-Heparin Plasma Pool 1	60	0.24	0.004	1.54	0.004	1.54
Li-Heparin Plasma Pool 2	60	1.90	0.029	1.53	0.046	2.42
K3-EDTA Plasma Pool 1	60	0.26	0.004	1.46	0.005	1.78
K3-EDTA Plasma Pool 2	60	1.90	0.030	1.60	0.045	2.36

Site C						
Elecsys 2010 and cobas 411 analyzers						
			Repeatability		Intermediate precision	
Sample	N	Mean S/CO	SD S/CO	CV %	SD S/CO	CV %
PC Rubella IgM 1	60	0.22	0.013	5.74	0.023	10.5
PC Rubella IgM 2	60	2.00	0.077	3.86	0.209	10.4
Serum Pool 1	60	0.21	0.007	3.11	0.020	9.53
Serum Pool 2	60	1.59	0.107	6.71	0.272	17.1
Serum Pool 3	60	6.39	0.277	4.34	0.694	10.9
Li-Heparin Plasma Pool 1	60	0.23	0.008	3.22	0.022	9.60
Li-Heparin Plasma Pool 2	60	2.00	0.079	3.96	0.183	9.14

K3-EDTA Plasma Pool 1	60	0.25	0.010	3.90	0.024	9.69
K3-EDTA Plasma Pool 2	60	2.01	0.056	2.79	0.172	8.59

Site D						
Elecsys 2010 and cobas e 411 analyzers						
	Repeatability			Intermediate precision		
Sample	Mean COI	SD	CV %	Mean COI	SD	CV %
Human Sample 1	0.20	0.005	2.41	0.20	0.006	2.97
Human Sample 2	1.29	0.016	1.23	1.31	0.024	1.86
Human Sample 3	3.57	0.037	1.03	6.69	0.271	4.06
PC Rubella IgM 1	0.19	0.003	1.38	0.20	0.008	4.07
PC Rubella IgM 2	1.81	0.021	1.14	1.95	0.080	4.09

Note: the panels used for the precision/reproducibility studies presented here have suboptimal samples regarding the cutoff. Such a panel configuration was acceptable at the time of the original submission. Going forward, newer and current recommendations reflected in published FDA guidelines establish the need for evaluation of samples with values very close to the cutoff (low positive, high negative) for the precision/reproducibility studies. See appropriate FDA guidance documents.

Quality Control:

Quality control is done using the Elecsys PreciControl Rubella IgM. The controls 1 and 2 should be run as single determinations at least once every 24 hours when the test is in use, once per reagent kit, and after every calibration. The control intervals and limits should be adapted to each laboratory's individual requirements. Results must be within the defined limits. If control values fall outside of the expected range(s), patient results should not be reported and samples and controls should be retested. The recommended quality control material is serum based. The user is responsible for providing alternate control material for plasma samples when necessary. Applicable government regulations and local guidelines for quality control should be followed.

b. *Linearity/assay reportable range:*

N/A

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

Traceability:

This method has been standardized against a Roche standard. The units have been selected arbitrarily.

Stability:

Reagents:

unopened at 2-8 °C	up to the stated expiration date
M, R1, R2 after opening at 2-8 °C	12 weeks
	2 weeks or
on MODULAR ANALYTICS E170, Elecsys 2010 and cobas e	12 weeks if stored alternately in the refrigerator and on the analyzers (up to 84 hours)
Cal1, Cal2 after opening at 2-8 °C	8 weeks
on Elecsys 2010 and cobas e 411 at 20-25 °C	up to 5 hours
on MODULAR ANALYTICS E170 and cobas e 601	use only once

Controls:

unopened at 2-8 °C	up to the stated expiration date
after opening at 2-8 °C	8 weeks
on the analyzers	up to 5 hours

Samples:

The potential influence of frozen human serum samples after storage at -20C for 3 months was evaluated using recovery of 3 negative, one low positive, and 3 positive samples vs. a fresh reference, and deemed satisfactory. Similarly, studies of 6 freeze thaw cycles, sample stability for 3 weeks at 4 C, and sample stability at 25 C for 3 days resulted in satisfactory recovery within the specified acceptance criteria.

d. Detection limits:

Range for the electrochemiluminescence signals (counts) for the calibrators:

Negative calibrator (Cal1): 500-2700 (Elecsys 2010, MODULAR ANALYTICS E170 and **cobas e** analyzers).

Positive calibrator (Cal2): 5500-30000 (Elecsys 2010, MODULAR ANALYTICS E170 and **cobas e** analyzers).

The Limit of Blank (LoB) was determined on Elecsys 2010 Immunoassay Analyzer as the 95th percentile of measurements of blank samples. 5 samples were measured 12 times with single determination. The measurements were then ordered according to their values and the 95th percentile was determined, interpolating between the results of 57th and 58th ranked samples as follows:
 $LoB = (Conc. Sample 57 + Conc. Sample 58)/2$.

The LoB was: 955 counts (corresponding to concentration of ~54.24 U/mL).

Limit of detection (LoD) was evaluated on Elecsys 2010 Immunoassay Analyzer according to the guidelines of CLSI EP 17-A. The LoD was determined as the lowest amount of Analyte in a sample that can be detected with 95% probability. 5 samples with low concentration were measured 12

times with single determination; the precision (SD) was calculated for each sample. A pooled estimate of precision over the five samples was then determined (SD_{total}). Calculation of the LoD was performed as follows:
 $LoD = LoB + 1.653 \times SD_{total}$.
 The resulting LoD was 362 counts (corresponding to a concentration ~61.53 U/mL)

e. *Analytical specificity:*

Cross-reactivity:

The specificity of the Elecsys Rubella IgM 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, VZV). The testing results are summarized in the table below. For all analytical specificity categories tested, 77.6 % overall agreement was observed between the Elecsys immunoassay and an FDA-cleared reference method.

Cross-reactant	N	IgM Elecsys/ Comparator Neg/Neg	IgM Elecsys/ Comparator Pos/Neg	IgM Elecsys/ Comparator Neg/Pos	IgM Elecsys/ Comparator Pos/Pos
ANA ^c	3	2	0	1	0
CMV	4	1	0	2	1
EBV ^c	1	0	0	1	0
FTA	5	5	0	0	0
HBV ^d	6	5	0	0	0
HCV	5	4	0	1	0
HIV 1/2	9	9	0	0	0
HSV	8	6	0	2	0
Mumps ^c	3	3	0	0	0
Parv B19 ^d	4	3	0	0	0
RH	7	3	3	1	0
VZV	5	3	0	2	0
Sub-total	60	44	3	10	1
Total	60	58			

c) Cross-reactivity not well assessed due to the limited sample size tested.

d) One sample was repeatedly equivocal by the reference method and was excluded from the calculations

Interference:

The impact of endogenous interfering substances on the Elecsys Rubella IgM Immunoassay was determined testing natural and spiked samples.

Calculations were based on signal-to-cutoff ratio (S/CO). Acceptance criteria was recovery within +/- 0.25 S/CO (≤ 0.5 S/CO) or 80-120% (> 0.5 S/CO), except for Rheumatoid Factor, for which acceptance criterion was concordance rate to predicate device $> 90\%$.

The assay is unaffected by icterus (bilirubin < 428 μ mol/L or < 25 mg/dL), hemolysis (Hb < 1.49 mmol/L or < 2.4 g/dL), lipemia (Intralipid < 1500 mg/dL), Immunoglobulin A up to 9.6 mg/mL, Immunoglobulin G up to 42 mg/mL and biotin < 205 nmol/L or < 50 ng/mL. Criterion: Recovery of

positive samples within $\pm 20\%$ of initial value. In patients receiving therapy with high biotin doses (i.e. > 5 mg/day), no sample should be taken until at least 8 hours after the last biotin administration. Rheumatoid factor was not observed to cause any consistent bias, but RF factor levels > 1650 IU/mL may lead to erroneous results in some instances. Elevated levels of unspecific human IgM may cause interference.

In vitro tests were performed on 18 commonly used pharmaceuticals (Acetylcysteine, Ampicillin-Na, Ascorbic acid, Ca-Dobesilate, Ciclosporine, Cefoxitin, Heparin, Intralipid, Levodopa, Methyldopa, Metronidazole, Phenylbutazone, Doxycycline, Acetylsalicylic acid, Rifampicin, Acetaminophen, Ibuprofen, and Theophylline) and in addition on folic acid. No interference with the assay was found.

f. Assay cut-off:

The cutoff for the Elecsys Rubella IgM assay was initially established by measuring 162 positive rubella samples from 18 commercially available seroconversion panels; and 298 negative samples collected from blood donors. The distribution of positive, equivocal and negative results was compared to results from various reference assays and the cutoffs were set as noted below. This setting revealed an excellent separation of negative and positive samples exhibiting only 2 equivocal results out of 460. The resulting cutoff was verified using another reagent kit lot; and was then applied to the performance evaluation studies described 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 Elecsys Rubella IgM assay can be interpreted as follows:

Non-reactive: < 0.8 COI; Indeterminate: $\geq 0.8 - < 1.0$ COI; Reactive: ≥ 1.0 COI

Samples with a cutoff index < 0.8 are non-reactive in the Elecsys Rubella IgM assay. Samples with a cutoff index between ≥ 0.8 and < 1.0 are considered indeterminate. The sample should be retested. In case the result is still indeterminate, a second sample should be collected e.g. within 1 week. A significant increase of the Rubella IgG antibody titer from a first to a second sample supports the diagnosis of acute Rubella infection. Samples with a cutoff index ≥ 1.0 are reactive in the Elecsys Rubella IgM assay.

The magnitude of the measured result above the cutoff is not indicative of the total amount of antibody present in the sample. The anti-Rubella IgM results in a given specimen, as determined by assays from different manufacturers, can vary due to differences in assay and reagent methods.

Calculation

The analyzer automatically calculates the cutoff based on the measurement of Cal1 and Cal2.

2. Comparison studies:

a. Method comparison with predicate device:

The performance of the Elecsys Rubella IgM assay was determined by percent agreement among negative samples and percent agreement among positive samples, against a consensus comparator method, in specific populations.

For the clinical routine and the banked positive cohorts, a consensus comparator method was defined using a total of three FDA-cleared predicate devices and a two out of three consensus result approach as described in the following table:

Predicate Test Results (In Any Order)			Final Reference Result
Result A	Result B	Result C	
+	+	(-, Equ, or +)	+
-	-	(-, Equ, or +)	-
Equ	Equ	(-, Equ, or +)	Equ
+	-	Equ	Equ

All specimens were tested according to the respective package inserts of the FDA-cleared Rubella IgM assays. The three FDA-cleared devices used were the Zeus Scientific Rubella IgM ELISA Test System, the Abbott Labs. AxSYM Rubella IgM Antibody Assay and the DPC Immulite IgM test. Equivocal results that remained equivocal after being retested were considered equivocal for the performance analysis. Any consensus equivocal result discordant with the Elecsys Rubella IgM test result was tallied against the Elecsys in the calculation of performance.

For the vaccine follow up cohort, the Zeus Rubella IgM device was used as the sole comparator.

b. Matrix comparison:

The effect of analyte detection in the presence of anticoagulants with the Elecsys Rubella IgM was determined on Elecsys 2010 Immunoassay Analyzer by comparing values obtained from samples drawn into Serum-gel Separation-, Li-Heparin-, Citrate-Plasma-, K₃-EDTA Plasma-, and Plasma Separation tubes. Reference was normal Serum tube without gel. Acceptance criterion for all measurements concerning Serum/Plasma interferences is recovery ≤ 0.5 S/CO ± 0.25 S/CO, > 0.5 S/CO mean recovery 80-120%.

The following tables summarize the results for the comparison between serum and 3 plasma matrices.

Plasma matrix	Number of positive specimens showing recovery to serum within various ranges		
	<10%	10% - 20%	$\geq 20\%$
Li-heparin	7	1	0
K ₃ -EDTA	3	6	0
Sodium Citrate	9	0	0

Plasma matrix	Number of negative specimens showing recovery to serum within various ranges		
	<0.1 COI	0.1 - 0.25 COI	>0.25 COI
Li-heparin	24	0	0
K ₃ -EDTA	23	0	0
Sodium Citrate	23	0	0

3. Clinical studies:

a. *Clinical Sensitivity:* N/A

b. *Clinical specificity:* N/A

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

Percent positive and percent negative agreement with a consensus comparator method was determined as specified under Comparison Studies (see above). Studies were carried out in three independent testing sites (two sites within the US, one in Germany).

Prospective US clinical study cohort:

501 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. 438 were from females (132 of whom were pregnant) and 63 were from males; ages ranged from 18-76 years. Samples were tested on the Elecsys 2010 analyzer and on three FDA-cleared devices, which were used to define a consensus comparator algorithm result using a two-out-of-three approach.

Clinical routine cohort (non-pregnant)

The following table summarizes the results for the clinical routine cohort (non-pregnant):

		Consensus Result Rubella IgM			Total
		Positive	Negative	Equivocal	
Elecsys Rubella IgM	Positive	0	3	0	3
	Equivocal	1	1	0	2
	Negative	0	364	0	364
	Total	1	368	0	369

Agreement classification ^e	Numerator/Denominator	Percent agreement (%)	95% confidence interval
Negative agreement	364/368	98.9	97.2 -99.7

Positive agreement	0/1	N/A	N/A
--------------------	-----	-----	-----

e) Discrepant equivocal results were counted against the Elecsys

Pregnant subjects:

The following tables summarize the overall results for pregnant subjects from the clinical routine cohort:

		Consensus Result Rubella IgM			Total
		Positive	Negative	Equivocal	
Elecsys Rubella IgM	Positive	0	0	0	0
	Equivocal	0	1	0	1
	Negative	0	131	0	131
	Total	0	132	0	132

Agreement classification ^d	Numerator/Denominator	Percent agreement (%)	95% confidence interval
Negative agreement	131/132	99.2	95.9 -99.98
Positive agreement	0/0	N/A	N/A

d) Discrepant equivocal results were counted against the Elecsys test

Preselected positive samples cohort:

Due to the extremely low prevalence of IgM positive subjects, 100 additional preselected samples from commercial sources were tested. 100 samples which had tested positive for Rubella IgM were purchased from a US commercial source. All samples were frozen sera. 50 were from females (2 of whom were pregnant) and 50 were from males; ages ranged from 24 - 51 years. Samples were tested in a blinded fashion (together with negative samples).

The following table summarizes the results for all subjects from this preselected cohort:

		Consensus Result Rubella IgM			Total
		Positive	Negative	Equivocal	
Elecsys Rubella IgM	Positive	100*	0	0	100
	Equivocal	0	0	0	0
	Negative	0	0	0	0
	Total	100	0	0	100

Agreement classification	Numerator/Denominator	Percent agreement (%)	95% confidence interval
Negative agreement	0/0	N/A	N/A

Positive agreement	100/100	100	96.4 - 100
--------------------	---------	-----	------------

* includes two pregnant subjects.

Vaccination follow up cohort:

Commercially available vaccination follow-up panels comprising 144 samples from 12 subjects (4 male, 8 unknown) were tested to evaluate detection of IgM after vaccination. The first positive bleed of the test was compared to the first positive bleed of the predicate assay, yielding 100 % agreement between the two methods, with 12/12 positive test results.

Instrument comparison:

Approach to the validation of the different instruments was addressed in a previous FDA decision, see file k072617 for additional details. A total of 313 samples, obtained from blood donors or purchased from commercial sources, were tested on both the Elecsys 2010 and cobas e 411 analyzers and the MODULAR ANALYTICS E170 and cobas e 601 analyzers. Samples had anti-Rubella IgM values ranging from 0.15 - 14.0 COI. The positive agreement was 102/103 or 99.0 % (95 % CI: 95 % - 100 %). The negative agreement was 207/208 or 99.5 % (95 % CI: 97 % - 100 %).

4. Clinical cut-off:

Not internationally standard exist for IgM, refer to cutoff section above for additional details.

5. Expected values/Reference range:

Reference Range:

below 0.8 COI	Non reactive
between = 0.8 and <1.0 COI	Indeterminate
equal to or above 1.0 COI	Reactive

Expected Values: N/A

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.