

Rubella IgM

IgM antibodies to Rubella virus

04618831 190

100 tests

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English

Please note

The measured anti-Rubella IgM value of a patient's sample can vary depending on the testing procedure used. The laboratory finding must therefore always contain a statement on the Rubella IgM assay used. Anti-Rubella IgM values determined on patient samples by different testing procedures cannot be directly compared with one another and could be the cause of erroneous medical interpretations. Therefore, the results reported by the laboratory to the physician should include: "The following results were obtained with the Elecsys Rubella IgM assay. Results from assays of other manufacturers cannot be used interchangeably."

Intended use

Immunoassay for the in vitro qualitative determination of IgM antibodies to Rubella virus in human serum and plasma.

The electrochemiluminescence immunoassay "ECLIA" is intended for use on the Roche Elecsys 2010 and MODULAR ANALYTICS E170 (Elecsys module) immunoassay analyzers.

Summary^{1,2,3,4,5,6,7}

Rubella virus is the etiological agent of German measles, a commonly mild rash disease which occurs usually during childhood. It is spread by small droplets via the respiratory route. Postnatal acquired infection is seldom associated with complications.

However, Rubella can be a serious disease when a pregnant woman becomes infected especially during the first trimester of pregnancy. Rubella virus can be transmitted through the placenta and can result in fetal death or may cause severe malformations to the fetus, commonly summarized as congenital Rubella syndrome (CRS). CRS is an important cause of blindness, deafness, congenital heart disease and mental retardation. Today infant vaccination programs and the vaccination of women in child-bearing age who are susceptible to Rubella infection have considerably reduced the incidence of acute Rubella infection and the incidence of CRS.

The detection of Rubella-specific antibodies is used to determine the immune status of an individual and to aid in the diagnosis of acute Rubella infection.

The presence of IgG antibodies to Rubella virus indicates a previous exposure either by vaccination or prior Rubella infection and is indicative of presumptive immunity.

The detection of Rubella-specific IgM antibodies is used as an aid in the diagnosis of acute Rubella infection. Seroconversion of specific Rubella antibodies or a significant rise of the IgG antibody titer from a first to a second sample may support the diagnosis of acute Rubella infection.

Recombinant Rubella-like particles (RLP) have proven to replace authentic Rubella virus as an antigen in diagnostic assays.

Test principle

μ-Capture test principle. Total duration of assay: 18 minutes.

- 1st incubation: 10 μL of sample are automatically prediluted 1:20 with Elecsys Diluent Universal. Biotinylated monoclonal anti-human IgM-specific antibodies and Rubella-specific recombinant antigen are added and react with anti-Rubella IgM antibodies present in the sample to form a complex.
- 2nd incubation: After addition of ruthenium-labeled^a Rubella-specific antibodies and 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 via a calibration curve which is instrument-specifically generated by 2-point calibration and a master curve provided via the reagent barcode.

a) Tris(2,2'-bipyridyl)ruthenium(II)-complex (Ru(bpy)₃²⁺)

Reagents - working solutions

- M Streptavidin-coated microparticles (transparent cap), 1 bottle, 6.5 mL: Streptavidin-coated microparticles 0.72 mg/mL; preservative.
- R1 Anti-h IgM-Ab-biotin; Rubella-specific recombinant antigen (gray cap), 1 bottle, 10 mL: Biotinylated monoclonal anti-h IgM antibody (mouse) > 500 ng/mL, Rubella-like particles (RLP) approx. 0.1 U/mL; sodium phosphate buffer pH 7.7; preservative.
- R2 Anti-Rubella~Ru(bpy)₃²⁺ (black cap), 1 bottle, 10 mL: Anti-Rubella antibodies labeled with ruthenium complex > 400 ng/mL; sodium phosphate buffer pH 7.7; preservative.
- Cal1 Negative calibrator 1 (white cap), 2 bottles of 1.0 mL each: Human serum, non-reactive for anti-Rubella IgM; preservative.
- Cal2 Positive calibrator 2 (black cap), 2 bottles of 1.0 mL each: Anti-Rubella IgM approx. 700 U/mL (Roche units) in buffer; preservative.

Precautions and warnings

For in vitro diagnostic use.

Exercise the normal precautions required for handling all laboratory reagents. Disposal of all waste material should be in accordance with local guidelines.

Safety data sheet available for professional user on request.

All human material should be considered potentially infectious.

The negative calibrator (Cal1) has been prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg and antibodies to HCV and HIV.

The testing methods applied were FDA-approved or cleared in compliance with the European Directive 98/79/EC, Annex II, List A.

Positive calibrator (Cal2): Materials of human origin were tested for HIV and hepatitis C. The findings were negative.

However, as no testing method can rule out the potential risk of infection with absolute certainty, the material should be treated just as carefully as a patient specimen. In the event of exposure the directives of the responsible health authorities should be followed.^{8,9}

The reagents may not be used after the stated expiration date. Avoid the formation of foam with all reagents and sample types (specimens, calibrators, and controls).

Reagent handling

The reagents in the kit are ready for use and are supplied in bottles compatible with the system.

Elecsys 2010 analyzer: The calibrators Cal1 and Cal2 should only be left on the analyzers during calibration at 20-25°C. After use, close the bottles as soon as possible and store at 2-8°C. Ensure that no calibration solution is trapped in the opened snap-cap. Because of possible evaporation effects, not more than 5 calibration procedures per calibrator bottle set should be performed.

MODULAR ANALYTICS E170 analyzer: Unless the entire volume is necessary for calibration on the analyzers, transfer aliquots of the ready-for-use calibrators into empty snap-cap bottles (CalSet Vials). Attach the supplied labels to these additional bottles. Store the aliquots for later use at 2-8°C. Perform **only one** calibration procedure per aliquot.

All information required for correct operation is read in via the respective reagent barcodes.

Storage and stability

Store at 2-8°C.

Store the Elecsys Rubella IgM reagent kit (M, R1, R2) **upright** in order to ensure complete availability of the microparticles during automatic mixing prior to use. Stability:

unopened at 2-8°C:	up to the stated expiration date
M, R1, R2 after opening at 2-8°C:	12 weeks
on MODULAR ANALYTICS E170,	2 weeks or
Elecsys 2010:	12 weeks if stored alternately in the refrigerator and on the analyzers (up to 84 hours)



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Cal1, Cal2 after opening at 2-8°C:	8 weeks
on Elecsys 2010 at 20-25°C:	up to 5 hours
on MODULAR ANALYTICS E170:	use only once

Store the calibrators **upright!** Ensure that no calibration solution is trapped in the opened snap-cap.

Specimen collection and preparation

Only the specimens listed below were tested in a sufficient number and found acceptable.

Serum collected using standard sampling tubes or tubes containing separating gel.

Li-heparin, K₃-EDTA, and sodium citrate plasma. Do not use plasma treated with sodium fluoride and potassium oxalate.

Criterion: Mean recovery of positive samples within 80-120% of serum value.

Stable for 3 weeks at 2-8°C, 3 days at 25°C, 3 months at -20°C.

The samples may be frozen 6 times.

The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube manufacturer.

Centrifuge samples containing precipitates and frozen samples before performing the assay. Lyophilized samples and samples and controls stabilized with azide (up to 1%) can be used. Do not use heat-inactivated samples.

Ensure the patients' samples, calibrators, and controls are at ambient temperature (20-25°C) before measurement.

Because of possible evaporation effects, samples and calibrators on the analyzers should be measured within 2 hours.

Materials provided

See "Reagents - working solutions" section for reagents.

- 2 x 6 bottle labels

Materials required (but not provided)

- Cat. No. 04618840, PreciControl Rubella IgM, 4 x 1 mL each of PreciControl Rubella IgM 1 and 2
- Cat. No. 11732277, Diluent Universal, 2 x 18 mL sample diluent or Cat. No. 03183971, Diluent Universal, 2 x 40 mL sample diluent
- Cat. No. 11776576, CalSet Vials, 2 x 56 empty snap-cap bottles
- General laboratory equipment
- Elecsys 2010 or MODULAR ANALYTICS E170 analyzer

Accessories for Elecsys 2010 analyzer:

- Cat. No. 11662988, ProCell, 6 x 380 mL system buffer
- Cat. No. 11662970, CleanCell, 6 x 380 mL measuring cell cleaning solution
- Cat. No. 11930346, Elecsys SysWash, 1 x 500 mL washwater additive
- Cat. No. 11933159, Adapter for SysClean
- Cat. No. 11706802, Elecsys 2010 AssayCup, 60 x 60 reaction vessels
- Cat. No. 11706799, Elecsys 2010 AssayTip, 30 x 120 pipette tips

Accessories for MODULAR ANALYTICS E170 analyzer:

- Cat. No. 12135019, ProCell M, 1 x 2 L system buffer
- Cat. No. 12135027, CleanCell M, 1 x 2 L measuring cell cleaning solution
- Cat. No. 03023141, PC/CC-Cups, 12 cups to prewarm ProCell M and CleanCell M before use
- Cat. No. 03005712, ProbeWash M, 12 x 70 mL cleaning solution for run finalization and rinsing during reagent change
- Cat. No. 03004899, PreClean M, 5 x 600 mL detection cleaning solution
- Cat. No. 12102137, AssayTip/AssayCup Combimagazine M, 48 magazines x 84 reaction vessels or pipette tips, waste bags
- Cat. No. 03023150, WasteLiner, waste bags
- Cat. No. 03027651, SysClean Adapter M

Accessories for all analyzers:

- Cat. No. 11298500, Elecsys SysClean, 5 x 100 mL system cleaning solution

Assay

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator manual for analyzer-specific assay instructions.

Resuspension of the microparticles takes place automatically before use.

Read in the test-specific parameters via the reagent barcode. If in exceptional cases the barcode cannot be read, enter the 15-digit sequence of numbers.

MODULAR ANALYTICS E170 and Elecsys 2010 analyzers: Bring the cooled reagent to approx. 20°C and place on the reagent disk (20°C) of the analyzer. Avoid the formation of foam. The system automatically regulates the temperature of the reagents and the opening/closing of the bottles.

Place the calibrators Cal1 and Cal2 in the sample zone of the analyzers.

Only keep open during calibration. All information necessary for calibration is encoded on the barcoded bottle labels and is read in automatically.

After calibration has been performed, store Cal1 and Cal2 at 2-8°C or discard (MODULAR ANALYTICS E170 analyzer).

Calibration

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

Calibration frequency: Calibration must be performed once per reagent lot using Elecsys Rubella IgM Cal1, Cal2, and fresh reagent (i.e. not more than 24 hours since the reagent kit was registered on the analyzer).

Renewed calibration is recommended as follows:

- after 1 month (28 days) when using the same reagent lot
- after 7 days (when using the same reagent kit on the analyzer)
- as required: e.g. quality control findings with Elecsys PreciControl Rubella IgM outside the specified limits
- more frequently when this is required by pertinent regulations

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

Negative calibrator (Cal1): 500-2700 (Elecsys 2010 and MODULAR ANALYTICS E170 analyzers), positive calibrator (Cal2): 5500-30000 (Elecsys 2010 and MODULAR ANALYTICS E170 analyzers).

Quality control

For quality control, use 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. Each laboratory should establish corrective measures to be taken if values fall outside the limits.

If necessary, repeat the measurement of the samples concerned.

Calculation

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

Interpretation of the results

Results obtained with the Elecsys Rubella IgM assay can be interpreted as follows:

Non-reactive: < 0.8 COI

Indeterminate: ≥ 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.



Rubella IgM

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Limitations - interference

A negative Rubella IgM test result, also in combination with a positive Rubella IgG result, does not completely rule out the possibility of acute Rubella infection:

- Specimens taken very early in the acute phase of infection may not contain detectable amounts of Rubella IgM antibodies.
- The immune response after Rubella infection varies considerably. Non-reactive results may preferentially occur in the late phase of acute infection by the Elecsys Rubella IgM assay.

The detection of IgM antibodies to Rubella virus in a single sample is not sufficient to prove an acute Rubella infection. Elevated IgM antibody levels may persist after natural infection and also after vaccination for a variable time period. Further tests or a combination of test methods should be done for clarification. The diagnosis of acute Rubella infection may be supported by a significant increase of the Rubella IgG antibody titer from a first to a second sample.

The results in HIV patients, in patients undergoing immunosuppressive therapy or in patients with other disorders leading to immune suppression should be interpreted with caution.

Specimens from neonates, cord blood, pretransplant patients or body fluids other than serum and plasma, such as urine, saliva or amniotic fluid have not been tested.

The assay is unaffected by icterus (bilirubin < 428 µmol/L or < 25 mg/dL), hemolysis (Hb < 1.49 mmol/L or < 2.4 g/dL), lipemia (Intralipid < 1500 mg/dL), and biotin < 205 nmol/L or < 50 ng/mL.

Criterion: Mean recovery of positive samples within ± 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.

No interference was observed from rheumatoid factors up to a concentration of 6210 IU/mL.

The high-dose hook effect does not lead to false-negative results in the Elecsys Rubella IgM assay.

In vitro tests were performed on 18 commonly used pharmaceuticals and in addition on folic acid. No interference with the assay was found.

As with many µ-capture assays an interference with unspecific human IgM is observed. Increasing amounts of unspecific human IgM may lead to a decrease in the recovery of positive samples with the Elecsys Rubella IgM assay.

As with all tests containing monoclonal mouse antibodies, erroneous findings may be obtained from samples taken from patients who have been treated with monoclonal mouse antibodies or have received them for diagnostic purposes.

In rare cases, interference due to extremely high titers of antibodies to streptavidin and ruthenium can occur.

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

Specific performance data

Representative performance data on the analyzers are given below. Results obtained in individual laboratories may differ.

Precision

Reproducibility was determined using Elecsys reagents, human sera, and controls (within-run n = 21, between-run n = 10); total precision on MODULAR ANALYTICS E170 analyzer was determined in a modified protocol (EP5-A) of the CLSI (Clinical and Laboratory Standards Institute; formerly NCCLS): 6 times daily for 10 days (n = 60). The following results were obtained:

Elecsys 2010 Sample	Within-run precision			Between-run precision		
	Mean COI	SD COI	CV %	Mean COI	SD COI	CV %
HS ^b , negative	0.198	0.005	2.4	0.20	0.006	3.0
HS, weakly positive	1.29	0.016	1.2	1.31	0.024	1.9
HS, positive	3.57	0.037	1.0	6.69	0.271	4.1
PC ^c Rubella IgM 1	0.190	0.003	1.4	0.20	0.008	4.1
PC Rubella IgM 2	1.81	0.021	1.1	1.95	0.080	4.1

b) HS = human serum
c) PC = PreciControl

MODULAR ANALYTICS E170 Sample	Within-run precision			Total precision		
	Mean COI	SD COI	CV %	Mean COI	SD COI	CV %
HS, negative	0.184	0.004	1.9	0.183	0.017	9.5
HS, weakly positive	1.06	0.011	1.0	1.00	0.027	2.7
HS, positive	4.12	0.049	1.2	3.96	0.108	2.7
PC Rubella IgM 1	0.183	0.002	1.3	0.180	0.020	10.9
PC Rubella IgM 2	1.72	0.023	1.3	1.59	0.053	3.4

Analytical specificity

390 samples containing potentially interfering substances were tested with the Elecsys Rubella IgM assay and commercially available comparison tests comprising specimens:

- containing IgM antibodies against HAV, HBcAg, CMV*, EBV, HSV, Parvo B19*, VZV, Toxoplasma gondii, measles and mumps
- positive for HIV (early infection), HCV (early infection), Treponema pallidum, Gonorrhoea and Chlamydia
- containing autoantibodies (AMA, ANA*, SMA*) and elevated titers of rheumatoid factor*
- after vaccination against HBV and influenza

Positive or indeterminate results were verified by a Rubella IgG avidity test or a third commercial Rubella IgM test. 7 false positive and 4 indeterminate samples were found for Elecsys Rubella IgM. The specificity (COI ≥ 0.8) in this group was found 97.2%. The lower confidence limit was found 95.4%.

*CMV IgM positive: 1 false positive and 1 indeterminate result out of 30 samples, ParvoB19 IgM: 2 false indeterminate results out of 30 samples; patients with autoantibodies: ANA: 3 false positive and 2 indeterminate results out of 47 samples, SMA: 1 false positive result out of 12 samples, RF: 3 false positive results out of 48 samples.

Clinical sensitivity

Acute Rubella infection

Of 109 samples from the early acute phase of Rubella infection (< 30 days after onset of symptoms) which were tested at two sites, 87 samples were found positive with the Elecsys Rubella IgM assay. 4 samples were found indeterminate (reactive) and 18 samples were found negative.

Of 17 samples from the late acute phase (≥ 30 days), 6 samples were found positive with the Elecsys Rubella IgM assay, 1 sample was found indeterminate (reactive) and 10 samples were found negative.

Persisting IgM after Rubella infection

Of 91 specimen from previously infected pregnant women where an acute Rubella infection was excluded at the time of bleeding, 66 samples were found negative with the Elecsys Rubella IgM assay, 10 samples were found indeterminate (reactive) and 15 samples were found positive.

Rubella vaccination

In 67 individuals comprising 265 samples after Rubella vaccination, Rubella IgM antibodies were detected with the Elecsys Rubella IgM assay up to 60-90 days.

Clinical specificity

Pre-selected negative samples

In 311 pre-selected Rubella IgM negative samples, 2 discordant positive and 3 indeterminate results were found with the Elecsys Rubella IgM assay.

Routine samples (antenatal screening)

A total of 1556 fresh samples obtained from clinical routine (antenatal screening) were tested at 2 different sites in comparison to commercially available Rubella IgM assays. Samples with reactive or indeterminate results were re-tested with a third commercial Rubella IgM test at site 1 and at site 2 in addition with a Rubella IgG avidity test at site 2.

Relative specificity after resolution

Site	N	Relative specificity (%) COI < 0.8	Lower confidence limit (%)
1	557	98.74 (547/554)	97.65
2	999	98.99 (983/993)	98.30

Site 1: 7 samples which were found positive or indeterminate with the Elecsys Rubella IgM assay were found negative with the comparison tests. 3 samples



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were found reactive with all comparison assays despite lacking signs of Rubella-related symptoms and thus excluded from the calculation of specificity.

Site 2: Of 16 samples which were positive or indeterminate with the Elecsys Rubella IgM assay, an acute Rubella infection was excluded within 10 samples by a Rubella IgG avidity test (index > 60%). 3 samples with an inconclusive Rubella IgG avidity test result and 3 samples which could not be further examined were excluded from the calculation of specificity.

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