04784618500V10.0

Elecsys CMV IgM

cobas®

REF		Σ	SYSTEM
			cobas e 411
04784618190	04784618500	100	**cobas e** 601
			cobas e 602

English

System information

For **cobas e** 411 analyzer: test number 580
For **cobas e** 601 and **cobas e** 602 analyzers: Application Code Number 011

Intended use

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

Results obtained with this assay are used as an aid in the diagnosis of recent CMV infections.

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

Regulatory status

This assay has been CE marked according to Directive 98/79/EC. Test performance has been established for diagnostic use and for testing of blood donations.

Summary

Cytomegalovirus (CMV), a member of the herpes virus family, is ubiquitous in all human populations, causing infections which are followed by life-long latency in the host with occasional reactivations.[1,2] The seroprevalence of antibodies in adults ranges from 40-100 % with inverse correlation to socioeconomic status.[1,2,3] CMV is transmitted through body fluids, including blood, genital secretions and breast milk. Saliva and urine of infected individuals also represent a prominent source of infection, and children, especially those attending day care facilities, are an important vector for viral spread.[2,3,4,5,6] In immunocompetent individuals primary CMV infection is usually mild or asymptomatic.[2,5] Patients commonly present with a mononucleosis-like syndrome, including fever, sore throat, cervical lymphadenopathy, malaise, headache, muscle ache and joint pains.[2,3,5,7] During pregnancy, CMV can cause congenital infection which may result in permanent physical and/or neurological sequelae to the child.[5] CMV infection can be primary, i.e. newly acquired, or secondary, i.e. due to reactivation of the latent virus or re-infection with a different viral strain.[3,5] Primary CMV infection is reported in 1-4 % of seronegative women during pregnancy and the risk of transmission to the fetus is estimated to be about 30-40 %.[3,4] Reactivation of CMV infection during pregnancy is reported in 10-30 % of seropositive women and, in this circumstance, the risk of transmission of the virus is about 1-3 %.[3,4,5] Overall, prenatal CMV infection occurs in 0.6-0.7 % of all life births in the developed world.[4,5,8] The majority of babies born with congenital CMV infection are asymptomatic at birth.[8,9,10] Of these 5-15 % still develop irreversible impairments, most frequently hearing loss, that can occur several months or even years after birth.[5,8,9,10] For babies symptomatic at birth, prognosis is very poor, and the vast majority will develop severe mental impairment and/or hearing loss.[5,8,9,10] Different studies have shown that the risk of symptomatic congenital disease in the fetus or newborn infant is high, when maternal primary infection takes place in early pregnancy before week 20 of gestation, and lower thereafter.[4,5] The congenital CMV infection caused by recurrent maternal infection seldom leads to symptomatic disease at birth.[4,5]

At risk for CMV infection and disease are also immunocompromised patients such as transplant recipients and HIV infected patients where the virus can cause life-threatening diseases.[11,12] The CMV status of transplant donors and recipients is very important, as it will determine prophylactic and pre-emptive treatment strategies against CMV. CMV-negative transplant recipients should receive donations from CMV-negative individuals or leukocyte depleted blood products. CMV can reside in latency in infected cells and free viral DNA load is usually low. The CMV status can still be determined by testing for CMV IgG antibodies.

Within the appropriate clinical context, the first step in diagnosing acute primary CMV infection is most commonly made by the detection of anti-CMV-specific IgG and IgM antibodies.[5] Samples being reactive for IgM antibodies indicate an acute, recent or reactivated infection.[2,4,5,12] For further analysis of a primary CMV infection the determination of the CMV IgG avidity is used as an aid.[2,4,5,12] A positive IgM result in combination with a low avidity index for IgG is a strong indication of a recent primary CMV infection.[4,5,12] Seroconversion to CMV IgM and IgG may also indicate a recent CMV infection.[2,3,4,5,12]

Test principle

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

- 1st incubation: 10 µL of sample are automatically prediluted 1:20 with Diluent Universal. Biotinylated monoclonal anti-h-IgM-specific antibodies are added.
- 2nd incubation: CMV-specific recombinant antigen labeled with a ruthenium complex[a)] and streptavidin-coated microparticles are added. Anti-CMV IgM antibodies present in the sample react with the ruthenium-labeled CMV-specific recombinant antigen. 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/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 ($Ru(bpy)_3^{2+}$)

Reagents - working solutions

The reagent rackpack (M, R1, R2) is labeled as CMVIGM.

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 (gray cap), 1 bottle, 9 mL:
Biotinylated monoclonal anti-h-IgM antibody (mouse) > 500 µg/L, MES buffer 50 mmol/L, pH 6.5; preservative.

R2 CMV-Ag~$Ru(bpy)_3^{2+}$ (black cap), 1 bottle, 9 mL:
CMV-specific antigen (recombinant, E. coli) labeled with ruthenium complex > 50 µg/L; MES buffer 50 mmol/L, pH 5.5; preservative.

CMVIGM Cal1 Negative calibrator 1 (white cap), 2 bottles of 1.0 mL each:
Human serum, negative for anti-CMV IgM; preservative.

CMVIGM Cal2 Positive calibrator 2 (black cap), 2 bottles of 1.0 mL each:
Anti-CMV IgM (human serum) in HEPES buffer, pH 7.4; bovine albumin; 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.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

Warning

Elecsys CMV IgM

cobas®

H317	May cause an allergic skin reaction.
Prevention:	
P261	Avoid breathing dust/fume/gas/mist/vapours/spray.
P272	Contaminated work clothing should not be allowed out of the workplace.
P280	Wear protective gloves.
Response:	
P333 + P313	If skin irritation or rash occurs: Get medical advice/attention.
P362 + P364	Take off contaminated clothing and wash it before reuse.
Disposal:	
P501	Dispose of contents/container to an approved waste disposal plant.

Product safety labeling follows EU GHS guidance.

Contact phone: all countries: +49-621-7590

All human material should be considered potentially infectious.

All products derived from human blood (CMVIGM Cal1, CMVIGM Cal2) are prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg and antibodies to HCV and HIV.

The serum containing anti-CMV IgM (CMVIGM Cal2) was sterile filtrated.

The testing methods used assays approved by the FDA or cleared in compliance with the European Directive 98/79/EC, Annex II, List A.

However, as no testing method can rule out the potential risk of infection with absolute certainty, the material should be handled with the same level of care as a patient specimen. In the event of exposure, the directives of the responsible health authorities should be followed.[13,14]

Avoid foam formation in 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.

cobas e 411 analyzer: The calibrators should only be left on the analyzer during calibration at 20-25 °C. After use, close the bottles as soon as possible and store upright at 2-8 °C.

Due to possible evaporation effects, not more than 5 calibration procedures per bottle set should be performed.

cobas e 601 and **cobas e** 602 analyzers: Unless the entire volume is necessary for calibration on the analyzers, transfer aliquots of the reconstituted calibrators into empty snap-cap bottles (CalSet Vials). Attach the supplied labels to these additional bottles. Store the aliquots at 2-8 °C for later use.

Perform **only one** calibration procedure per aliquot.

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

Please note for **cobas e** 602 analyzers: Both the vial labels, and the additional labels (if available) contain 2 different barcodes. Please turn the vial cap 180° into the correct position so that the barcode between the yellow markers can be read by the system. Place the vial on the analyzer as usual.

Storage and stability

Store at 2-8 °C.

Do not freeze.

Store the Elecsys reagent kit **upright** in order to ensure complete availability of the microparticles during automatic mixing prior to use.

Stability of the reagent rackpack	
unopened at 2-8 °C	up to the stated expiration date
after opening at 2-8 °C	12 weeks
on **cobas e**	2 weeks or 6 weeks if stored alternately in the refrigerator and on the analyzers (up to 80 hours on the analyzer)

Stability of the calibrators	
unopened at 2-8 °C	up to the stated expiration date
after opening at 2-8 °C	8 weeks
on **cobas e** 411 at 20-25 °C	up to 5 hours
on **cobas e** 601 and **cobas e** 602 at 20-25 °C	use only once

Store calibrators **upright** in order to prevent the calibrator solution from adhering to the snap-cap.

Specimen collection and preparation

Only the specimens listed below were tested and found acceptable.

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

Li-heparin, Na-heparin, K_2-EDTA, K_3-EDTA, ACD, CPD, CP2D, CPDA and Na-citrate plasma.

Criterion: Mean recovery of serum value: negative samples ± 0.2 COI (cutoff-index); boderline/reactive samples: 80-120 %.

Sampling devices containing liquid anticoagulants have a dilution effect resulting in lower COI values for individual patient specimens.
In order to minimize dilution effects it is essential that respective sampling devices are filled completely according to manufacturer's instructions.

Stable for 4 weeks at 2-8 °C, 7 days at 25 °C, 3 months at -20 °C (± 5 °C). The samples may be frozen 5 times.

The sample types listed were tested with a selection of sample collection tubes or systems 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/collection system manufacturer.

Specimens should not be subsequently altered with additives (biocides, anti-oxidants or substances that could possibly change the pH of the sample) in order to avoid erroneous findings.

Pooled samples and other artificial material may have different effects on different assays and thus may lead to discrepant findings.

Centrifuge samples containing precipitates and frozen samples before performing the assay. Lyophilized samples can be used.

Do not use heat-inactivated samples.

Ensure the samples, calibrators and controls are at 20-25 °C prior to measurement.

Due to possible evaporation effects, samples, calibrators and controls on the analyzers should be analyzed/measured within 2 hours.

The performance of the Elecsys CMV IgM assay has not been established with cadaveric samples or body fluids other than serum and plasma.

Materials provided

See "Reagents – working solutions" section for reagents.

Materials required (but not provided)

- REF 04784626190, PreciControl CMV IgM, 16 x 1.0 mL
- REF 11732277122, Diluent Universal, 2 x 16 mL sample diluent or REF 03183971122, Diluent Universal, 2 x 36 mL sample diluent
- REF 11776576322, CalSet Vials, 2 x 56 empty snap-cap bottles
- General laboratory equipment
- **cobas e** analyzer

Additional materials for the **cobas e** 411 analyzer:

- REF 11662988122, ProCell, 6 x 380 mL system buffer
- REF 11662970122, CleanCell, 6 x 380 mL measuring cell cleaning solution

- REF 11930346122, Elecsys SysWash, 1 x 500 mL washwater additive
- REF 11933159001, Adapter for SysClean
- REF 11706802001, AssayCup, 60 x 60 reaction cups
- REF 11706799001, AssayTip, 30 x 120 pipette tips
- REF 11800507001, Clean-Liner

Additional materials for **cobas e** 601 and **cobas e** 602 analyzers:

- REF 04880340190, ProCell M, 2 x 2 L system buffer
- REF 04880293190, CleanCell M, 2 x 2 L measuring cell cleaning solution
- REF 03023141001, PC/CC-Cups, 12 cups to prewarm ProCell M and CleanCell M before use
- REF 03005712190, ProbeWash M, 12 x 70 mL cleaning solution for run finalization and rinsing during reagent change
- REF 12102137001, AssayTip/AssayCup, 48 magazines x 84 reaction cups or pipette tips, waste bags
- REF 03023150001, WasteLiner, waste bags
- REF 03027651001, SysClean Adapter M

Additional materials for all analyzers:

- REF 11298500316, ISE Cleaning Solution/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's manual for analyzer-specific assay instructions.

Resuspension of the microparticles takes place automatically prior to 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.

Bring the cooled reagents to approximately 20 °C and place on the reagent disk (20 °C) of the analyzer. Avoid foam formation. The system automatically regulates the temperature of the reagents and the opening/closing of the bottles.

Place the calibrators in the sample zone.

All the information necessary for calibrating the assay is automatically read into the analyzer.

After calibration has been performed, store the calibrators at 2-8 °C or discard (**cobas e** 601 and **cobas e** 602 analyzers).

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 CMVIGM Cal1, CMVIGM 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:

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

- 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 PreciControl CMV IgM outside the defined limits
- more frequently when this is required by pertinent regulations

Range for the electrochemiluminescence signals (counts) for the calibrators:
Negative calibrator (CMVIGM Cal1): 500-1600
Positive calibrator (CMVIGM Cal2): 2800-16000

Quality control

For quality control, use PreciControl CMV IgM.

Controls for the various concentration ranges should be run individually at least once every 24 hours when the test is in use, once per reagent kit, and following each calibration.

The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

If necessary, repeat the measurement of the samples concerned.

Follow the applicable government regulations and local guidelines for quality control.

Note: The controls are not barcode-labeled and therefore the controls must run on all instruments as non-Roche controls. The control values and ranges have to be entered manually (except for the **cobas e** 602 analyzer). Please refer to the corresponding section in the operator's manual.

The exact lot-specific target values and ranges are printed on the value sheet which is included in the control kit or reagent kit (or electronically available).

Calculation

The analyzer automatically calculates the cutoff based on the measurement of CMVIGM Cal1 and CMVIGM 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 CMV IgM assay can be interpreted as follows:

Non-reactive: < 0.7 COI

Indeterminate: ≥ 0.7 - < 1.0 COI

Reactive: ≥ 1.0 COI

Samples with a cutoff index < 0.7 are non-reactive in the Elecsys CMV IgM assay.

Samples with a cutoff index between ≥ 0.7 and < 1.0 are considered indeterminate. The sample should be retested. In case the result is still indeterminate, a second sample should be tested e.g. within the following 2-3 weeks.

Samples with a cutoff index ≥ 1.0 are reactive in the Elecsys CMV 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-CMV IgM results in a given specimen, as determined by assays from different manufacturers, can vary due to differences in reagents and assay methods.

Limitations - interference

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

- Individuals at the early stage of acute infection may not exhibit detectable amounts of CMV IgM antibodies. In some of these individuals an indeterminate or low positive result with the Elecsys CMV IgG assay may be found and indicate an early acute infection. A second sample should be tested e.g. within 2 weeks. The detection of CMV IgM and/or a significant increase of the Elecsys CMV IgG antibody titer in the second sample supports the diagnosis of acute CMV infection.[15,16]
- The individual immune response following CMV infection varies considerably.

  In some individuals non-reactive results may occur in the late phase of acute infection by the Elecsys CMV IgM assay.

The detection of IgM antibodies against CMV in a single sample is not sufficient to prove an acute CMV infection. In single cases elevated IgM antibody levels may persist even for years after initial infection. For further clarification additional laboratory tests (e.g. CMV IgG and IgG avidity) or combination of tests should be performed and results should be assessed in conjunction with the patient's medical history and clinical symptoms.

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 ≤ 342 µmol/L or ≤ 20 mg/dL), hemolysis (Hb ≤ 0.310 mmol/L or ≤ 0.500 g/dL), lipemia (Intralipid ≤ 1500 mg/dL) and biotin (≤ 410 nmol/L or ≤ 100 ng/mL).

Criterion: Mean recovery of positive samples within ± 20 % of serum value.

Samples should not be taken from patients receiving therapy with high biotin doses (i.e. > 5 mg/day) until at least 8 hours following the last biotin administration.

No interference was observed from rheumatoid factors up to a concentration of 2000 IU/mL.

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

Sera from patients with primary EBV infections can demonstrate positive results in the Elecsys CMV IgM assay. This is not unexpected as both viruses belong to the herpes virus family and this potential interference is known for CMV IgM assays.[16] As with many µ-capture assays, an interference with unspecific IgM is observed. Increasing amounts of unspecific IgM may lead to a decrease in the recovery of positive samples with the Elecsys CMV IgM assay.

In rare cases, interference due to extremely high titers of antibodies to analyte-specific antibodies, streptavidin or ruthenium can occur. These effects are minimized by suitable test design.

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

Precision was determined using Elecsys reagents, human sera and controls in a protocol (EP5-A2) of the CLSI (Clinical and Laboratory Standards Institute): 2 runs per day in duplicate each for 21 days (n = 84); repeatability n = 21. The following results were obtained:

cobas e 411 analyzer						
	Repeatability			**Intermediate precision**		
Sample	Mean COI	SD COI	CV %	Mean COI	SD COI	CV %
HS[b], negative	0.188	0.004	2.1	0.175	0.004	2.4
HS, low positive	1.52	0.032	2.1	1.62	0.056	3.4
HS, high positive	14.2	0.295	2.1	13.9	0.438	3.2
PC[c] CMV IgM 1	0.185	0.006	3.1	0.171	0.005	2.8
PC CMV IgM 2	2.04	0.052	2.6	1.98	0.103	5.3

b) HS = human serum

c) PC = PreciControl

cobas e 601 and **cobas e** 602 analyzers						
	Repeatability			**Intermediate precision**		
Sample	Mean COI	SD COI	CV %	Mean COI	SD COI	CV %
HS, negative	0.172	0.004	2.0	0.184	0.010	5.2
HS, low positive	1.17	0.027	2.3	1.68	0.082	4.9
HS, high positive	15.0	0.297	2.0	14.0	0.524	3.8
PC CMV IgM 1	0.164	0.003	1.8	0.182	0.010	5.2
PC CMV IgM 2	1.97	0.033	1.7	1.96	0.119	6.1

Analytical specificity

433 potentially cross reacting samples were tested with the Elecsys CMV IgM assay and a comparison CMV IgM assay comprising the following specimens:

- containing antibodies against HBV, HAV, HCV, HIV*, HTLV, EBV**, HSV***, VZV, Parvo B19***, Rubella****, Treponema pallidum, Toxoplasma gondii
- containing autoantibodies***** (ANA, anti-tissue, RF)

* HIV: 8 discordant samples were found out of 70 samples.
** EBV: 13 discordant samples were found out of 48 samples.
*** HSV, Parvo B19: 1 discordant sample was found in each group.
**** Rubella: 2 discordant samples were found.
***** Autoantibodies: 7 discordant samples were found out of 73 samples.

An overall agreement of 92.3 % (381/413) was found in these specimens with the Elecsys CMV IgM assay and the comparison test. 377 samples were found concordantly negative and 4 samples were found positive. 20 samples were found indeterminate either with the Elecsys CMV IgM assay or the comparison test.

Clinical sensitivity

Sensitivity in primary infections

A total of 365 frozen samples from pregnant women with primary CMV infection including sequential and single samples analyzed by commercially available CMV IgM assays were tested with the Elecsys CMV IgM assay at 4 different sites. For calculation of sensitivity confirmed positive samples had a low avidity index or were clinically characterized. Indeterminate samples were counted as positives. Samples with a high avidity index and all discrepant samples or concordant negative samples with a moderate avidity index were excluded.

Site	N	Sensitivity (%)	
		Elecsys CMV IgM assay	Comparison CMV IgM test
1[d]	180	93.0 (106/114)	94.7 (108/114)
2	57	96.5 (55/57)	96.5 (55/57)
3	39[e]	91.2 (31/34)	79.4 (27/34)
	35[f]	93.1 (27/29)	100 (29/29)
4[g]	54	92.3 (48/52)	98.1 (51/52)

d) 66 samples were excluded due to high/moderate avidity.

e) 5 samples were excluded due to moderate avidity and concordant negative results for CMV IgM.

f) 6 samples were excluded due to moderate/high avidity and concordant negative results for CMV IgM.

g) 2 samples were excluded due to moderate avidity and discrepant CMV IgM results.

Specificity in past infection

A total of 158 frozen samples from pregnant women with past CMV infection, analyzed by commercial CMV assays, were tested with the Elecsys CMV IgM assay at 4 different sites. All samples were pre-selected positive for CMV IgG, negative for CMV IgM and a high avidity index showing absence of acute infection.

Relative specificity in past infections

Site	N	Relative specificity (%)	
		Elecsys CMV IgM assay	Comparison CMV IgM test
1[h]	48	98	100
2	30	100	100
3[i]	50	84	86
4	30	100	100

h) 1 sample was found indeterminate with the Elecsys CMV IgM assay and negative with the comparison assay.

i) 8 samples were positive with the Elecsys CMV IgM assay; 7 samples were equivocal with the comparison assay.

Capability to discriminate the persisting IgM after CMV infection

A total of 68 frozen samples from pregnant women analyzed by commercial CMV IgM assays were tested with the Elecsys CMV IgM assay at 3 different sites. All samples were pre-selected positive for CMV IgG and CMV IgM and a high avidity index showing absence of acute infection.

Capability to discriminate the persisting CMV IgM

Site	N	Elecsys CMV IgM assay tested/reactive	Comparison CMV IgM test tested/reactive
1[j]	20	20/6	20/20
2[k]	28	28/4	28/28
3[j]	20	20/7	20/20

j) 14 samples were discrepant negative with the Elecsys CMV IgM assay.

k) 24 samples were discrepant negative with the Elecsys CMV IgM assay.

l) 12 samples were discrepant negative with the Elecsys CMV IgM assay.

Specificity in pre-selected negative samples

A total of 173 frozen samples from pregnant women in which a CMV infection was excluded and analyzed by commercial CMV IgM assays were tested with the Elecsys CMV IgM assay at 4 different sites.

Site	N	Specificity (%)	
		Elecsys CMV IgM assay	Comparison CMV IgM test
1	50	100	100
2[m)]	50	98	100
3[n)]	23	100	95.7
4	50	100	100

m) 1 sample was found positive with the Elecsys CMV IgM assay.

n) 1 sample was found equivocal with the comparison assay.

Clinical specificity

A total of 1646 fresh samples from clinical routine (blood donors, site 1) were tested at 3 different sites (pregnancy testing, site 2 and 3) with the Elecsys CMV IgM assay in comparison to competitor assays. The IgG avidity test was used to resolve discrepant results.

Relative specificity after resolution

Site	N	Relative specificity Elecsys CMV IgM assay %	Lower confidence limit %	Relative specificity Comparison CMV IgM test %	Lower confidence limit %
1[o)]	511	98.8 (495/501)	97.4	96.6 (484/501)	94.6
2[p)]	616	97.1 (574/591)	95.4	93.4 (552/591)	91.1
3[q)]	519	97.0 (492/507)	95.2	92.9 (471/507)	90.3

o) 10 samples were excluded due to moderate avidity or missing avidity result.

p) 10 samples were confirmed positive by low avidity index; 15 samples were excluded due to moderate or missing avidity result.

q) 3 samples were confirmed positive by low avidity index; 9 samples were excluded due to moderate or missing avidity result.

References

1 Cannon MJ, Schmid DS, Hyde TB. Review of cytomegalovirus seroprevalence and demographic characteristics associated with infection. Rev Med Virol 2010;20:202-213.

2 Johnson J, Anderson B, Pass RF. Prevention of maternal and congenital cytomegalovirus infection. Clin Obstet Gynecol 2012;55:521-530.

3 Yinon Y, Farine D, Yudin MH. Screening, diagnosis, and management of cytomegalovirus infection in pregnancy. Obstet Gynecol Surv 2010;65:736-743.

4 Buonsenso D, Serranti D, Gargiullo L, et al. Congenital cytomegalovirus infection: current strategies and future perspectives. Eur Rev Med Pharmacol Sci 2012;16:919-935.

5 Coll O, Benoist G, Ville Y, et al. WAPM Perinatal Infections Working Group. Guidelines on CMV congenital infection. J Perinat Med 2009;37:433-445.

6 Joseph S, Beliveau C, Muecke C, et al. Cytomegalovirus as an occupational risk in daycare educators. Paediatr Child Health 2006;11:401-407.

7 Lazzarotto T, Guerra B, Lanari M, et al. New advances in the diagnosis of congenital cytomegalovirus infection. J Clin Virol 2008;41:192-197.

8 Lombardi G, Garofoli F, Stronati M. Congenital cytomegalovirus infection: treatment, sequelae and follow-up. J Matern Fetal Neonatal Med 2010;23Suppl3:45-48.

9 Elliott SP. Congenital cytomegalovirus infection: an overview. Infect Disord Drug Targets 2011;11:432-436.

10 Lazzarotto T, Guerra B, Gabrielli L, et al. Update on the prevention, diagnosis and management of cytomegalovirus infection during pregnancy. Clin Microbiol Infect 2011;17:1285-1293.

11 Plosa EJ, Esbenshade JC, Fuller MP, et al. Cytomegalovirus infection. Pediatr Rev 2012;33:156-163.

12 Ross SA, Novak Z, Pati S, et al. Overview of the diagnosis of cytomegalovirus infection. Infect Disord Drug Targets 2011;11:466-474.

13 Occupational Safety and Health Standards: Bloodborne pathogens. (29 CFR Part 1910.1030). Fed. Register.

14 Directive 2000/54/EC of the European Parliament and Council of 18 September 2000 on the protection of workers from risks related to exposure to biological agents at work.

15 Revello MG, Gerna G. Diagnosis and Management of Human Cytomegalovirus Infection in the Mother, Fetus, and Newborn Infant. Clin Microbiol Rev 2002;15(4):680-715.

16 Genser B, Truschnik-Wilders M, Stünzner D, et al. Evaluation of Five Commercial Enzyme Immunoassays for the Detection of Human Cytomegalovirus-Specific IgM Antibodies in the Absence of a Commercially Available Gold Standard. Clin Chem Lab Med 2001;39(1): 62-70.

For further information, please refer to the appropriate operator's manual for the analyzer concerned, the respective application sheets and the Method Sheets of all necessary components (if available in your country).

A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see dialog.roche.com for definition of symbols used):

CONTENT	Contents of kit
SYSTEM	Analyzers/Instruments on which reagents can be used
REAGENT	Reagent
CALIBRATOR	Calibrator
→	Volume for reconstitution
GTIN	Global Trade Item Number

CE 0123

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com

Roche