ms_04784596190V8.0

# CMV IgG

**IgG antibodies to Cytomegalovirus**

cobas®

| REF | Σ | SYSTEM |
|---|---|---|
| | | Elecsys 2010 |
| | | MODULAR ANALYTICS E170 |
| **04784596** 190 | 100 | **cobas e** 411 |
| | | **cobas e** 601 |
| | | **cobas e** 602 |

**English**

**Please note**

The measured CMV IgG 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 CMV IgG assay method used.
CMV IgG 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 CMV IgG assay. Results from assays of other manufacturers cannot be used interchangeably."

**Intended use**

Immunoassay for the in vitro quantitative determination of IgG antibodies to cytomegalovirus in human serum and plasma.

Results with this assay are used to indicate past or recent infection with CMV.

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

**Summary**

References[1,2,3,4,5,6]

Cytomegalovirus, 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 as well as recurrent infections. The seroprevalence of antibodies in adults ranges from 40-100 % with inverse correlation to socioeconomic status. Transmission of infection requires intimate contact with infected excretions such as saliva, urine, cervical and vaginal excretions, semen, breast milk and blood.

CMV infections are usually mild and asymptomatic. However, primary maternal CMV infection during pregnancy carries a high risk of intrauterine transmission which may result in severe fetal damage, including growth and mental retardation, jaundice and CNS abnormalities. Those who are asymptomatic at birth may develop hearing defects or learning disabilities later in life. Prenatal CMV infection occurs in approximately 0.2-2.5 % of all life births.

About 10 % of seropositive women have reactivation of CMV during gestation, but the transmission rate to the fetus is about 1 % from non-primary infection compared to 40 % following primary infection. After a primary infection with CMV an individual may undergo reinfection with an exogenous virus or reactivation of latent virus.

At risk for severe CMV disease are also immunocompromised patients such as transplant recipients and HIV infected patients where the virus can cause life-threatening diseases. For these patients seronegative blood products have to be provided. Serologic tests can be used to identify seronegative blood donors and blood products. The determination of CMV IgG antibodies is used to assess the serological status of an individual and is indicative for an acute or past infection.

A first step in diagnosing acute primary CMV infection is most commonly made by the detection of anti-CMV-specific IgG and IgM antibodies. Samples being reactive for IgM antibodies indicate an acute, recent or reactivated infection. For further analysis of a primary CMV infection the determination of the CMV IgG avidity is used as an aid. A positive IgM result in combination with a low avidity index for IgG is a strong indication of a primary CMV infection within the last 4 months. Seroconversion to CMV IgM and IgG also establishes the diagnosis of a recent CMV infection.

**Test principle**

Sandwich principle. Total duration of assay: 18 minutes.

- 1st incubation: 20 µL of sample, biotinylated recombinant CMV-specific antigens, and CMV-specific recombinant antigens labeled with a ruthenium complex[a)] 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/ProCell M. 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 ($Ru(bpy)_3^{2+}$)

**Reagents - working solutions**

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

M Streptavidin-coated microparticles (transparent cap), 1 bottle, 6.5 mL:
Streptavidin-coated microparticles 0.72 mg/mL; preservative.

R1 CMV-Ag~biotin (gray cap), 1 bottle, 9 mL:
Biotinylated CMV-specific antigen (recombinant, E. coli), > 400 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 > 400 µg/L; MES buffer 50 mmol/L, pH 6.5; preservative.

CMVIGG Cal1 Negative calibrator 1 (white cap), 2 bottles of 1.0 mL each:
Human serum, non-reactive for anti-CMV IgG; buffer; preservative.

CMVIGG Cal2 Positive calibrator 2 (black cap), 2 bottles of 1.0 mL each:
Human serum, reactive for anti-CMV IgG, approx. 40 U/mL; 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.

Both calibrators (CMVIGG Cal1, CMVIGG Cal2) have been 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 IgG (CMVIGG Cal2) was sterile filtrated.

The testing methods applied were FDA-approved 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.[7,8]

Avoid foam formation in all reagents and sample types (specimens, calibrators and controls).

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### Reagent handling

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

Elecsys 2010 and **cobas e** 411 analyzers: The calibrators should only be left on the analyzers 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.

MODULAR ANALYTICS E170, **cobas e** 601 and **cobas e** 602 analyzers: 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 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:* Both the vial labels, and the additional labels (if available) contain 2 different barcodes. The barcode between the yellow markers is for **cobas** 8000 systems only. If using a **cobas** 8000 system, please turn the vial cap 180° into the correct position so the barcode can be read by the system. Place the vial on the instrument 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 the analyzers | 3 weeks |

| *Stability of the calibrators* | |
|---|---|
| unopened at 2-8 °C | up to the stated expiration date |
| 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, **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 in a sufficient number and found acceptable.

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

Li-heparin, $K_2$-EDTA and $K_3$-EDTA plasma.

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

Stable for 4 weeks at 2-8 °C, 7 days at 25 °C, 6 months at -20 °C. The samples may be frozen 5 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.

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 and heat-inactivated samples can be used.

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.

### Materials provided

See “Reagents – working solutions” section for reagents.

### Materials required (but not provided)

- REF 04784600190, PreciControl CMV IgG, 8 x 1 mL each of PreciControl CMV IgG 1 and 2
- 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
- Elecsys 2010, MODULAR ANALYTICS E170 or **cobas e** analyzer

Accessories for Elecsys 2010 and **cobas e** 411 analyzers:

- 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, Elecsys 2010 AssayCup, 60 x 60 reaction vessels
- REF 11706799001, Elecsys 2010 AssayTip, 30 x 120 pipette tips

Accessories for MODULAR ANALYTICS E170, **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 Combimagazine M, 48 magazines x 84 reaction vessels or pipette tips, waste bags
- REF 03023150001, WasteLiner, waste bags
- REF 03027651001, SysClean Adapter M

Accessories 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 (MODULAR ANALYTICS E170, **cobas e** 601 and **cobas e** 602 analyzers).

### Calibration

Traceability: This method has been standardized against the internal Roche standard for CMV IgG. No international standard is available for CMV.

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Every Elecsys CMV IgG reagent set has a barcoded label containing specific information for calibration of the particular reagent lot. The predefined master curve is adapted to the analyzer using CMVIGG Cal1 and CMVIGG Cal2.

*Calibration frequency:* Calibration must be performed once per reagent lot using CMVIGG Cal1, CMVIGG 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 PreciControl CMV IgG outside the defined limits
- more frequently when this is required by pertinent regulations

**Quality control**

For quality control, use PreciControl CMV IgG.

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. 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 analyte concentration of each sample in U/mL.

*Interpretation of the results*

Results obtained with the Elecsys CMV IgG assay can be interpreted as follows:

Non-reactive: < 0.5 U/mL

Indeterminate: 0.5-< 1.0 U/mL

Reactive: ≥ 1.0 U/mL

Samples with concentrations < 0.5 U/mL are considered non-reactive in the Elecsys CMV IgG assay. These individuals are considered not to be infected with CMV and therefore susceptible to primary infection.

Samples with concentrations between 0.5 U/mL and < 1.0 U/mL are considered indeterminate. These samples should be retested. In case the result is still indeterminate, a second sample should be collected e.g. within 2 weeks.

Samples with concentrations ≥ 1.0 U/mL are considered positive for IgG antibodies to CMV and indicate either acute or past infection. Such individuals are potentially at risk of transmitting the virus (e.g. mother to fetus) but are at current not necessarily contagious.

For the diagnosis of acute CMV infection further tests have to be performed e.g. the determination of CMV IgM antibodies and the CMV IgG avidity. A positive IgM result in combination with a low avidity index for IgG is a strong indication of a primary CMV infection within the last 4 months.

The diagnosis may be supported by a significant increase of the CMV IgG antibody titer from a first to a second sample taken e.g. within 3-4 weeks.

*Note: An indeterminate or low positive result may already indicate an early acute CMV infection (also if the sample is non-reactive for CMV IgM antibodies).*

The anti-CMV IgG results in a given specimen, as determined by assays from different manufacturers, can vary due to differences in assay and reagent methods. Therefore, the results reported by the laboratory to the physician should include: "The following results were obtained with the Elecsys CMV IgG assay. Results from assays of other manufacturers cannot be used interchangeably."

**Limitations - interference**

A negative test result does not completely rule out the possibility of an infection with CMV. Individuals may not exhibit any detectable IgG antibodies at the early stage of acute infection.

The detection of CMV-specific IgG antibodies in a single sample indicates a previous exposure to CMV but is not always sufficient to distinguish between an acute or latent infection (irrespective of the level of the IgG antibody titer).

In rare cases of primary CMV infection IgG antibody may be present before a specific IgM antibody response is detected. It is recommended that a follow-up sample be tested after 2 weeks. If the CMV IgG antibody titer remains stable, a primary infection can be excluded.[1,9]

Elecsys CMV IgG results should be used in conjunction with the patient's medical history, clinical symptoms and other laboratory tests, e.g. CMV-specific IgM results, CMV IgG avidity results.

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.

Among a panel of 142 positive samples within the measuring range no high-dose hook effect was observed (no increasing signals upon dilution). However, the occurrence of a high-dose hook effect cannot be excluded in other cohorts.

The assay is unaffected by icterus (bilirubin < 1129 µmol/L or < 66 mg/dL), hemolysis (Hb < 0.310 mmol/L or < 0.500 g/dL), lipemia (Intralipid < 2000 mg/dL) and biotin (< 246 nmol/L or < 60 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 1500 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.

In rare cases, interference due to extremely high titers of antibodies to immunological components, 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.

**Limits and ranges**

**Measuring range**

0.25-500 U/mL (defined by the Limit of Detection and the maximum of the master curve). Values below the Limit of Blank are reported as < 0.15 U/mL. Values above the Limit of Blank but below the Limit of Detection will not be flagged by the instrument. Values above the measuring range are reported as > 500 U/mL (or up to 10000 U/mL for 20-fold diluted samples).

**Lower limits of measurement**

*Limit of Blank (LoB) and Limit of Detection (LoD)*

Limit of Blank = 0.15 U/mL

Limit of Detection = 0.25 U/mL

The Limit of Blank and Limit of Detection were determined in accordance with CLSI (Clinical and Laboratory Standards Institute) EP17-A requirements.

The Limit of Blank is the 95$^{th}$ percentile value from n ≥ 60 measurements of analyte-free samples over several independent series. The Limit of Blank corresponds to the concentration below which analyte-free samples are found with a probability of 95 %.

The Limit of Detection is determined based on the Limit of Blank and the standard deviation of low concentration samples. The Limit of Detection corresponds to the lowest analyte concentration which can be detected (value above the Limit of Blank with a probability of 95 %).

# CMV IgG

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### Dilution

Samples with anti-CMV IgG concentrations above the measuring range can be diluted with Diluent Universal. The recommended dilution is 1:20 (either automatically by the MODULAR ANALYTICS E170, Elecsys 2010 and **cobas e** analyzers or manually). The concentration of the diluted sample must be ≥ 15 U/mL.

After manual dilution, multiply the result by the dilution factor.

After dilution by the analyzers, the MODULAR ANALYTICS E170, Elecsys 2010 and **cobas e** software automatically takes the dilution into account when calculating the sample concentration.

Manual dilution can also be made with human serum negative for CMV IgG.

*Note:* Antibodies to CMV are heterogeneous. This may lead to non-linear dilution behavior.

### Expected values

The prevalence of IgG antibodies to CMV varies considerably depending upon geographical location and socioeconomic status of the population studied.

The Elecsys CMV IgG assay was used to test 616 samples from clinical routine in Germany (site 1) and 520 samples from clinical routine in Israel (site 2). Out of these 334 (54.2 %, Germany) and 415 samples (79.8 %, Israel) were found positive or indeterminate with the Elecsys CMV IgG assay.

A distribution of these values is given in the following table:

| U/mL | Site 1, Germany, n = 616 | | Site 2, Israel, n = 520 | |
|---|---|---|---|---|
| | N | % of total | N | % of total |
| < 0.5 | 282 | 45.8 | 105 | 20.2 |
| 0.5-< 1 | 4 | 0.6 | 2 | 0.4 |
| ≥ 1-< 10 | 15 | 2.4 | 2 | 0.4 |
| 10-< 100 | 62 | 10.1 | 71 | 13.7 |
| 100-< 300 | 91 | 14.8 | 114 | 21.9 |
| 300-< 500 | 65 | 10.6 | 84 | 16.2 |
| > 500 | 97 | 15.0 | 142 | 27.3 |

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

### 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-A) of the CLSI (Clinical and Laboratory Standards Institute): 2 runs per day in duplication each for 21 days (n = 84); repeatability n = 21. The following results were obtained:

| Elecsys 2010 and **cobas e** 411 analyzers | | | | | | |
|---|---|---|---|---|---|---|
| | **Repeatability** | | | **Intermediate precision** | | |
| Sample | Mean U/mL | SD U/mL | CV % | Mean U/mL | SD U/mL | CV % |
| HS[b], low positive | 1.07 | 0.009 | 0.8 | 1.17 | 0.038 | 3.3 |
| HS, medium positive | 53.8 | 0.629 | 1.2 | 54.8 | 2.14 | 3.9 |
| HS, high positive | 444 | 7.58 | 1.7 | 437 | 14.3 | 3.3 |
| PC[c] CMV IgG 1 | 1.37 | 0.012 | 0.9 | 1.40 | 0.045 | 3.2 |
| PC CMV IgG 2 | 24.6 | 0.218 | 0.9 | 24.6 | 0.811 | 3.3 |

b) HS = human serum

c) PC = PreciControl

| MODULAR ANALYTICS E170, **cobas e** 601 and **cobas e** 602 analyzers | | | | | | |
|---|---|---|---|---|---|---|
| | **Repeatability** | | | **Intermediate precision** | | |
| Sample | Mean U/mL | SD U/mL | CV % | Mean U/mL | SD U/mL | CV % |
| HS, low positive | 1.10 | 0.015 | 1.3 | 1.14 | 0.045 | 4.0 |
| HS, medium positive | 56.3 | 1.50 | 2.7 | 53.1 | 2.37 | 4.5 |
| HS, high positive | 458 | 3.16 | 0.7 | 460 | 16.2 | 3.5 |
| PC CMV IgG 1 | 1.38 | 0.033 | 2.4 | 1.38 | 0.045 | 3.2 |
| PC CMV IgG 2 | 25.9 | 0.456 | 1.8 | 24.1 | 0.890 | 3.7 |

### Analytical specificity

439 potentially cross reacting samples were tested with the Elecsys CMV IgG assay and a comparison CMV IgG 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)

An overall agreement of 96.6 % (422/437) was found in these specimens with the Elecsys CMV IgG assay and the comparison test. 110 samples were found concordantly negative and 312 samples were found positive. 2 samples were found indeterminate either with the Elecsys CMV IgG assay or the comparison test.

* HSV, HCV: 2 discordant samples were found in each group.

** HBV, EBV, VZV, Treponema pallidum, Toxoplasma gondii: 1 discordant sample was found in each group.

*** Parvo B19, autoantibodies: 3 discordant samples were found in each group.

### Agreement in primary infections

A total of 368 frozen samples from pregnant women (acute, recent and late phase) including sequential and single samples analyzed by commercially available CMV IgG assays were tested with the Elecsys CMV IgG assay at 4 different sites.

Agreement to comparative assays

| Site | N | Agreement[d] % | Concordant reactive | Concordant non-reactive | Discrepant |
|---|---|---|---|---|---|
| 1[e] | 181 | 96.1 | 172 | 2 | 7 |
| 2[f] | 57 | 96.5 | 52 | 3 | 2 |
| 3 | 40[g] | 97.5 | 39 | 0 | 1 |
| | 36[h] | 94.4 | 34 | 0 | 2 |
| 4[i] | 54 | 90.7 | 43 | 6 | 5 |

d) All indeterminate samples counted positive.

e) 6 samples were found discordant positive with the Elecsys CMV IgG assay; 1 sample was found discordant negative with the Elecsys CMV IgG assay.

f) 1 sample was found discordant positive with the Elecsys CMV IgG assay; 1 sample was found discordant negative with the Elecsys CMV IgG assay.

g) 1 sample was found discordant negative with the Elecsys CMV IgG assay.

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

i) 4 samples were found discordant negative with the Elecsys CMV IgG assay; 1 sample was found discordant indeterminate with the Elecsys CMV IgG assay; the comparison assay was negative.

### Agreement in past infection

A total of 158 frozen samples from pregnant women with past CMV infection analyzed by commercially available CMV IgG assays were tested with the Elecsys CMV IgG assay at 4 different sites. A 100 % agreement for the Elecsys CMV IgG assay was found with the competitor assays.

### Agreement in pre-selected negative samples

A total of 162 frozen samples from pregnant women in which a CMV infection was excluded and analyzed by commercially available CMV IgG assays were tested with the Elecsys CMV IgG assay at 4 different sites. In 3 sites a 100 % agreement of the Elecsys CMV IgG assay was found with the competitor assays, whereas at site 4 the Elecsys CMV IgG assay

showed 1 discrepant positive and 1 discrepant indeterminate result (agreement 96 %).

### Method comparison

A total of 1668 fresh samples obtained from clinical routine (blood donors and pregnancy testing) were tested with the Elecsys CMV IgG assay at 3 different sites in comparison to commercially available CMV IgG assays.

Agreement to comparative assays

| Site | N | Agreement[j] % | Concordant reactive | Concordant non-reactive | Discrepant |
|---|---|---|---|---|---|
| 1[k] | 532 | 98.9 | 206 | 320 | 6 |
| 2[l] | 616 | 96.8 | 316 | 279 | 21 |
| 3[m] | 520 | 99.4 | 413 | 103 | 4 |

j) All indeterminate samples counted positive.

k) 4 samples were found indeterminate with the Elecsys CMV IgG assay and negative with the comparison assay; 2 samples were found discrepant negative with the Elecsys CMV IgG assay.

l) 13 samples were found discrepant positive with the Elecsys CMV IgG assay; 4 samples were found indeterminate with the Elecsys CMV IgG assay and negative with the comparison assay; 2 samples were found discrepant negative with the Elecsys CMV IgG assay; 1 sample was found negative with the Elecsys CMV IgG assay and indeterminate with the comparison assay; 1 sample was found positive with the Elecsys CMV IgG assay and indeterminate with the comparison assay.

m) 1 sample was found indeterminate with the Elecsys CMV IgG assay and negative with the comparison assay; 2 samples were found discrepant negative with the Elecsys CMV IgG assay; 1 sample was found indeterminate with the Elecsys CMV IgG assay and positive with the comparison assay.

### References

1 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.

2 Munro SC, Hall B, Whybin LR, et al. Diagnosis of and Screening for Cytomegalovirus Infection in Pregnant Women. J Clin Microbiol 2005;43(9):4713-4718.

3 Lazzarotto T, Gabrielli L, Lanari M, et al. Congenital Cytomegalovirus Infection: Recent Advances in the Diagnosis of Maternal Infection. Hum Immunol 2004;65:410-415.

4 Guerra B, Simonazzi G, Banfi A, et al. Impact of diagnostic and confirmatory tests and prenatal counseling on the rate of pregnancy termination among women with positive cytomegalovirus immunoglobulin M antibody titers. Am J Obstet Gynecol 2007;196:221-223.

5 Duff P. A thoughtful algorithm for the accurate diagnosis of primary CMV infection in pregnancy. Am J Obstet Gynecol 2007;196:196-197.

6 Ljungman P. Risk of cytomegalovirus transmission by blood products to immunocompromised patients and means for reduction. Brit J Haematol 2004;125:107-116.

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

8 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.

9 Weber B, Fall EM, Berger A, et al. Screening of blood donors for human cytomegalovirus (HCMV) IgG antibody with an enzyme immunoassay using recombinant antigens. J Clin Virol 1999;14:173-181.

For further information, please refer to the appropriate operator's manual for the analyzer concerned, the respective application sheets, the product information 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.

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



CE 0123

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