# Elecsys CMV IgG Avidity

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| REF | | Σ | SYSTEM |
|---|---|---|---|
| 07027095119 | 07027095500 | 100; equals to 50 CMV IgG avidity determinations | cobase801 |

English

System information

| Short name | Assay type | To be used for |
|---|---|---|
| CMVAVI | cobas e flow | samples with unknown Elecsys CMV IgG titer |
| CMVAVI H | cobas e flow | samples with Elecsys CMV IgG titer > 500 U/mL |
| CMVAVI L | cobas e flow | samples with Elecsys CMV IgG titer ≤ 500 U/mL |

Intended use

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

The electrochemiluminescence immunoassay "ECLIA" is intended for use on the cobas e 801 immunoassay analyzer.

Note: Please note that the catalogue number appearing on the package Insert retains only the first 8 digits of the licensed 11-digit Catalogue Number: 07027095190 for the CMV IgG Avidity Assay. The last 3-digit-190 have been replaced by -119 for logistic purpose.

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.[2,3,4,5,7]

During pregnancy, CMV can cause congenital infection which may result in permanent physical and/or neurological sequelae in 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, as they are likely to 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. During latency, CMV resides in infected cells and the 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]

The CMV IgG avidity assay measures the functional binding affinity of CMV IgG antibodies in response to infection. The antibodies produced during the primary response have lower antigen avidity than the antibodies produced later on.[2,5,10] Low avidity is encountered approximately up to 18-20 weeks after onset of symptoms in immunocompetent subjects.[5,10] However, individual variation does exist in the rate of avidity maturation. In rare cases low avidity results can be observed up to 6 months or even longer after the onset of infection. The avidity testing should be performed early in gestation. Low avidity CMV IgG antibodies detected before the 16$^{th}$-18$^{th}$ week of pregnancy in combination with positive CMV IgM result is a strong evidence for recent primary infection.[3,5,10] A high avidity result later after gestation (after 20th week of gestation) cannot rule out a primary infection earlier in gestation when low avidity CMV IgG may have been present.[3] A high avidity index during the first 12-16 weeks of pregnancy can be considered indicative of past infection.[3,5,7,10]

Test principle

The test principle is based on two parallel measurements that are implemented into a cobas e flow (see also section "cobas e flows").

The first measurement is a standard CMV IgG determination. For the second measurement, the sample is treated with the CMV IgG Avidity Pretreatment (CMVAV PT) prior to the immunoreaction. The CMVAV PT contains components which interfere with the binding of low avidity CMV IgG antibodies.

The avidity (%) of the CMV specific antibodies is automatically assessed by determining the ratio of both measurements.

The Elecsys CMV IgG Avidity assay uses the sandwich principle. Total duration of assay is 18 minutes for both reference measurement and CMVAV PT treated measurement.

- 1st incubation: 12 µL of sample (or pretreated sample, respectively), biotinylated recombinant CMV specific antigens, and CMV-specific recombinant antigens labeled with a ruthenium complex[a)] form a sandwich complex. In case of the CMVAV PT treated measurement, only high avidity CMV antibodies are able to build up the sandwich complex, while the complex with low avidity CMV antibodies is dissolved.
- 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 II 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 cobas link.

a) Tris(2,2'-bipyridyl)ruthenium(II)-complex ($Ru(bpy)_3^{2+}$)

Reagents - working solutions

The cobas e pack (M, R1, R2) and the pretreatment reagent (PT) are labeled as CMVAV.

M Streptavidin-coated microparticles, 1 bottle, 6.4 mL:
Streptavidin-coated microparticles 0.72 mg/mL; preservative.

R1 CMV-Ag~biotin, 1 bottle, 9.5 mL:
Biotinylated CMV- specific antigen (recombinant, E. coli), > 400µg/L
2- (N- morpholino)ethanesulfonic acid (MES) buffer 50 mmol/L, pH 6.5; preservative.

R2 CMV-Ag~ $Ru(bpy)_3^{2+}$, 1 bottle, 9.5 mL:
CMV−specific antigen (recombinant, E. coli) labeled with ruthenium complex > 400 µg/L; MES buffer 50 mmol/L, pH 6.5; preservative.

PT CMV Avidity pretreatment, 1 bottle, 5.5 mL:
0.8 M Guanidine chloride, CMV- specific antigen (recombinant, E. coli); MES buffer 50 mmol/L, pH 6.5; preservative.

# Elecsys CMV IgG Avidity

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

CMVAV Cal2 Positive calibrator 2 (black cap), 2 bottles of 1.0 mL each: Human serum, reactive for anti-CMV IgG, approximately 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.

The calibrators (CMVAV Cal1, CMVAV 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 (CMVAV 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 (M, R1, R2, PT) in the kit are ready-for-use and are supplied in **cobas e** packs.

*Calibrators*

The calibrators are supplied ready-for-use in bottles compatible with the system.

Unless the entire volume is necessary for calibration on the analyzer, 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 available via the **cobas** link.

**Storage and stability**

Store at 2-8 °C.

Do not freeze.

Store the **cobas e** pack **upright** in order to ensure complete availability of the microparticles during automatic mixing prior to use.

| Stability of the **cobas e** pack and the pretreatment reagent: | |
|---|---|
| unopened at 2-8 °C | up to the stated expiration date |
| on the **cobas e** 801 analyzer | 16 weeks |

| Stability of the calibrators: | |
|---|---|
| unopened at 2-8 °C | up to the stated expiration date |
| after opening at 2-8 °C | up to 8 weeks |
| on the **cobas e** 801 analyzer 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, $K_2$-EDTA and $K_3$-EDTA plasma.

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

Stable for 7 days at 20-25 °C, 4 weeks at 2-8 °C, 6 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 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 thawed samples before performing the assay. Lyophilized samples and heat-inactivated samples can be used.

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

Due to possible evaporation effects, samples and calibrators 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, 16 x 1.0 mL
- REF 05942322190, PreciControl CMV IgG Avidity, for 6 x 1.0 mL
- REF 11776576322, CalSet Vials, 2 x 56 empty snap-cap bottles
- REF 07299001190, Diluent Universal, 45.2 mL sample diluent
- General laboratory equipment
- **cobas e** 801 analyzer

Accessories for the **cobas e** 801 analyzer:

- REF 06908799190, ProCell II M, 2 x 2 L system solution
- REF 04880293190, CleanCell M, 2 x 2 L measuring cell cleaning solution
- REF 07485409001, Reservoir Cups, 8 cups to supply ProCell II M and CleanCell M
- REF 06908853190, PreClean II M, 2 x 2 L wash solution
- REF 05694302001, Assay Tip/Assay Cup tray, 6 magazines x 6 magazine stacks x 105 assay tips and 105 assay cups, 3 wasteliners
- REF 07485425001, Liquid Flow Cleaning Cup, 2 adaptor cups to supply ISE Cleaning Solution/Elecsys SysClean for Liquid Flow Cleaning Detection Unit
- REF 07485433001, PreWash Liquid Flow Cleaning Cup, 1 adaptor cup to supply ISE Cleaning Solution/Elecsys SysClean for Liquid Flow Cleaning PreWash Unit
- 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.

Place the cooled (stored at 2-8 °C) **cobas e** pack on the reagent manager. Avoid foam formation. The system automatically regulates the temperature of the reagents and the opening/closing of the **cobas e** pack.

*Calibrators:*

Place the calibrators in the sample zone.

Read in all the information necessary for calibrating the assay.

**Calibration**

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

The predefined master curve is adapted to the analyzer using CMVAV Cal1 and CMVAV Cal2.

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

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

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Renewed calibration is recommended as follows:

- after 12 weeks when using the same reagent lot
- after 28 days when using the same **cobas e** pack on the analyzer
- as required: e.g. quality control findings outside the defined limits

**Quality control**

For quality control, use PreciControl CMV IgG and PreciControl CMV IgG Avidity.

Controls for the various concentration ranges should be run individually at least once every 24 hours when the test is in use, once per **cobas e** pack, 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.

**Calculation**

The CMV IgG Avidity **cobas e** flow automatically calculates the avidity of CMV specific IgG antibodies in the sample. The CMV IgG avidity of the sample is shown as the main result of the **cobas e** flow (Avidity ratio in %) together with its qualitative interpretation (Avidity low/grey-zone/high). Additionally, the CMV IgG titer (U/mL) of the sample and the corresponding qualitative interpretation (non-reactive/borderline/reactive) are shown as a subresult.

Main result and subresult contents are also uploaded to the Laboratory Information System (LIS).
Note: CMV IgG avidity (%) can only be determined for CMV IgG reactive samples (≥ 1.0 U/mL).

**Interpretation of the results**

Results obtained with the Elecsys CMV IgG Avidity assay are interpreted as follows:

| Numeric result | Result message | Further action |
|---|---|---|
| < 45.0 % | Avidity low | None |
| 45.0-54.9 % | Avidity gray-zone | No clinical interpretation can be deduced from a gray-zone result. It is recommended to take a follow-up sample within an appropriate period of time (e.g. 2-4 weeks) and repeat testing. |
| ≥ 55.0 % | Avidity high | None |
| - | No avidity calculation possible | Depending on the subresult, retesting with a different **cobas e** flow might be recommended (see table below). |

Recommendations in case of the result message "No avidity calculation possible":

| Subresult | Used cobas e flow | Further action |
|---|---|---|
| CMV IgG < 1 U/mL or "below measuring range" | **CMVAVI** or **CMVAVI L** | None, CMV IgG titer too low for avidity determination. |
| CMV IgG "below measuring range" | **CMVAVI H** | Repeat avidity determination with **cobas e** flow "CMVAVI L" or "CMVAVI". |
| CMV IgG "above measuring range" | **CMVAVI** or **CMVAVI H** | None, sample exceeds the extended measuring range of the assay, no avidity determination possible. |
| CMV IgG "above measuring range" | **CMVAVI L** | Repeat avidity determination with **cobas e** flow "CMVAVI H". |

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

In case of a CMV IgG avidity result discordant to the patient's medical history, clinical symptoms and other laboratory tests, e.g. CMV-specific IgG and IgM results, further tests should be performed to verify the result and testing of a follow up sample is recommended.

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

**cobas e flows**

**cobas e** flows are procedures to enable a fully automated sequence of measurements and the calculation of assay combinations to perform decision algorithms.

The following **cobas e** flows are available to perform the CMV IgG Avidity assay:

| cobas e flow | Function |
|---|---|
| CMVAVI | **cobas e** flow "CMV IgG Avidity-all titer" performs a fully automated CMV IgG Avidity determination comprising the complete Elecsys measuring range for CMV IgG antibodies of 0.25-10000 U/mL; triggers the automated dilution and re-run of the diluted sample if the sample initially exceeded a CMV IgG reactivity of 500 U/mL (= upper limit of the standard measuring range). Preferentially to be used if the CMV IgG titer of the sample is unknown or was not determined with the Elecsys CMV IgG assay. |
| CMVAVI L | **cobas e** flow "CMV IgG Avidity-low titer" performs a fully automated CMV IgG Avidity determination comprising the standard measuring range for CMV IgG antibodies of 0.25-500 U/mL; samples with Elecsys CMV IgG titers > 500 U/mL are not processed any further. Preferentially to be used if the CMV IgG titer of the sample is known to be in the standard measuring range of the Elecsys CMV IgG assay. |
| CMVAVI H | **cobas e** flow "CMV IgG Avidity-high titer" performs a fully automated CMV IgG Avidity determination exclusively comprising the extended measuring range for CMV IgG antibodies of 500-10000 U/mL; samples with Elecsys CMV IgG titers < 500 U/mL cannot be analyzed. Preferentially to be used if the CMV IgG titer of the sample is known to be in the extended measuring range of the Elecsys CMV IgG assay. |

**Note:** For CMVAVI and CMVAVI H provide Diluent Universal on the analyzer to enable automated pre-dilution of the sample.

**Limitations - interference**

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.

There is no high-dose hook effect at CMV IgG concentrations up to 2500 U/mL.

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The effect of the following endogenous substances and pharmaceutical compounds on assay performance was tested. Interferences were tested up to the listed concentrations and no impact on results was observed.

*Endogenous substances*

| Compound | Concentration tested |
|---|---|
| Bilirubin | ≤ 1129 µmol/L or ≤ 66 mg/dL |
| Hemoglobin | ≤ 0.310 mmol/L or ≤ 500 mg/dL |
| Intralipid | ≤ 2000 mg/dL |
| Biotin | ≤ 368 nmol/L or ≤ 90 ng/mL |
| Rheumatoid factors | ≤ 1500 IU/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.

*Pharmaceutical substances*
In vitro tests were performed on 16 commonly used pharmaceuticals. No interference with the assay was found.

In addition, the following special anti-viral drugs were tested. No interference with the assay was found.

*Special anti-viral drugs*

| Drug | Concentration tested |
|---|---|
| Ganciclovir | ≤ 800 mg/L |
| Valganciclovir | ≤ 900 mg/L |

In rare cases, interference due to extremely high titers of antibodies to 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 CMV IgG (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 CMV IgG on the subresult level. 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 CMV IgG on the subresult level.

An extended measuring range of 500-10000 U/mL CMV IgG applies to measurements of samples that were pre-diluted with Diluent Universal (see section "Dilution").

*Limit of Blank and Limit of Detection*

Limit of Blank = 0.15 U/mL CMV IgG

Limit of Detection = 0.25 U/mL CMV IgG

The Limit of Blank and Limit of Detection were determined in accordance with CLSI (Clinical and Laboratory Standards Institute) EP17-A2 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 %).

**Dilution**

Samples with CMV IgG concentrations above the standard measuring range of the assay (> 500 U/mL) should be analyzed again with a CMV IgG Avidity **cobas e** flow that supports the extended measuring range (i.e. "CMVAVI" or "CMVAVI H"). In these **cobas e** flows, the sample is automatically pre-diluted in a 1:20 ratio with Diluent Universal. Please make sure to provide Diluent Universal on the analyzer if running CMVAVI or CMVAVI H.

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

**Specific performance data**

Representative performance data on the analyzer is given below. Results obtained in individual laboratories may differ.

**Precision**

Precision was determined using Elecsys reagents, samples and controls in a protocol (EP05-A3) of the CLSI (Clinical and Laboratory Standards Institute): 2 runs per day in duplicate each for 21 days (n = 84). The following results were obtained:

| **cobas e** 801 analyzer | | | | | | |
|---|---|---|---|---|---|---|
| | **Repeatability** | | | **Intermediate precision** | | |
| Sample | Mean Avi% | SD Avi% | CV % | Mean Avi% | SD Avi% | CV % |
| HSP[b)] 1, low avidity | 6.52 | 0.324 | 5.0 | 6.52 | 0.392 | 6.0 |
| HSP 2, gray-zone | 49.6 | 0.770 | 1.6 | 49.6 | 0.808 | 1.6 |
| HSP 3, high avidity | 94.8 | 1.37 | 1.4 | 94.8 | 1.37 | 1.4 |
| PC[c)] CMV IgG Avidity 1 | 24.0 | 0.477 | 2.0 | 24.0 | 0.523 | 2.2 |
| PC CMV IgG Avidity 2 | 87.2 | 1.50 | 1.7 | 87.2 | 1.61 | 1.8 |

b) HSP = human specimen (serum/plasma)

c) PC = PreciControl

**Analytical specificity**

439 potentially cross reacting samples were tested with the Elecsys CMV IgG assay (which equals to the Elecsys CMV IgG Avidity reference measurement) 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 Avidity reference measurement 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.

**Sensitivity**

*Sensitivity (concordance of low avidity results with primary infections):*

The sensitivity of the CMV IgG avidity assay is defined as the percentage of samples of CMV primary infections (characterized by reference laboratories) detected to contain low avidity CMV IgG antibodies.

Overall 183 single and sequential samples collected by reference laboratories and characterized (based on diagnostic testing and if available, clinical indications) to be from primary CMV infections were investigated. 31 samples showed a gray-zone result and were excluded from calculation.

| Sample type | Sensitivity % | Lower 95 % confidence limit % | Upper 95 % confidence limit % |
|---|---|---|---|
| Diagnostic | 96.1 (74/77) | 89.0 | 99.2 |
| Pregnant women | 93.4 (99/106) | 86.9 | 97.3 |
| Total | 94.5 (173/183) | 90.2 | 97.4 |

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*Relative sensitivity (concordance of low avidity results to a commercial CMV IgG avidity assays):*

Single specimens from randomly selected blood donor samples with CMV IgG seroconversion from the previous to the actual donation and characterized to contain CMV IgG low avidity antibodies with a commercial CMV IgG avidity assays were investigated. In 23 samples out of 26 samples low avidity CMV IgG antibodies were detected. 1 sample showed a gray-zone result.

**Specificity**

*Specificity (concordance of high avidity results with late infections):*

The specificity of the CMV IgG avidity assay is defined as the percentage of samples of CMV late infections (characterized by reference laboratories) detected to contain high avidity CMV IgG antibodies.

A total of 95 single samples collected by a reference laboratory and characterized (based on diagnostic testing) to be from late CMV infections were investigated.

12 samples showed a gray-zone result and were excluded from calculation.

| Sample type | Specificity % | Lower 95 % confidence limit % | Upper 95 % confidence limit % |
|---|---|---|---|
| Diagnostic | 90.9 (40/44) | 78.3 | 97.5 |
| Pregnant women | 100 (51/51) | 93.0 | 100 |
| Total | 95.8 (91/95) | 89.6 | 98.8 |

*Relative specificity (concordance of high avidity results in CMV IgG reactive, CMV IgM non-reactive samples indicating the absence of a primary infection):*

A total of 375 samples from blood donor testing and pregnancy screening (calculated from CMV IgG reactive, CMV IgM non-reactive samples with a concordant high avidity results in a comparison methods indicating the absence of a primary infection) were investigated. 24 samples showed a gray-zone result and were excluded from calculation.

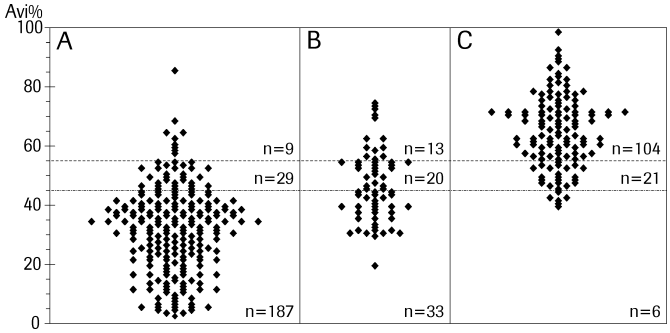
| Sample type | Relative specificity % | Lower 95 % confidence limit % | Upper 95 % confidence limit % |
|---|---|---|---|
| Blood donors | 97.9 (137/140) | 93.9 | 99.6 |
| Pregnant women | 100 (235/235) | 98.4 | 100 |
| Total | 99.2 (372/375) | 97.7 | 99.8 |

**Distribution of avidity**

The ability to discriminate between acute and late CMV infection is shown with 422 single and sequential samples collected by reference laboratories and classified into one of the following categories:

- Category A: < 90 days after presumed onset of infection or date of first bleed (single and sequential samples of patients initially suffering from a CMV primary infection); n = 225 samples
- Category B: 90-180 days after presumed onset of infection or date of first bleed (single and sequential samples of patients initially suffering from a CMV primary infection); n = 66 samples
- Category C: > 180 days after presumed onset of infection or date of first bleed (single and sequential samples of patients initially suffering from a CMV primary infection); n = 131 samples

The exact distribution of low avidity, gray-zone and high avidity results is given in the following diagram:

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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.


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 (for USA: see https://usdiagnostics.roche.com for definition of symbols used):

| | |
|---|---|
| CONTENT | Contents of kit |
| SYSTEM | Analyzers/Instruments on which reagents can be used |
| REAGENT | Reagent |

# Elecsys CMV IgG Avidity

cobas®

| | |
|---|---|
| CALIBRATOR | Calibrator |
| → | Volume after reconstitution or mixing |
| GTIN | Global Trade Item Number |



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