

MAGLUMI CMV IgM (CLIA)



130212006M



100



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FOR PROFESSIONAL USE ONLY
Store at 2...8 °C



**COMPLETELY READ THE INSTRUCTIONS BEFORE
PROCEEDING**



SYMBOLS EXPLANATIONS



Authorized Representative in Europe



Manufacturer



Attention. See Instructions For Use



Contents of kit



In vitro diagnostic medical device
(In vitro diagnostic use)



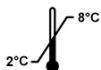
Lot number



Catalogue Code



Expiry date (Use by...)



Temperature limitation
(store at 2...8 °C)



Number of tests



Keep away from sunlight



Keep upright

INTENDED USE

The kit has been designed for the qualitative determination of CMV IgM in human serum.

The method can be used for samples over the range of 0-30 AU/ml.

The test has to be performed on the MAGLUMI chemiluminescence immunoassay (CLIA) fully auto analyzer (Including MAGLUMI 1000, MAGLUMI 2000, MAGLUMI 2000 Plus and new developed models).

SUMMARY AND EXPLANATION OF THE TEST

Human cytomegalovirus (hCMV) is a member of the Herpesviridae family and is one of the human herpesviruses pathogenic for man. It is ubiquitous, species-specific and is spread by close human contact. The viral capsid, which has a DNA core, is icosahedral in shape and is formed of 162 capsomers. One or more oval membranes containing lipids surround the capsid.

hCMV infection can be primary or secondary. Primary infection may be acquired through different transmission routes and in different periods of life (i.e., congenital and post-natal infections). Following primary infection, hCMV enters a latency phase during which the virus can be found in B lymphocytes. Subsequent reactivation of viral replication (secondary infection) may take place concomitantly with changes in the relationship between host and virus, such as pregnancy, serious illness, immunosuppressive therapy or stress.

Congenital infection is transmitted transplacentally or at birth and can occur even if pregnant women already present antibodies to hCMV (re-infection with exogenous virus). If seronegative women contract primary hCMV infection during pregnancy, sequelae may be abortion, stillbirth or neonatal malformation. This is the case even if the birth of a normal child is possible in almost 50% of maternal infections. The clinical picture of congenital hCMV infection is always severe and includes psychomotor retardation, deafness, retinochoroiditis, microcephaly, hydrocephalus, cardiac disease, hepatitis, hepatosplenomegaly, thrombocytopenia. The mortality rate is quite high.

Most individuals (40-90%) acquire primary hCMV infection during childhood or adulthood. Post-natal infections are transmitted through close contact with infected biological fluids (urine, saliva, breast milk, semen, cervical secretions, faeces), infected blood products and, occasionally, organ transplants. In immunocompetent individuals, the clinical picture of postnatal hCMV infection is usually mild or asymptomatic. The commonest signs include fever, malaise, and increased serum transaminase levels without jaundice.

By contrast in immunocompromized patients (organ transplant recipients, patients with AIDS, lymphoproliferative diseases or cancer), symptoms may be severe because of disseminated and/or visceral infection, and include splenomegaly, pneumonia, haemolytic anemia, myocarditis and encephalitis. In these patients the disease may be fatal.

The immune response to hCMV involves synthesis of IgM antibodies some weeks after infection by hCMV and, one week later, of IgG antibodies. Levels of IgM to hCMV usually increase for some weeks and decrease slowly thereafter, in four to six months. Occasionally, IgM may circulate for years.

Specific IgM assay is instrumental in diagnosing acute hCMV infection, which remains difficult to identify from symptoms alone. However, it is not always possible to distinguish between primary and secondary infection, because reactivation may induce synthesis of IgM in immunocompromized patients.

Specific IgG assay is useful in distinguishing subjects who have acquired the disease from those who have not. This is particularly important in order to adopt suitable prophylaxis in susceptible individuals.

Determination of immune status to hCMV is of particular importance. (a) In immunocompromised patients, in whom the disease may have serious consequences; (b) in young fertile or pregnant women, so as to avoid virus transmission to the foetus; (c) in organ transplant recipients and donors and (d) in blood donors. White blood cells, namely polymorphonuclear leucocytes, may carry hCMV which may infect blood or organ recipients.

Detection of IgM to hCMV allows adequate treatment to be administered, as needed. Prophylaxis of hCMV infection may be achieved by administration of high-titered virus-specific immunoglobulin preparations. In addition, overt disease may be treated with specific antiviral agents.

PRINCIPLE OF THE TEST

Indirect immunoluminometric assay;

Mouse anti-human IgM is used to label ABEI, and use purified CMV antigen to coat nano magnetic microbeads. Sample, Calibrator or Control with Buffer and nano magnetic microbeads coated with CMV antigen are mixed thoroughly and incubated at 37°C, forming a sandwich; After sediment in a magnetic field, decant the supernatant, then cycle washing for 1 time. Then add ABEI Label, incubation and washing for the 2nd time. Subsequently, the starter reagents are added and a flash chemiluminescent reaction is initiated. The light signal is measured by a photomultiplier as RLU within 3 seconds and is proportional to the concentration of CMV IgM present in controls or samples.

CONT

KIT COMPONENTS

Material Supplies

Reagent Integral for 100 determinations	
Nano magnetic microbeads: TRIS buffer, 1.2% (W/V), 0.2%NaN ₃ , coated with CMV antigen.	2.5ml
Calibrator Low: bovine serum, 0.2%NaN ₃ .	2.5ml
Calibrator High: bovine serum, 0.2%NaN ₃	2.5ml
Buffer: Goat anti-Human IgA 1.2%(W/V), Goat anti-Human IgG, 0.2%NaN ₃ , BSA	12.5ml
ABEI Label: Mouse anti-human IgM labeled ABEI contains BSA, 0.2%NaN ₃ .	22.5ml
Diluent: Goat anti-Human IgA 1.2%(W/V), Goat anti-Human IgG, 0.2%NaN ₃ , BSA	25ml
All reagents are provided ready-to-use.	

Please prepare 0.9% sodium chloride solution in case of insufficient diluents.

Reagent Vials in kit box	
Internal Quality Control: containing BSA, 0.2%NaN ₃ . (target value refer to Quality Control Information date sheet)	2.0ml

Accessories Required But Not Provided

MAGLUMI Reaction Module	REF: 630003
MAGLUMI Starter 1+2	REF: 130299004M
MAGLUMI Wash Concentrate	REF: 130299005M
MAGLUMI Light Check	REF: 130299006M



Preparation of the Reagent Integral

Before the sealing is removed, gentle and careful horizontal shaking of the Reagent Integral is essential (avoid foam formation!) Remove the sealing and turn the small wheel of the magnetic microbeads compartment to and fro, until the colour of the 081120521-v1.0-EN

suspension has changed into brown. Place the Integral into the reagent area and let it stand there for 30 min. During this time, the magnetic microbeads are automatically agitated and completely resuspended.

Do not interchange integral component from different reagents or lots!

Storage and Stability

- Sealed: Stored at 2-8°C until the expiry date.
- Opened: Stable for 4 weeks. To ensure the best kit performance, it is recommended to place opened kits in the refrigerator if it's not going to be used on board during the next 12 hours.



- Keep upright for storage.



- Keep away from direct sunlight.

CALIBRATION AND TRACEABILITY

Traceability

To perform an accurate calibration, we have provided the test calibrators standardized against the SNIBE internal reference substance.

Calibrators in the Reagent Kit are from Fitzgerald.

2) 2-Point Recalibration

Via the measurement of calibrators, the predefined master curve is adjusted (recalibrated) to a new, instrument-specific measurement level with each calibration.

3) Frequency of Recalibration

- After each exchange of lot (Reagent Integral or Starter Reagents).
- Every 4 weeks and/or each time a new Integral is used (recommendation).
- After each servicing of the MAGLUMI Fully Auto analyzer.
- If controls are beyond the expected range.

SPECIMEN COLLECTION AND PREPARATION

Sample material: serum

Collect 5.0ml venous blood into Blood Collection Tube (Tube without anticoagulant or coagulant, Anticoagulation tube with EDTA-K₂ or EDTA-Na₄ can be used. Anticoagulation tube with heparin sodium is not recommended). Centrifuge and gain serum. Store at 2-8°C: 24 hours, for longer storage periods: freeze to below -20°C

Avoid repeated freezing and thawing cycles, stored samples should be thoroughly mixed prior to use (Vortex mixer).

Please ask local representative of SNIBE for more details if you have any doubt.

Vacuum Tubes

- Blank tubes are recommended type for collecting samples.
- Please ask SNIBE for advice if special additive must be used in sample collecting.

Specimen Conditions

- Do not use specimens with the following conditions:
 - heat-inactivated specimens;
 - Cadaver specimens or body fluids other than human serum;
 - Obvious microbial contamination.
- Use caution when handling patient specimens to prevent cross contamination. Use of disposable pipettes or pipette tips is recommended.
- Inspect all samples for bubbles. Remove bubbles with an applicator stick prior to analysis. Use a new applicator stick for each sample to prevent cross contamination.

- Serum specimens should be free of fibrin, red blood cells or other particulate matter.
- Ensure that complete clot formation in serum specimens has taken place prior to centrifugation. Some specimens, especially those from patients receiving anticoagulant or thrombolytic therapy, may exhibit increased clotting time. If the specimen is centrifuged before a complete clot forms, the presence of fibrin may cause erroneous results.

Preparation for Analysis

- Patient specimens with a cloudy or turbid appearance must be centrifuged prior to testing. Following centrifugation, avoid the lipid layer (if present) when pipetting the specimen into a sample cup or secondary tube.
- Specimens must be mixed **thoroughly** after thawing by **low** speed vortexing or by gently inverting, and centrifuged prior to use to remove red blood cells or particulate matter to ensure consistency in the results. Multiple freeze-thaw cycles of specimens should be avoided.
- All samples (patient specimens or controls) should be tested within 3 hours of being placed on board the MAGLUMI System. Refer to the SNIBE service for a more detailed discussion of onboard sample storage constraints.

Storage

- If testing will be delayed for more than 8 hours, remove serum from the serum separator, red blood cells or clot. Specimens removed from the separator gel, cells or clot may be stored up to 24 hours at 2-8°C.
- Specimens can be stored up to 30 days frozen at -20°C or colder.

Shipping

- Before shipping specimens, it is recommended that specimens be removed from the serum or plasma separator, red blood cells or clot. When shipped, specimens must be packaged and labeled in compliance with applicable state, federal and international regulations covering the transport of clinical specimens and infectious substances. Specimens must be shipped frozen (dry ice). Do not exceed the storage time limitations identified in this section of the package insert.

WARNING AND PRECAUTIONS FOR USERS



- For use in *IN-VITRO* diagnostic procedures only.
- Package insert instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

Safety Precautions

CAUTION: This product requires the handling of human specimens.

- The calibrators in this kit are prepared from bovine serum products. However, because no test method can offer complete assurance that HIV, Hepatitis B Virus or other infectious agents are absent; these reagents should be considered a potential biohazard and handled with the same precautions as applied to any serum or plasma specimen.
- All samples, biological reagents and materials used in the assay must be considered potentially able to transmit infectious agents. They should therefore be disposed of in accordance with the prevailing regulations and guidelines of the agencies holding jurisdiction over the laboratory, and the regulations of each country. Disposable materials must be incinerated; liquid waste must be decontaminated with sodium hypochlorite at a final concentration of 5% for at least half an hour. Any materials to be reused must be

autoclaved using an overkill approach (USP 24, 2000, p.2143). A minimum of one hour at 121 °C is usually considered adequate, though the users must check the effectiveness of their decontamination cycle by initially validating it and routinely using biological indicators.

- It is recommended that all human sourced materials be considered potentially infectious and handled in accordance with the OSHA Standard on Bloodborne Pathogens 13. Biosafety Level 214 or other appropriate biosafety practices should be used for materials that contain or are suspected of containing infectious agents.
- This product contains Sodium Azide; this material and its container must be disposed of in a safe way.
- Safety data sheets are available on request.

Handling Precautions

- Do not use reagent kits beyond the expiration date.
- Do not mix reagents from different reagent kits.
- Prior to loading the Reagent Kit on the system for the first time, the microbeads requires mixing to re-suspend microbeads that have settled during shipment.
- For microbeads mixing instructions, refer to the KIT COMPONENTS, Preparation of the Reagent Integral section of this package insert.
- To avoid contamination, wear clean gloves when operating with a reagent kit and sample.
- Over time, residual liquids may dry on the kit surface, please pay attention the silicon film still exists on the surface of the kit.
- For a detailed discussion of handling precautions during system operation, refer to the SNIBE service information.

TEST PROCEDURE

To ensure proper test performance, strictly adhere to the operating instructions of the MAGLUMI Fully Auto analyzer. Each test parameter is identified via a RFID tag on the Reagent Integral. For further information please refer to the MAGLUMI Chemiluminescence Analyzer Operating Instructions.

Auto dilution 1:11 20µl +200µl	Sample Diluent
20µl +100µl +20µl	Diluted Sample, calibrator or controls Buffer Nano magnetic microbeads
10 min	Incubation
400µl	Cycle washing
+200µl	ABEI Label
10 min	Incubation
400µl	Cycle washing
3 s	Measurement

DILUTION

Samples with concentrations above the measuring range can be diluted. After manual dilution, multiply the result by the dilution factor. After dilution by the analyzers, the analyzer software automatically takes the dilution into account when calculating the sample concentration.

Availability of sample dilution by analyzer please refers to the MAGLUMI analyzer user software program. Dilution settings please follow MALGUMI analyzer operating instructions.

QUALITY CONTROL

- Observe quality control guidelines for medical laboratories
- Use suitable controls for in-house quality control. Controls should be run at least once every 24 hours when the test is in use, once per reagent kit and after every calibration. The control intervals should be adapted to each laboratory's individual requirements. Values obtained should fall within the

defined ranges. Each laboratory should establish guidelines for corrective measures to be taken if values fall outside the range.

LIMITATIONS OF THE PROCEDURE

1) Limitations

Use CMV IgM value as a kind of auxiliary material for other testing data when in diagnosis. Assay results should be utilized in conjunction with other clinical and laboratory data to assist the clinician in making individual patient management decisions.

A skillful technique and strict adherence to the instructions are necessary to obtain reliable results. Bacterial contamination of samples or repeated freeze-thaw cycles may affect the test results. Assay results should be utilized in conjunction with other clinical and laboratory data to assist the clinician in making individual patient management decisions.

2) Interfering Substances

No interference with test results is seen by concentrations of bilirubin < 0.06mg/ml, haemoglobin < 16mg/dl or triglycerides < 12.5mg/ml.

3) HAMA

Patient samples containing human anti-mouse antibodies (HAMA) may give falsely elevated or decreased values. Although HAMA-neutralizing agents are added, extremely high HAMA serum concentrations may occasionally influence results.

RESULTS

1) Calculation of Results

1. The analyzer automatically calculates the CMV IgM concentration in each sample by means of a calibration curve which is generated by a 2-point calibration master curve procedure. The results are expressed in AU/ml. For further information please refer to the MAGLUMI Chemiluminescence Analyzer Operating Instructions.

2. Test results need NOT to multiply dilution rate!

2) Interpretation of Results

Results obtained with the MAGLUMI CMV IgM assay can be interpreted as follows:

Non-reactive: A result less than 2 AU/ml (< 2 AU/ml) is considered to be negative.

Reactive: A result greater than or equal to 2 AU/ml is (≥ 2 AU/ml) considered to be positive.

Since there is no CMV IgM international standard material yet, different IVD manufacturer have different traceability chain. Therefore results from assays of other manufacturers cannot be used interchangeably.

PERFORMANCE CHARACTERISTICS

1) Precision

Intra-assay coefficient of variation was evaluated on 3 different levels of control serum repeatedly measured 20 times in the same run, calculating the coefficient of variation.

Intra-assay precision

Control	Mean(AU/ml)	SD(AU/ml)	CV%
Level 1	1.62	0.09	5.54
Level 2	7.62	0.38	4.94
Level 3	18.59	0.95	5.11

Inter-assay coefficient of variation was evaluated on three batches of kits. Repeatedly measured 3 different levels of control serum 21 times, calculating the coefficient of variation.

Inter-assay precision

Control	Mean(AU/ml)	SD(AU/ml)	CV%
Level 1	1.59	0.14	8.87
Level 2	7.49	0.64	8.54
Level 3	19.11	1.65	8.64

2) Analytical Sensitivity

The sensitivity is defined as the concentration of CMV IgM equivalent to the mean RLU of 20 replicates of the zero standard plus two standard deviations corresponding to the concentration from the standard curve. The sensitivity is typically less than 0.25 AU/ml.

3) Specificity

The specificity of the CMV IgM assay system was assessed by measuring the apparent response of the assay to various potentially cross reactive analytes.

When CMV IgG, Rubella IgG, Rubella IgM, Toxo IgG, Toxo IgM, HSV-1/2IgG, HSV-1/2IgM separately reach a concentration of 30AU/ml, measured Toxo IgG is negative. No cross reaction with the IgG or IgM antibody of HAV, HBV, HCV, HIV, syphilis, EBV. The ELISA diagnosed RF or ANA positive, which is non CMV infected sample, this reagent's determination results show negative.

4) Recovery

Consider calibrator high of known concentration as a sample, dilute it by 1:2 ratio with diluents, and measure its diluted concentration for 10 times. Then calculate the recovery of measured concentration and expected concentration. The recovery should be within 90% -110%.

Expected	Mean Measuring	Recovery
9.8 AU/ml	9.6 AU/ml	98%

5) Linearity

Use CMV IgM calibrator to prepare the six-point standard curve, measuring all points' RLU except point A, and then do four-parameter linear fitting in double logarithm coordinate, the absolute linear correlation coefficient(r) should be bigger than 0.9800.

Calibrator Point	Concentration AU/ml	Absolute linear correlation coefficient (r)
A	0.0	
B	1.0	r=0.9844
C	3.0	
D	8.0	
E	15.0	
F	30.0	

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