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VIDAS® CMV IgM (CMVM)

IVD

VIDAS® CMV IgM is an automated qualitative enzyme immunoassay for use on the VIDAS® family instruments, for the detection of anti-cytomegalovirus IgM (CMVM) in human serum, using the ELFA technique (Enzyme Linked Fluorescent Assay).

SUMMARY AND EXPLANATION

Cytomegalovirus (CMV) is a herpesvirus which can cause serious diseases in infants and adults. CMV can persist in the human body for several years and can cause recurrent infections or be transmitted to other individuals.
CMV infections are very common; 60 to 85% of the population have been infected but most cases are asymptomatic.
1 to 3% of women are infected during pregnancy and in 1 out of every 2 cases the infection is passed on to the fetus. The infection is most often asymptomatic but in about 5% of cases, the consequences can be very severe: hepatosplenomegaly, hydrocephalus, microcephalism, prematurity. Fetal death is frequent (1, 2).
Even in cases of asymptomatic infection, approximately 10% of infants show sensorineural after-effects, such as deafness or partial or total blindness.
In immunocompromised patients (HIV positive or organ transplanted), CMV infections can be severe (3).
The detection of anti-CMV IgM can be useful in the diagnosis of current primary infection, particularly in pregnant women (4, 5, 6).
The anti-CMV IgM present in approximately 70% of primary infections, generally persist 16 to 20 weeks after infection, and may reappear irregularly during reactivation (7).

PRINCIPLE

The assay principle combines a two-step enzyme immunoassay sandwich method with a final fluorescent detection (ELFA).
The Solid Phase Receptacle (SPR) serves as the solid phase as well as the pipetting device. Reagents for the assay are ready-to-use and pre-dispensed in the sealed reagent strips.
All of the assay steps are performed automatically by the instrument. The reaction medium is cycled in and out of the SPR device several times.
After IgG and rheumatoid factor adsorption, the sample is cycled in and out of the SPR device for a specified length of time. Anti-CMV IgM antibodies present in the specimen will bind to the CMV antigen coating the interior of the SPR device. Unbound components are eliminated during the washing steps.
An alkaline phosphatase-labeled mouse monoclonal anti-human IgM antibody is cycled in and out of the SPR device and binds to the human anti-CMV IgM coated on the SPR device. A final wash step removes unbound components.
During the final detection step, the substrate (4-Methyl-umbelliferyl phosphate) is cycled in and out of the SPR device. The conjugate enzyme catalyzes the hydrolysis of this substrate into a fluorescent product (4-Methyl-umbelliferone), the fluorescence of which is measured at 450 nm. At the end of the assay, results are automatically calculated by the instrument in relation to the calibration curve stored in memory, and then printed out.

CONTENT OF THE KIT (30 TESTS):

30 CMVM Strips [a]	STR	Ready-to-use.
30 CMVM Solid Phase Receptacles	SPR	Ready-to-use. Interior of SPR devices coated with CMV antigen (cell culture of the virus of the AD169 strain).
CMVM Positive Control 1 x 1.3 mL (liquid)	C1	Ready-to-use. Human serum* containing anti-CMV IgM + 1 g/L sodium azide. MLE data indicate the index: confidence interval ("Control C1 (+) Test Value Range).
Negative Control [b] 1 x 1.9 mL (liquid)	C2	Ready-to-use. Phosphate buffer + protein stabilizer of animal origin + preservatives.
CMVM Standard 1 x 1.8 mL (liquid)	S1	Ready-to-use. Human serum* containing anti-CMV IgM + 1 g/L sodium azide.
Specifications for the factory master data required to calibrate the test: • MLE data (Master Lot Entry) provided in the kit, or • MLE bar code printed on the box label.		
1 Package insert provided in the kit or downloadable from www.biomerieux.com/techlib.		

* This product has been tested and shown to be negative for HBs antigen, antibodies to HIV1, HIV2 and HCV. However, since no existing test method can totally guarantee their absence, this product must be treated as potentially infectious. Therefore, usual safety procedures should be observed when handling.

(a) DANGER H318 / P280 / P305 + P351 + P338

(b) WARNING EUH208 / H317 / P261 / P280 / P302 + P352

Hazard statements

EUH208: Contains 2-methyl-2H-isothiazolin-3-one. May produce an allergic reaction.
H317: May cause an allergic skin reaction.
H318: Causes serious eye damage.

Precautionary statements

P261: Avoid breathing dust/fume/gas/mist/vapours/spray.
P280: Wear protective gloves/protective clothing/eye protection/face protection.
P302 + P352: IF ON SKIN: Wash with plenty of soap and water.
P305 + P351 + P338: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.

For further information, please refer to the Safety Data Sheet

The SPR device

The interior of the SPR device is coated during production with purified CMV antigen. Each SPR device is identified by the CMVM code. Only remove the required number of SPR devices from the pouch and **carefully reseal the pouch after opening.**

The Strip

The strip consists of 10 wells covered with a labeled, foil seal. The label comprises a bar code which mainly indicates the assay code, kit lot number and expiration date. The foil of the first well is perforated to facilitate the introduction of the sample. The last well of each strip is a cuvette in which the fluorometric reading is performed. The wells in the center section of the strip contain the various reagents required for the assay

Description of the CMVM Strip

Wells	Reagents
1	Sample well.
2	IgG and rheumatoid factor adsorbant (anti-human IgG goat serum) + 1 g/L sodium azide (300 µL).
3	IgG and rheumatoid factor adsorbant (anti-human IgG goat serum) + 1 g/L sodium azide (600 µL).
4	Pre-wash solution: phosphate (10 mmol/L) pH 7.2 + Tween + protein and chemical stabilizers + 1 g/L sodium azide (600 µL).
5 - 7 - 8 - 9	Wash solution: TRIS (50 mmol/L) pH 7.4 + 1 g/L sodium azide (600 µL).
6	Conjugate: Alkaline phosphatase-labeled monoclonal anti-human IgM antibodies (mouse) + 1 g/L sodium azide (400 µL).
10	Reading cuvette with substrate: 4-Methyl-umbelliferyl phosphate (0.6 mmol/L) + diethanolamine DEA (0.62 mol/L or 6.6%, pH 9.2) + 1 g/L sodium azide (300 µL).

MATERIALS AND DISPOSABLES REQUIRED BUT NOT PROVIDED

- Pipette with disposable tip to dispense 100 µL.
- Powderless, disposable gloves.
- For other specific materials and disposables, please refer to the Instrument User Manual.
- Instrument of the VIDAS® family.

WARNINGS AND PRECAUTIONS

- **For *in vitro* diagnostic use only.**
- **For professional use only.**
- **This kit contains products of human origin. No known analysis method can totally guarantee the absence of transmissible pathogenic agents. It is therefore recommended that these products be treated as potentially infectious and handled observing the usual safety precautions (see Laboratory Biosafety Manual - WHO - Geneva - latest Edition).**
- This kit contains products of animal origin. Certified knowledge of the origin and/or sanitary state of the animals does not totally guarantee the absence of transmissible pathogenic agents. It is therefore recommended that these products be treated as potentially infectious and handled observing the usual safety precautions (do not ingest or inhale).
- Do not use the SPR devices if the pouch is pierced.
- Do not use visibly deteriorated STRs (damaged foil or plastic).
- Do not use reagents after the expiration date indicated on the box label.
- Do not mix reagents (or disposables) from different lots.
- Use **powderless** gloves, as powder has been reported to cause false results for certain enzyme immunoassay tests.
- Kit reagents contain sodium azide which can react with lead or copper plumbing to form explosive metal azides. If any liquid containing sodium azide is disposed of in the plumbing system, drains should be flushed with water to avoid build-up.
- Refer to the hazard statements "H" and the precautionary statements "P" above.
- Spills should be wiped up thoroughly after treatment with liquid detergent or a solution of household bleach containing at least 0.5% sodium hypochlorite. See the User Manual for cleaning spills on or in the instrument. Do not autoclave solutions containing bleach.
- The instrument should be regularly cleaned and decontaminated (see the User Manual).

STORAGE CONDITIONS

- Store the VIDAS® CMV IgM kit at 2-8°C.
- **Do not freeze reagents.**
- **Store all unused reagents at 2-8°C.**
- After opening the kit, check that the SPR pouch is correctly sealed and undamaged. If not, do not use the SPR devices.
- **Carefully reseal the pouch with the desiccant inside after use to maintain stability of the SPR devices and return the complete kit to 2-8°C.**
- If stored according to the recommended conditions, all components are stable until the expiration date indicated on the label.

SPECIMENS

Specimen Type and Collection

Human serum.

It is recommended that each laboratory checks the compatibility of used collection tubes.

It is recommended not to use hemolyzed, lipemic, icteric, or inactivated samples, and, if possible, to collect a new sample.

Refer to the section **PERFORMANCE – Study of drugs and other potentially interfering substances** for the compounds tested.

Specimen Stability

Samples can be stored at 2-8°C in stoppered tubes for up to 5 days; if longer storage is required, freeze the sera at -25 ± 6°C.

A study performed on frozen samples over a period of 2 months, showed that the quality of results is not affected.

Avoid successive freezing and thawing.

INSTRUCTIONS FOR USE

For complete instructions, see the User Manual.

Reading Master Lot Data

Before each new lot of reagents is used, enter the specifications (or factory master data) into the instrument using the master lot entry (MLE) data.

If this operation is not performed **before initiating the tests**, the instrument will not be able to print results.

Note: the master lot data need to be entered only once for each lot.

It is possible to enter MLE data **manually or automatically** depending on the instrument (refer to the User Manual).

Calibration

Calibration, using the standard provided in the kit, must be performed each time a new lot of reagents is opened, after the master lot data have been entered. Calibration should then be performed every 14 days. This operation provides instrument-specific calibration curves and compensates for possible minor variations in assay signal throughout the shelf-life of the kit.

The standard, identified by S1, must be tested **in duplicate** (see User Manual). The standard value must be within the set RFV (Relative Fluorescence Value) range. If this is not the case, recalibrate.

Procedure

1. **Only remove the required reagents from the refrigerator and allow them to come to room temperature for at least 30 minutes.**
2. Use one "CMVM" strip and one "CMVM" SPR device for each sample, control or standard to be tested. **Make sure the storage pouch has been carefully resealed after the required SPR devices have been removed.**
3. The test is identified by the "CMVM" code on the instrument. The standard must be identified by "S1", and tested **in duplicate**. If the positive control is to be tested, it should be identified by C1. If the negative control is to be tested, it should be identified by C2.

4. Mix the standard, controls and samples using a vortex-type mixer (for serum separated from the pellet).
5. **For this test, the standard, control, and sample test portion is 100 µL.**
6. Insert the "CMVM" SPR devices and "CMVM" strips into the instrument. Check to make sure the color labels with the assay code on the SPR devices and the Reagent Strips match.
7. Initiate the assay as directed in the User Manual. All the assay steps are performed automatically by the instrument.
8. Restopper the vials and return them to 2–8°C after pipetting.
9. The assay will be completed within approximately 60 minutes. After the assay is completed, remove the SPR devices and strips from the instrument.
10. Dispose of the used SPR devices and strips into an appropriate receptacle.

RESULTS AND INTERPRETATION

Once the assay is completed, results are analyzed automatically by the computer. Fluorescence is measured twice in the Reagent Strip's reading cuvette for each sample tested. The first reading is a background reading of the substrate cuvette before the SPR device is introduced into the substrate. The second reading is taken after incubating the substrate with the enzyme remaining on the interior of the SPR device. The RFV (Relative Fluorescence Value) is calculated by subtracting the background reading from the final result. This calculation appears on the result sheet.
The index (ratio of the fluorescent signal found for the serum to be tested, over the standard signal stored in the memory) is calculated by the instrument.

This index and the interpretation are indicated on the result sheet.

Threshold and Interpretation of Results

Index	Interpretation
i < 0.70	Negative
0.70 ≤ i < 0.90	Equivocal
i ≥ 0.90	Positive

Repeat the assay for indexes between 0.70 and 0.90. If after verification interpretation is still equivocal, repeat the assay on a new sample collected 10 to 15 days later.
Interpretation of test results should be made taking into consideration the patient's history, and the results of any other tests performed.
As no international standard is available for the determination of anti-CMV IgM, the VIDAS® CMV IgM reagent is calibrated against collection sera.

QUALITY CONTROL

One positive control and one negative control are included in each VIDAS® CMVM kit.
These controls must be performed immediately after opening a new kit to ensure that reagent performance has not been altered. Each calibration must also be checked using these controls. The instrument will only be able to check the control values if they are identified by C1 and C2.
Results cannot be validated if the control values deviate from the expected values.

Note

It is the responsibility of the user to perform Quality Control in accordance with any local applicable regulations.

LIMITATIONS OF THE METHOD

Interference may be encountered with certain sera containing antibodies directed against reagent components. For this reason, assay results should be interpreted as part of a complete clinical profile.
The detection of anti-CMV IgM may be difficult in immunocompromised patients. The diagnosis of cytomegalovirus infection or non-infection in immunocompromised patients should not be based solely on the determination of anti-CMV IgM. Interpretation of VIDAS® CMV IgM test results should be made taking into consideration the patient's history and the results of any other tests performed (viral culture, viral DNA, anti-CMV IgG, etc.).
VIDAS® CMV IgM has not been validated for use with specimens collected post mortem or neonatal specimens (cord blood, etc.).

PERFORMANCE

The VIDAS® CMV IgM reagent was evaluated at an external site in comparison with 3 other commercially available EIA methods.
The presence or absence of anti-CMV IgM in each sample was determined by taking into account the concordant results obtained with at least 2 or 3 of the commercially available tests.
Equivocal samples were excluded from the performance calculation.

Sensitivity Study of VIDAS® CMV IgM

During the evaluation, 43 typically anti-CMV IgM positive samples were tested. The following results were obtained with VIDAS® CMV IgM:

N = 43		VIDAS® CMV IgM		
		Positive	Equivocal	Negative
Status	Positive	37	2	4*

* The 4 specimens that were found to be negative were all collected from transplant patients.

Sensitivity: 90.24%
95% Confidence Interval: 76.87 – 97.28%.

Specificity Study of VIDAS® CMV IgM

During the evaluation, 171 typically anti-CMV IgM-negative samples were tested. The following results were obtained with VIDAS® CMV IgM:

N = 171		VIDAS® CMV IgM		
		Positive	Equivocal	Negative
Status	Negative	1	1	169

Specificity: 99.41%
95% Confidence Interval: 96.65 – 99.90%.

Specificity Study of VIDAS® CMV IgM on potentially interfering samples

This study was carried out using 171 serum samples with the following characteristics:
- 40 serum samples from patients with HIV1 virus,
- 11 serum samples from infants less than 3 months old,
- 57 serum samples from pregnant women,
- 17 serum samples from carriers of Epstein-Barr virus,
- 5 serum samples from carriers of varicella virus.
- 5 serum samples from carriers of herpes virus,
- 16 serum samples from subjects possessing antinuclear antibodies,
- 20 serum samples from subjects possessing rheumatoid factor.

158 out of the 171 serum samples were diagnosed as anti-CMV IgM-negative. The following results were obtained with VIDAS® CMV IgM:

N = 158		VIDAS® CMV IgM		
		Positive	Equivocal	Negative
Status	Negative	2*	2	154

*One sample belongs to the group of subjects with rheumatoid factor, the second to the group of patients with antinuclear antibodies.

Specificity: 98.72%
95% Confidence Interval: 95.34 – 99.66%.

Within-Run Reproducibility

3 samples were tested 30 times in the same run.

Sera	Mean Index	Standard Deviation	Intra-Assay CV %
High positive	1.63	0.09	5.52
Low positive	1.00	0.06	6.00
Negative	0.08	0.01	12.50

Between-Run Reproducibility

3 samples were tested singly in 10 different runs on the same VIDAS instrument.

Sera	Mean Index	Standard Deviation	Inter-Assay CV %
High positive	1.51	0.06	3.97
Low positive	0.96	0.05	5.21
Negative	0.14	0.06	42.86

The figures in the above tables are given for information only.

Study of drugs and other potentially interfering substances

Potential interference by commonly used drugs and other substances was studied according to CLSI EP07-A2 recommendations. No significant interference was detected up to the maximum concentrations indicated below.

Tested substances	Maximum concentrations
Hemoglobin	3.98 g/L
Lipids	17 g/L
Bilirubin	300 mg/L
Albumina	60 g/L

RANGE OF EXPECTED VALUES

The incidence of cytomegalovirus infection differs according to the populations studied. In developed countries, the percentage of CMV-positive women between 15-30 years of age does not exceed 40-50%.

WASTE DISPOSAL

Dispose of used or unused reagents as well as any other contaminated disposable materials following procedures for infectious or potentially infectious products.
It is the responsibility of each laboratory to handle waste and effluents produced according to their type and degree of hazardousness and to treat and dispose of them (or have them treated and disposed of) in accordance with any applicable regulations.

LITERATURE REFERENCES

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INDEX OF SYMBOLS

Symbol	Meaning
REF	Catalogue number
IVD	*In Vitro* Diagnostic Medical Device
	Manufacturer
	Temperature limit
	Use by date
LOT	Batch code
	Consult Instructions for Use
	Contains sufficient for <n> tests
	Date of manufacture

LIMITED WARRANTY

bioMérieux warrants the performance of the product for its stated intended use provided that all procedures for usage, storage and handling, shelf life (when applicable), and precautions are strictly followed as detailed in the instructions for use (IFU).
Except as expressly set forth above, bioMerieux hereby disclaims all warranties, including any implied warranties of merchantability and fitness for a particular purpose or use, and disclaims all liability, whether direct, indirect or consequential, for any use of the reagent, software, instrument and disposables (the "System") other than as set forth in the IFU.

REVISION HISTORY

Change type categories:

N/A	Not applicable (First publication)
Correction	Correction of documentation anomalies
Technical change	Addition, revision and/or removal of information related to the product
Administrative	Implementation of non-technical changes noticeable to the user

Note: *Minor typographical, grammar, and formatting changes are not included in the revision history.*

Release date	Part Number	Change Type	Change Summary
2019-02	06637N	Technical	CONTENT OF THE KIT (30 TESTS)
2019-05	06637O	Administrative	LIMITED WARRANTY
		Technical	SPECIMENS
			PERFORMANCE - Study of drugs and other potentially interfering substances
2019-11	046052-04	Technical	CONTENT OF THE KIT (30 TESTS) WARNINGS AND PRECAUTIONS

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