30 אפריל, 2013

לקוחות נכבדים,

הנדון:**Vidas CMV Avidity (CMVA)**

חברת אילקס שמחה להודיע על השקת ערכה חדשה לבדיקת CMV Avidity במכשיר ה- Vidas.

יתרונות הערכה:

הקטנת טווח ה- borderline בערכי הייחוס-

- low avidity, אינדיקציה להדבקה טרייה (מתחת ל- 3 חודשים) < 0.4
- Equivocal, אין אבחנה האם מדובר בהדבקה טרייה או הדבקה מהעבר 0.4 -0.65
- high avidity, אינדיקציה להדבקה מהעבר (מעל ל- 3 חודשים) > 0.65

לתשומת ליבכם, הקיט הישן לבדיקת CMV Avidity (מק"ט 5-30203) ישווק **עד סוף שנת 2013.**

ערוץ תקשורת של הקיט החדש – CMVA.

להלן הנתונים החדשים להזמנת הקיט החדש:

שם פריט	מק"ט אילקס
Vidas CMV Avidity	5-413557

מצ"ב מידע מחברת BioMerieux

למידע נוסף ניתן לפנות ל:
עילית ליזרמן, 054-6686183
אורלי דויטש, 054-5686303

בברכה,
עילית ליזרמן
אילקס מדיקל בע"מ.

אילקס מדיקל בע"מ - בניין קודאק, רח' התנופה 7, איזור תעשייה קרית אריה, ת.ד. 10249, פתח תקווה 49002
טל. 03-9385501 פקס. 03-9385500 sales@ilexmedical.com www.ilexmedical.com

IVD

VIDAS® CMV IgG Avidity II (CMVA)

VIDAS CMV IgG Avidity II is an automated qualitative test for use on the VIDAS family of instruments, for the determination of anti-CMV IgG avidity in human serum, using the ELFA technique (Enzyme Linked Fluorescent Assay). This test is an aid in diagnosing CMV infections. VIDAS CMV IgG Avidity II is intended to be used with the VIDAS CMV IgG assay (Ref. 30 204).

SUMMARY AND EXPLANATION

The diagnosis of Cytomegalovirus (CMV) infection in immunocompetent patients (1) in general and in pregnant women (2) in particular, is serological. It is based on the observation of a seroconversion. It is impossible, in the presence of IgM, to assess the date of infection or to distinguish a primary infection from a reactivation, a re-infection or a polyclonal stimulation. This information is nevertheless essential in an obstetrical situation for prenatal diagnosis (3) (4). The aim of the determination of anti-CMV IgG avidity is to obtain more accurate diagnosis and confirm or exclude CMV primary infections (1).
The addition of an agent which disrupts the Ag-Ab link (such as urea) (5) during an ELISA test has little effect on the high avidity antibody link, but great effect on that of the weak avidity antibodies. Comparison of results obtained with and without a dissociating agent corresponds to one measure of avidity.

VIDAS CMV IgG Avidity II is a simple technique which enables weak avidity antibodies to be differentiated from high avidity antibodies. The detection of high avidity antibodies is a strong indication of a primary infection of more than 3 months, whereas the detection of weak avidity antibodies is a strong indication of a primary infection of less than 3 months.

PRINCIPLE

VIDAS CMV IgG Avidity II uses strips and SPRs of the VIDAS CMV IgG kit (ref. 30 204).
Avidity reveals the strength of the link between an antibody and a plurivalent antigen.
This avidity is determined by two VIDAS CMV IgG assays (ref. 30 204):
The first assay is the reference. For the second assay, the wash buffer in well 4 of the VIDAS CMV IgG strip is replaced with the urea buffer included in the VIDAS CMV IgG Avidity II kit.

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 for the assay. Reagents for the assay are ready-to-use and pre-dispensed in the sealed reagent strips, except the urea buffer (R1).

All of the assay steps are performed automatically by the instrument. The reaction medium is cycled in and out of the SPR several times.
If anti-CMV IgG are present in the sample, they form complexes with the antigen coated to the solid phase. In the strip without urea buffer, non-specific antibodies are eliminated by washing, whereas specific antibodies remain coated to the solid phase. In the strip containing urea buffer, washing with the dissociating agent changes antigen-antibody links. Only antibodies with high avidity remain bound to the solid phase, whereas antibodies with low avidity are eliminated.
Alkaline phosphatase-labeled human anti-IgG antibodies (conjugate) are then cycled in and out of the SPR and bind with any human IgG coated on the interior of the SPR. Unbound components are eliminated during the washing steps.
During the final detection step, the substrate (4-Methyl-umbelliferyl phosphate) is cycled in and out of the SPR. 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. The intensity of the fluorescence is proportional to the concentration of antibodies present in the sample.
At the end of the assay, the results in RFV (Relative Fluorescence Value) for each strip are used to calculate the avidity index, determined as the RFV ratio obtained for the Test strip (with urea buffer), divided by the RFV obtained with the Reference strip.

CONTENT OF THE KIT (30 TESTS):

Urea buffer 4 x 5 ml (liquid)	R1	TRIS + urea + preservative.
High avidity control 1 x 1.5 ml (liquid)	C H	Human serum* containing anti-CMV IgG (index ≥ 0.70) + preservative.
Low avidity control 1 x 1.5 ml (liquid)	C L	Human serum* containing anti-CMV IgG (index ≤ 0.30) + preservative.
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.

Each CMVA assay requires 2 VIDAS CMV IgG strips and SPRs (ref. 30 204).

REAGENTS, MATERIALS AND DISPOSABLES REQUIRED BUT NOT PROVIDED

- VIDAS CMV IgG (ref. 30 204)
- Pipette with disposable tip to dispense 100 and 600 µl.
- Powderless, disposable gloves.
- For other specific materials and disposables, please refer to the Instrument User's Manual.
- VIDAS family instrument.

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).**
- Do not use reagents after the expiration date indicated on the 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.
- 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's 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's Manual).

STORAGE CONDITIONS

- Store the VIDAS CMV IgG Avidity II kit at 2-8°C.
- **Do not freeze reagents.**
- **Store all unused reagents at 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:

Refer to the VIDAS CMV IgG package insert (ref. 30 204).

Specimen stability:

Refer to the VIDAS CMV IgG package insert (ref. 30 204).

INSTRUCTIONS FOR USE

For complete instructions, see the Instrument User's Manual.

Any samples to be assayed by VIDAS CMV IgG Avidity II must have been previously tested using VIDAS CMV IgG (ref. 30 204): samples with titers greater than 400 aU/ml will have been diluted according to the package insert (ref. 30 204) in order to obtain a working titer (6 - 400 aU/ml).

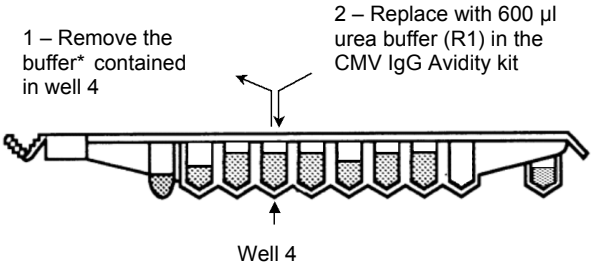
Note: Determination of avidity is only applicable to samples with VIDAS CMVG titers between 6 and 400 aU/mL.

It is strongly recommended to determine the anti-CMV IgG avidity using anti-CMV IgM-positive samples only. In particular, IgM-negative samples with a low IgG titer (< 12 aU/ml) will have to be interpreted with caution.

Procedure

1. **Only remove the required reagents from the refrigerator and wait 30 minutes before using.**
2. Use two "CMVG" strips and two "CMVG" SPRs from the same lot for each sample or control to be tested. **Make sure the storage pouch has been carefully resealed after the required SPRs have been removed.**
3. Preparation of **Test strip**: pierce well 4 (identified by the letter U) on one of the two CMVG strips using a pipette tip; carefully push back the aluminum foil covering the opening.

CMV IgG STRIP



The strip which now contains urea is the Test strip.

* This buffer contains a preservative (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.

4. The test is identified by the "CMVA" code on the instrument (to do so, refer to the Instrument User's Manual). If the controls need to be tested, they should be identified by CH and CL **and entered as patient samples on the instrument**.
5. Mix the controls and samples using a vortex-type mixer (for serum separated from the pellet).
6. **For this test, the control and sample test portion in each sample well on the two strips for the "CMVA" assay is 100 µL.**
7. Insert the "CMVG" SPRs and "CMVG" strips into the instrument according to the loading plan. Check to make sure the color labels with the assay code on the SPRs and the Reagent Strips match.
8. Initiate the assay as directed in the User's Manual. All the assay steps are performed automatically by the instrument.
9. Restopper the vials and return them to 2-8°C after pipetting.
10. The assay will be completed within approximately 40 minutes. After the assay is completed, remove the SPRs and strips from the instrument.
11. Dispose of the used SPRs and strips into an appropriate recipient.

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® is introduced into the substrate. The second reading is taken after incubating the substrate with the enzyme remaining on the interior of the SPR. The RFV (Relative Fluorescence Value) is calculated by subtracting the background reading from the final result. This calculation appears on the result sheet.
The results are calculated by the instrument using a CMV IgG calibration curve which is stored by the instrument; concentrations are expressed in RFV and aU/ml.
If the IgG concentrations are lower than 6 aU/ml or greater than 400 aU/ml with the Reference strip (without urea buffer), the avidity index calculation is uninterpretable. If the result of the Reference strip is greater than 400 aU/ml, repeat the assay using two new CMVG strips and an appropriate dilution.

CALCULATION OF AVIDITY INDEX

For each patient sample or control, the avidity index is calculated as follows: (*)

$$\text{Index} = \frac{\text{RFV Test strip}}{\text{RFV Reference strip}}$$

(*) : manual or automatic calculation depending on the VIDAS family instrument used.

Interpretation of the avidity index is as follows:

Avidity	Interpretation
index < 0.40	Low avidity IgG
0.40 ≤ index < 0.65	Borderline avidity
index ≥ 0.65	High avidity IgG

An avidity index greater than or equal to 0.65 is a strong indication of a primary infection dating back more than 3 months.
An avidity index lower than 0.40 is a strong indication of a primary infection dating back less than 3 months. (6).
For these results, confirmation using another serum collected 3 or 4 weeks later may be justified depending on the clinicobiological context.

An avidity index between 0.40 and 0.65 does not enable to distinguish a recent infection from a former infection. For these samples, depending on the context, other markers and/or avidity determination methods should be used and/or a new serum sample (collected 3 or 4 weeks later) should be tested (7).

In all cases, refer to current legislation concerning repeat sample testing, in particular as regards following up pregnant women.

QUALITY CONTROL

CMVG reagents used for this assay must have been previously controlled with quality controls included in the VIDAS CMVG kit; refer to the VIDAS CMV IgG (ref. 30 204) package insert.
Two controls (CH and CL) are included in each VIDAS CMV IgG Avidity II kit. These controls must be performed immediately after opening a new kit to ensure that reagent performance has not been altered.
The user must check that the avidity indexes obtained for the CH and CL controls are conform to the values indicated on each control label.
Results cannot be validated if one of the avidity indexes is outside the acceptable values indicated.

Note

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

LIMITATIONS OF THE METHOD

- The results of this assay must be interpreted taking into consideration the patient's history, and the results of any other tests performed.
- Results may not be valid in patients who have received blood transfusions or other blood products within the past few months.
- VIDAS CMV IgG Avidity II has not been validated for use with specimens collected post mortem.
- Interference may be encountered with certain sera containing antibodies directed against reagent components.

PERFORMANCE

Studies performed using VIDAS CMV IgG Avidity II gave the following results:

Precision

Between-run reproducibility:

4 samples were tested singly in 8 different runs using 8 lots of VIDAS CMV IgG.

	Serum 1	Serum 2	Serum 3	Serum 4
Mean index	0.91	0.83	0.39	0.07
CV %	4.9	3.7	1.9	12

Clinical study

430 samples were tested at three sites:

- 320 samples with CMV (IgG-positive / IgM-negative) serology or clinical results which evoke a former infection (sera collected more than 3 months after the onset of infection).
- 110 samples with primary infection collected less than 3 months after the onset of infection.

The presumed date of infection was determined as accurately as possible, based on the study of clinical files, the increase in specific IgG and the appearance of IgM.

For 110 samples with primary infection (infection < 3 months) the diagnostic agreement was 97.3% [$_{95\%}$ CI: 92.2-99.4%] (avidity index < 0.65), including 83 samples with an avidity index < 0.40.

For 320 samples with a former infection (infection > 3 months), the diagnostic agreement was 97.8% [$_{95\%}$ CI: 95.5-99.1] (avidity index ≥ 0.40), including 279 samples with an avidity index ≥ 0.65.

For 279 samples with a former infection (infection > 6 months) the diagnostic agreement was 98.9% [$_{95\%}$ CI: 96.9-99.8%] (avidity index ≥ 0.40), including 265 samples with an avidity index ≥ 0.65.

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 nature 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

1. DUSSAIX E., CHANTOT S., HARZIC M., GRANGEOT-KEROS L. CMV-IgG avidity and CMV-IgM concentration in both immunocompromised and immunocompetent patients. Pathologie Biologie, 1996, 44(5), 405-410.
2. GRANGEOT-KEROS L., MAYAUX M.J., LEBON P., FREYMUTH F., EUGENE G., STRICKER R., and DUSSAIX E. Value of cytomegalovirus (CMV) IgG avidity index for the diagnosis of primary CMV infection in pregnant women. The Journal of Infectious Diseases, 1997, 175, 944-946.
3. LAZZAROTTO T., SPEZZACATENA P., VARINI S., GABRIELLI L., PRADELLI P., GUERRA B., LANDINI M.P. Anticytomegalovirus (Anti-CMV) immunoglobulin G avidity in identification of pregnant women at risk of transmitting congenital CMV infection. Clinical and Diagnostic Laboratory Immunology, 1999, 127-129.
4. RUELLAN-EUGENE G., BARJOT P., CAMPET M., VABRET A., HERLICOVIEZ M., MULLER G., LEVY G., GUILLOIS B. and FREYMUTH F. Evaluation of virological procedures to detect fetal human cytomegalovirus infection: avidity of IgG antibodies, virus detection in amniotic fluid and maternal serum. Journal of Medical Virology, 1996, 50, 9 -15.
5. BLACKBURN N.K., BESSELAAR T.G., SCHOUB B.D., and O'CONNELL K.F. Differentiation of primary cytomegalovirus infection from reactivation using the urea denaturation test for measuring antibody avidity. Journal of Medical Virology, 1991, 33, 6-9.
6. VAULOUP-FELLOUS C, GRANGEOT-KEROS L, GUILLET M, HESKIA F, DUGUA J-M. Study of new cut-off values for the VIDAS ® CMV IgG Avidity kit and comparison to the Liaison and a home made technique. 14th Annual Meeting of the European Society for Clinical Virology 21- 24 September 2011 POSTER P099.
7. BACCARD-LONGERE M., FREYMUTH F., COINTE D et al – Multicenter evaluation of a rapid and convenient method for determination of cytomegalovirus immunoglobulin G avidity - Clinical and diagnostic laboratory immunology, Mar. 2001, Vol.8, n°2, p. 429-431.

INDEX OF SYMBOLS

Symbol	Meaning
REF	Catalogue number
IVD	In Vitro Diagnostic Medical Device
	Manufacturer
	Temperature limitation
	Use by
LOT	Batch code
	Consult Instructions for Use
	Contains sufficient for <n> tests

WARRANTY

bioMérieux disclaims all warranties, express or implied, including any implied warranties of MERCHANTABILITY AND FITNESS FOR A PARTICULAR USE. bioMérieux shall not be liable for any incidental or consequential damages. IN NO EVENT SHALL BIOMERIEUX'S LIABLITY TO CUSTOMER UNDER ANY CLAIM EXCEED A REFUND OF THE AMOUNT PAID TO BIOMERIEUX FOR THE PRODUCT OR SERVICE WHICH IS THE SUBJECT OF THE CLAIM.

BIOMÉRIEUX

bioMérieux SA
Chemin de l'Orme
69280 Marcy-l'Etoile - France

RCS LYON 673 620 399
Tel. 33 (0)4 78 87 20 00
Fax 33 (0)4 78 87 20 90
www.biomerieux.com

CE 0459