VIDAS®EBV VCA/EA IgG (VCAG)

IVD

VIDAS EBV VCA/EA IgG is an automated test for use on the VIDAS family instruments, for the qualitative detection of anti-VCA and anti-EA IgG in human serum using the ELFA technique (Enzyme Linked Fluorescent Assay). Detection of these specific antibodies is an aid in diagnosing infectious mononucleosis (IM).

SUMMARY AND EXPLANATION

The Epstein-Barr virus (EBV, also called Human Herpesvirus 4 (HHV4)) is ubiquitous. It was identified as the cause of infectious mononucleosis (IM). In adolescents and young adults, EBV may cause an infectious mononucleosis still known as Pfeiffer's disease (glandular fever) or the kissing disease. In young children, EBV infection is usually asymptomatic.

Transmission mainly occurs through contact with saliva. Indeed, EBV replication takes place in the oropharyngeal epithelial cells where the virions are released into the saliva by infected B-lymphocytes.

Over 95% of the adult population carries the virus. As this virus generally remains dormant in the body, reactivation may occur, particularly in immunocompromised patients. While reactivated EBV infection is asymptomatic in immunocompetent carriers, it is however associated with clinical disorders and a high morbidity and mortality rate in immunocompromised patients.

Diagnosis of IM is mainly based on clinical symptoms (sore throat, fever and swollen lymph glands). Serology is used to confirm diagnosis of IM and exclude illnesses such as lymphoma and leukemia, which may produce IM-type symptoms. Mononucleosis syndrome may also be caused by other pathogenic agents (cytomegalovirus, HHV6, adenovirus, rubella virus, mumps virus, HIV, hepatitis A virus, influenza A & B viruses and toxoplasma gondii).

Serologic diagnosis of IM includes non-specific tests such as the detection of heterophile antibodies, as well as EBV-specific tests. The latter tests are based on the detection of antibodies produced by the host in response to different antigens produced during the viral cycle. During the lytic phase, EBV early antigens (EA) are produced, then viral capsid antigens (VCA) are expressed at the same time as the viral genome. During the latent cycle, Epstein-Barr nuclear antigens (EBNA) are synthesized.

When IM occurs, heterophile antibodies appear in 60-80% of cases, anti-EA antibodies in 70-80% of cases, anti-VCA IgM antibodies in 100% of cases and anti-VCA IgG antibodies in nearly 100% of cases.

During the convalescent phase, anti-VCA IgG antibodies persist and approximately 95% of patients produce anti-EBNA IgG antibodies (1, 2, 3, 4, 5).

The VIDAS tests enable the detection of anti-EA IgG and anti-VCA IgG antibodies (VIDAS EBV VCA/EA IgG), anti-VCA IgM antibodies (VIDAS EBV VCA IgM) and anti-EBNA IgG antibodies (VIDAS EBV EBNA IgG).

Global interpretation of these assays is useful in diagnosing IM and establishing the stage of infection (see the following table):

VIDAS EBV VCA IgM	VIDAS EBV VCA/EA IgG	VIDAS EBV EBNA IgG	**Interpretation of VIDAS EBV (combined results)**
-	-	-	Seronegative subject (non infected)
+	-	-	Early-phase IM / primary infection (2)
+	+	-	Acute IM / primary infection
-	+	+ (1)	Seropositive subject (past infection)
-	-	+	Isolated EBNA IgG (2)
-	+	-	Isolated VCA/EA IgG (2)
+	+	+	Indeterminate profile (2)

-: Absence of antibodies.

+: Presence of antibodies.

(1) in rare cases, anti-EBNA antibodies are not detected in seropositive subjects who have had a past infection.

(2) to be checked using a specimen collected 1 to 2 weeks later.

PRINCIPLE

The assay principle combines a 2-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 strip.

All of the assay steps are performed automatically by the instrument. The reaction medium is cycled in and out of the SPR several times.

In the first step, the sample is diluted and then cycled in and out of the SPR. The anti-VCA and/or EA antibodies in the sample will bind to the VCA P18 and EA P54 antigens coated on the interior of the SPR wall. Unbound components are eliminated during the washing steps. During the second step, mouse monoclonal anti-human IgG antibodies in Fab' form, conjugated to alkaline phosphatase, are cycled in and out of the SPR and will attach to any human IgG bound to the antigen. 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 antibody present in the sample. At the end of the assay, the results are automatically calculated by the instrument in relation to the stored standard S1, and then printed out.

CONTENT OF THE KIT (30 TESTS):

30 EBV VCA/EA IgG Strips	STR	Ready-to-use.
30 EBV VCA/EA IgG SPRs 1 x 30	SPR	Ready-to-use. Interior of SPRs coated with VCA P18 and EA P54 antigens.
EBV VCA/EA IgG Positive Control 1 x 1,2 ml (liquid)	C1	Pool of human sera* containing anti-VCA IgG in a phosphate buffer pH 7.4 + 50 g/l BSA + preservatives. MLE data indicate the index: confidence interval ("Control C1 (+) Test Value Range").
Negative Control 1 x 1.9 ml (liquid)	C2	Ready-to-use. Phosphate buffer + protein stabilizer of animal origin+ preservatives. MLE data indicate the index: confidence interval ("Control C2 (-) Test Value Range").
Standard EBV VCA/EA IgG 1 x 2 ml (liquid)	S1	Pool of human sera* containing anti-VCA IgG in a phosphate buffer pH 7.4 + 50 g/l BSA + preservatives.
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 Clip Seal		
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 surface antigen, and 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.

The SPR

The interior of the SPR® is coated during production with VCA P18 and EA P54 antigens. Each SPR is identified by the code VCAG. Only remove the required number of SPRs from the pouch and **carefully reseal the pouch after opening using the clip seal provided**.

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 VCAG strip

Wells	Reagents
1	Sample well.
2	Sample diluent: Phosphate buffered saline + Tween 20 0.05% pH 7.2 + 5 g/l BSA + preservatives (600 µl).
3 - 4 - 5 - 7 - 8	Wash buffer: Phosphate buffered saline + Tween 20 0.25% pH 7.8 + preservatives (600 µl).
6	Conjugate: alkaline phosphatase-labeled mouse monoclonal anti-human IgG antibodies in Phosphate buffered saline pH 6.1 + protein stabilizers + preservatives (400 µl).
9	Sample diluent: Phosphate buffered saline + Tween 20 0.05% + 5 g/l BSA pH 7.2 + preservatives (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).

* Signal Word: **DANGER**

Hazard statement

H318 : Causes serious eye damage.

Precautionary statement

P280 :Wear protective gloves/protective clothing/eye protection/face protection.
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, refer to the Material Safety Data Sheet.

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'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).**
- 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®s 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.
- The substrate in well 10 contains an irritant agent (6.6% diethanolamine). 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'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 EBV VCA/EA IgG 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 SPRs.
- **To maintain stability of the remaining SPRs, carefully reseal the pouch after use with the desiccant inside using the clip seal provided, 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 (glass or plastic plain tube with coagulation activator and tube with separation gel).
It is recommended that each laboratory validate the type of collection tube used.

Sample-related interference

None of the following factors have been found to significantly influence this assay.
- hemolysis (after spiking samples with hemoglobin: 0 to 300 µmol/l (monomer)),
- lipemia (after spiking samples with lipids: 0 to 30 mg/ml equivalent in triglycerides),
- bilirubinemia (after spiking samples with bilirubin: 0 to 610 µmol/l).

However, it is recommended not to use samples that are clearly hemolyzed, lipemic or icteric and, if possible, to collect a new sample.

Specimen preparation:

Plain tubes: wait for samples to coagulate and **centrifuge** according to the tube manufacturer's recommendations to eliminate fibrin.
Other tubes: follow the tube manufacturer's recommendations for use.
Frozen-stored samples: after thawing, these samples must be homogenized before analysis.

Sample stability

Samples can be stored in stoppered tubes for up to 5 days at 2-8°C; if longer storage is required, freeze the sera at -25 ± 6°C.
Do not exceed 3 freeze/thaw cycles.
A study performed on samples frozen for 6 months, showed that the quality of results is not affected.

INSTRUCTION FOR USE

For complete instructions, see the User's Manual.
Reading VIDAS® Protocole Test Change (PTC) protocol data and MLE data

When using the assay for the first time:
With the external instrument barcode reader,
1. Scan the PTC barcode(s) at the end of the package insert. or downloadable from www.biomerieux.com/techlib. This reading allows VIDAS® PTC protocol data to be transferred to the instrument software for its update.
2. Scan the MLE data on the box label.

Note: If the MLE data have been read before the VIDAS® PTC protocol, read the MLE data again.

When opening a new lot of reagents:
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 only be entered once for each lot.

It is possible to enter MLE data **manually or automatically** depending on the instrument (refer to the User's 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 28 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 **triplicate** (see User's 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 "VCAG" strip and on "VCAG" SPR® for each sample, control or standard to be tested. **Make sure the storage pouch has been carefully resealed after the required SPRs have been removed.**
3. The test is identified by the "VCAG" code on the instrument. The standard must be identified by "S1" and tested in triplicate. If the positive control is to be tested, it should be identified by "C1". If the negative control needs 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 "VCAG" SPRs and "VCAG" strips into the instrument. Check to make sure the color labels with the assay code on the SPRs and the Reagent Strips match.
7. Initiate the assay as directed in the User's 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 results are obtained within approximately 40 minutes. After the assay is completed, remove the SPRs and strips from the instrument.
10. Dispose of the used SPRs and strips into an appropriate biohazard 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 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 RFV obtained for each sample is interpreted by the VIDAS system as follows:

Test value = patient RFV / standard RFV

This test value and the interpreted result are also included on the result sheet. The test value is interpreted as follows:

Test Value (TV)	Results
≤ 0.09	Negative
0.10 ≤ VT ≤ 0.20	Equivocal
≥ 0.21	Positive

IM diagnosis is based on the biological interpretation of test results taking into account the patient's history and the results of the other VIDAS EBV assays (VIDAS EBV EBNA IgG ref. 30 235 and VIDAS EBV VCA IgM ref. 30 237). Please refer to the VIDAS interpretation table on page 1 of this package insert.

It is advisable to check the equivocal results using a second specimen collected one or two weeks later.

QUALITY CONTROL

One positive control and one negative control are included in each VIDAS EBV VCA/EA IgG kit.
These controls must be performed immediately after opening a new kit to ensure that reagent performance has not been altered. Each calibration must 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

- Biological interpretation for the diagnosis of IM must be based on at least the results of the 3 VIDAS EBV assays (VIDAS EBV EBNA IgG ref. 30 235, VIDAS EBV VCA/EA IgG ref. 30 236 and VIDAS EBV VCA IgM ref. 30 237).
- In the presence of negative results for the 3 VIDAS markers and suspicion of IM, collect a second specimen one or two weeks later and test the two samples simultaneously.
- A positive VCA/EA IgG result (non-differentiated result) does not rule out a recent EBV infection if a negative result is obtained for the VCA IgM and EBNA IgG markers.
- In some cases, at the end of the acute phase of IM (transitional phase), isolated anti-VCA/EA IgG antibodies may be encountered (drop in anti-VCA IgM antibodies and late appearance of anti-EBNA IgG antibodies).
- A negative VIDAS EBV VCA/EA IgG result does not exclude the presence of antibodies directed against VCA P23 protein.
- In rare cases, anti-EBNA antibodies are not detected in seropositive subjects who have a past infection.
- In rare cases, only anti-EBNA antibodies are detected:
- in seropositive subjects who have a past infection,
- in children under 6 months of age (passive transfer of maternal anti-EBNA IgG antibodies),
- in transfused subjects.
- The performance characteristics of this test have not been established for use within the scope of blood donation.
- The performance characteristics of this test have not been established for immunocompromised or immunosuppressed patients (transplanted patients).
- This test has not been validated for use in the diagnosis of nasopharyngeal carcinoma (NPC).
- Certain negative samples may have a test value < 0.
- Cross reactivity or interference may be encountered with certain sera containing antibodies directed against reagent components. For this reason, assay results should be interpreted taking into consideration the patient's history and the results of the two other tests: VIDAS EBV VCA IgM and VIDAS EBV EBNA IgG.

USUAL VALUES

In Western countries, only 5% of adults are never affected by an EBV infection; thus, the antibodies characteristic of a past infection (EBNA and VCA IgG) reach a prevalence rate of 95%.

PERFORMANCE

Performance studies conducted using the VIDAS EBV VCA/EA IgG assay gave the following results:

Precision

Three samples were tested for 10 days in 2 runs per day and 2 replicates per run, with 2 reagent lots on 3 instruments (N = 240).

Mean index of negative sample varies between 0.00 and 0.01.

The **intra-run precision** (repeatability) and the **total precision intra-lot** (intra-run, inter-run, inter-day, inter-calibration, inter-instrument reproducibility) were calculated using this protocol, based on the recommendations of the **NCCLS/CLSI document EP5 A2, volume 24 number 25**.

Lot 1		Repeatability		Inter-run precision		Inter-instrument precision		Total precision	
Sample	Index	Standard deviation	CV (%)	Standard deviation	CV (%)	Standard deviation	CV (%)	Standard deviation	CV (%)
Sample 1	0.26	0.01	5.2	0.01	3.0	0.01	5.4	0.02	8.7
Sample 2	1.21	0.04	3.7	0.05	3.9	0.03	2.8	0.08	7.0

Lot 2		Repeatability		Inter-run precision		Inter-instrument precision		Total precision	
Sample	Index	Standard deviation	CV (%)	Standard deviation	CV (%)	Standard deviation	CV (%)	Standard deviation	CV (%)
Sample 1	0.26	0.02	5.8	0.01	2.0	0.01	3.5	0.02	7.5
Sample 2	1.23	0.05	4.2	0.02	1.8	0.00	0.0	0.07	5.8

Sensitivity - Specificity

Specificity and sensitivity performance was established on 2 lots of VIDAS EBV EBNA IgG reagent using 621 samples characterized for their EBV status (past infections, primary infections including 53 early-phase primary infections, seronegatives) and including 93 fresh serum samples. The status of the samples was determined on the basis of the available demographic (patient age) and clinical data, and the results obtained with the routine methods used by the expert site's laboratory.

	Reference populations for sensitivity calculation	Reference population for specificity calculation
VIDAS EBV VCA/EA IgG	Acute primary infections and past infections	Seronegatives

The following consolidated results were obtained:
The 21 samples were found to be equivocal with the VIDAS EBV VCA/EA IgG assay and were not taken into account for the sensitivity and specificity calculations.
The 53 samples characterized as early-phase primary infections were not taken into account for the total sensitivity calculation.

	Sensitivity				**Specificity**
Population	**Total sensitivity****	Early-phase primary infections**	Acute primary infections	Past infections	**Seronegatives**
Positive	**377**	25	120	257	**0**
Negative	**14**	19	9	5	**165**
Total*	**391**	44	129	262	**165**
%*	**96.42**	NA	93.02	98.09	**100**
95% confidence interval	**94.02 – 97.88**	NA	87.13 – 96.33	95.54 – 99.20	**97.63 - 100**

- *Equivocal results were not taken into account for the calculations.

** Early-phase primary infections are characterized by the presence of anti-VCA IgM and the absence of anti-VCA IgG with the EIA tests routinely used by the expert site.
NA: Not applicable

Concordance study

Comparison with two other EIA methods

A study was performed at an external site, using 526 samples, to establish the concordance between the VIDAS EBV VCA/EA IgG kit and two other automated EIA methods.

The discordances between the methods were analyzed on the basis of the EBV clinical status of the samples determined by the expert site, taking into consideration the patient's history and serological evolution.

		EA IgG and VCA IgG EIA			
		Positive	Equivocal	Negative	Total
VIDAS EBV VCA/EA IgG	Positive	302	1	15****	318
	Equivocal	12	0	9	21**
	Negative	6***	2	179	187
	Total*	308	3	194	
Concordance % *		95.82%			

*The equivocal results for each of the VIDAS and EIA assays were not taken into account for the calculations.
** Among the 21 samples, 1 is seronegative, 16 are primary infections and 4 are past infections.
*** The 6 samples are primary infections.
**** Among the 15 samples, 10 are primary infections and 5 are past infections.

Comparison with the clinical status of the specimen

A study was performed to establish the concordance between the EBV status defined by the expert site, and the global status obtained using the results of the 3 VIDAS EBV VCA/EA IgG, VIDAS VCA IgM and VIDAS EBNA IgG reagents. The clinical status of EBV and the global interpretations of the 3 VIDAS assays were defined by the expert site taking into consideration the patient's history and serological evolution.

		Reference serological status				
		Seronegatives	Total primary infections		Total past infections	
			Early-phase primary infections	Acute primary infections	Past infections	Isolated VCA IgG
VIDAS Serological status	Seronegatives	159	6	3	0	0
	Primary infections (early-phase and acute)	4	37	120	0	5
	Past infections	0	0	0	224	4
	Isolated VCA/EA IgG	0	5	3	7	12
	Isolated EBNA IgG	2	0	0	5	0
	Indeterminate	1	5	10	8	1
	Total*	165	48	126	236	21
Total concordance %*		92.62%				

*The indeterminate EBV statuses (4.03%) were not taken into account for the calculations.

CROSS REACTIVITY AND INTERFERENCES

Cross-reactivity

The notion of cross-reactivity is the study of samples which are negative for the test to be evaluated and positive for the potentially interfering pathology. The presence of these potentially interfering pathologies must not modify the interpretation of the evaluated test. The equivocal results were not taken into account for the analysis.
The results of the 136 samples tested are presented in the following table:

Pathology	Number of sera tested	Number of cross reactions	Number of equivocal results
Toxo IgG	10	0	1
CMV IgG	12	0	0
VZVG	30	0	0
HSV IgG	7	0	0
Rheumatoid factor	12	0	0
Rub IgG	7	0	0
HAMA	3	0	0
Parvo B19 IgG	17	0	0

Pathology	Number of sera tested	Number of cross reactions
HAVT	4	1
HHV6	8	0
HCV	5	0
HIV	4	0
HBsT	5	0
HBcT	5	0
HBs Ag	5	0
ANA	2	0

Among all the samples tested, only one sample with anti-HAV antibodies showed cross-reactivity with a weakly positive index (index = 0.21).

Interferences

The notion of interference is the study of samples which are positive for the test to be evaluated and positive for the potentially interfering pathology. The presence of these potentially interfering pathologies must not modify the interpretation of the evaluated test.
124 samples of potentially interfering pathologies (Toxo IgG, HBs Ag, Rub IgG, HBcT, HBsT, ANA+, HCV, HIV, CMV IgG, VZV IgG, HAVT, HSV IgG, FR, Parvo B19 IgG, HAMA and HHV6 IgG) with anti-VCA/EA IgG antibodies, were tested.
There was no change in the interpretation of the VIDAS EBV VCA/EA IgG test results.
No interference was observed with the VIDAS EBV VCA/EA IgG test.

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. Seigneurin JM. Infections à virus Epstein-Barr . Encycl Méd Chir (Editions Scientifiques et Médicales Elsevier SAS, Paris, tous droits réservés), Maladies infectieuses,8-070-K-10, 2001, 12 p.
2. Fafi-Kremer S., Seigneurin J-M., Morand P. La mononucléose infectieuse (MNI) "revisitée", Virologie 2007, 11: 13-26 p.
3. H.B. Jenson, Virologic Diagnosis, Viral Monitoring, and treatment of Epstein-Barr Virus Infectious Mononucleosis, Current Infectious Disease Reports, 2004, vol 6, p 200-207.
4. R.D. Hess, Routine Epstein Barr Virus Diagnostics from the Laboratory Perspective: still challenging after 35 years, Journal of Clinical Microbiology, 2004, vol 2, n° 8, p 3381-3387.
5. K.F.Macsween and D.H.Crawford, Epstein Barr virus – recent advances, The Lancet Infectious Diseases, 2003, vol 3, p 131-140.

INDEX OF SYMBOLS

Symbol	Meaning
REF	Catalog 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

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 LIABILITY 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.

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
2015/01	14120E	Administrative	INDEX OF SYMBOLS REVISION HISTORY
		Technical	CONTENT OF THE KIT (30 TESTS) WARNINGS AND PRECAUTIONS
2015/06	14120F	Technical	CONTENT OF THE KIT (30 TESTS) INSTRUCTIONS FOR USE
2016/05	14120G	Technical	CONTENT OF THE KIT (30 TESTS)

BIOMÉRIEUX
bioMérieux SA
376 Chemin de l'Orme
69280 Marcy-l'Etoile - France
673 620 399 RCS LYON
Tél. 33 (0)4 78 87 20 00
Fax 33 (0)4 78 87 20 90
www.biomerieux.com

CE