CE 1023

IVD

For Professional Use Only

# AmpliSens® *EBV / CMV / HHV6*-screen-FRT

PCR kit

## Instruction Manual

**AmpliSens®**

EC REP

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## 1. INTENDED USE

**AmpliSens® *EBV / CMV / HHV6*-screen-FRT** PCR kit is an *in vitro* nucleic acid amplification test for qualitative detection and quantification of *Epstein-Barr virus* (*EBV*) DNA, *Human Herpes Virus* type 6 (*HHV6*) DNA and *human cytomegalovirus* (*CMV*) DNA in clinical materials (whole human blood, white blood cells, viscera biopsy material, saliva, oropharyngeal swabs, and cerebrospinal fluid (liquor)) by using real-time hybridization-fluorescence detection.

The results of PCR analysis are taken into account in complex diagnostics of disease.

## 2. PRINCIPLE OF PCR DETECTION

*CMV, EBV* and *HHV6* detection by polymerase chain reaction (PCR) with hybridization-fluorescence detection includes DNA extraction from clinical samples and PCR amplification of pathogen genome specific region with real-time hybridization-fluorescence detection. During DNA extraction from clinical material, human genomic DNA (endogenous internal control) is amplified. Endogenous internal control (IC Glob) allows controlling both PCR-analysis stages (DNA extraction and PCR amplification), material sampling, and storage adequacy. Then, the obtained samples are amplified using specific primers and polymerase (TaqF). In real-time PCR, the amplified product is detected using fluorescent dyes. These dyes are linked to oligonucleotide probes which bind specifically to the amplified product during thermocycling. The real-time monitoring of the fluorescence intensities during the real-time PCR allows the detection of accumulating product without re-opening the reaction tubes after the PCR run. **AmpliSens® *EBV / CMV / HHV6*-screen-FRT** PCR kit uses “hot-start”, which greatly reduces the frequency of nonspecifically primed reactions. “Hot-start” is guaranteed by separation of nucleotides and Taq-polymerase by using a chemically modified polymerase (TaqF). Chemically modified polymerase (TaqF) is activated by heating at 95 ºC for 15 min.

## 3. CONTENT

**AmpliSens® *EBV / CMV / HHV6*-screen-FRT** PCR kit is produced in 1 form:

AmpliSens® *EBV / CMV / HHV6*-screen-FRT PCR kit variant FRT-100 F (for use with RG, Mx) **REF** R-V48(RG,iQ,Mx)-CE.

**AmpliSens® *EBV / CMV / HHV6*-screen-FRT** PCR kit variant FRT-100 F includes:

| *Reagent* | *Description* | *Volume, ml* | *Quantity* |
|---|---|---|---|
| **PCR-mix-1-FRT *EBV / CMV / HHV6* / Glob** | colorless clear liquid | 0.6 | 2 tubes |
| **PCR-mix-2-FRT** | colorless clear liquid | 0.3 | 2 tubes |
| **Polymerase (TaqF)** | colorless clear liquid | 0.03 | 2 tubes |
| **RNA-buffer** | colorless clear liquid | 0.6 | 1 tube |
| **DNA calibrator KSG1** | colorless clear liquid | 0.2 | 1 tube |
| **DNA calibrator KSG2** | colorless clear liquid | 0.2 | 1 tube |
| **Negative Control (C-)*** | colorless clear liquid | 1.2 | 2 tubes |
| **Positive Control DNA *EBV / CMV / HHV6* and human DNA**** | colorless clear liquid | 0.1 | 2 tubes |

* must be used in the extraction procedure as Negative Control of Extraction.

** must be used in the extraction procedure as Positive Control of Extraction (PCE).

AmpliSens® *EBV / CMV / HHV6*-screen-FRT PCR kit is intended for 110 reactions, including controls.

## 4. ADDITIONAL REQUIREMENTS

- DNA extraction kit.
- Disposable powder-free gloves and laboratory coat.
- Automated pipettors (dosers) of variable volumes (from 5 to 20 µl and from 20 to 200 µl).
- Disposable tips with aerosol barriers (100 or 200 µl) in tube racks.
- Tube racks
- Vortex mixer/desktop centrifuge.
- PCR box.
- Personal thermocyclers (for example, Rotor-Gene 3000 or Rotor-Gene 6000 (Corbett Research, Australia); Rotor-Gene Q (Qiagen, Germany) iQ5 and iCycler iQ (Bio-Rad, USA), Mx3000P (Stratagene, USA) or equivalent).
- Disposable polypropylene microtubes for PCR with 0.2 or 0.1 ml capacity (for example, Axygen, USA).
- Refrigerator for 2–8 °C.
- Deep-freezer for ≤ –16 °C.
- Waste bin for used tips.

## 5. GENERAL PRECAUTIONS

The user should always pay attention to the following:

- Use sterile pipette tips with aerosol barriers and use new tip for every procedure.
- Store and handle amplicons away from all other reagents.

- Thaw all components thoroughly at room temperature before starting detection.
- When thawed, mix the components and centrifuge briefly.
- Use disposable gloves, laboratory coats, protect eyes while samples and reagents handling. Thoroughly wash hands afterward.
- Do not eat, drink, smoke, apply cosmetics, or handle contact lenses in laboratory work areas.
- Do not use a kit after its expiration date.
- Dispose of all samples and unused reagents in compliance with local authorities requirements.
- Samples should be considered potentially infectious and handled in a biological cabinet in accordance with appropriate biosafety practices.
- Clean and disinfect all sample or reagent spills using a disinfectant, such as 0.5% sodium hypochlorite or another suitable disinfectant.
- Avoid contact with the skin, eyes and mucosa. If skin, eyes and mucosa contact, immediately flush with water, seek medical attention.
- Material Safety Data Sheets (MSDS) are available on request.
- Use of this product should be limited to personnel trained in the techniques of DNA amplification.
- The laboratory process must be one directional, it should begin in the Extraction Area and then move to the Amplification and Detection Areas. Do not return samples, equipment and reagents to the area in which the previous step was performed.

Some components of this kit contain sodium azide as a preservative. Do not use metal tubing for reagent transfer.

## 6. SAMPLING AND HANDLING

Obtaining samples of biological materials for PCR-analysis, transportation and storage is described in manufacturer's handbook [1]. It is recommended that this handbook is read before starting work.

**AmpliSens®** ***EBV* / *CMV* / *HHV6*-screen-FRT** PCR kit is intended for the analysis of DNA extracted by DNA extraction kits from whole human blood, white blood cells, viscera biopsy material, saliva, oropharyngeal swabs, and cerebrospinal fluid (liquor).

*Whole peripheral and umbilical blood*

Before extraction, it is necessary to pretreat blood. Transfer 1.0 ml of hemolytic (**REF** 137, it is manufactured by Federal Budget Institute of Science "Central Research Institute for Epidemiology") and 0.25 ml of whole blood to 1.5 ml Eppendorf-type tube using a new tip. Carefully mix the contents of the tube by vortexing and incubate it for 10 min under periodic stirring. Centrifuge tubes at 8,000 rpm for 2 min. Remove the supernatant with a vacuum

aspirator. Do not disturb the pellet. After washing, the pellet should be white. A small quantity of pinkish film above the pellet (erythrocyte debris) is allowed. Washing with hemolytic can be repeated if required. Thus obtained leukocyte pellet should be lysed immediately (in case of extraction with RIBO-prep, add 300 µl of Solution for Lysis and then isolate DNA according to the RIBO-prep instruction manual; do not add Solution for Lysis again). The pellet can be also stored at ≤ –68 °C for a long time.

*Packed white cells of peripheral and/or umbilical blood*

Packed white cells are obtained from peripheral and/or umbilical blood. Blood can be stored for 6 hours after sampling at room temperature. To obtain white cells, centrifuge blood at 800–1,600 g (3,000 rpm) for 20 min. Then, collect the white film formed on the surface of the supernatant and pretreat it as described for whole peripheral and umbilical blood. White cells of peripheral and umbilical blood can be stored at temperature ≤ –68 °C for a long time.

## 7. WORKING CONDITIONS

**AmpliSens® *EBV / CMV / HHV6*-screen-FRT** PCR kit should be used at 18–25 °C.

## 8. PROTOCOL

### 8.1. DNA Extraction

It is recommended to use the following nucleic acid extraction kits:

- RIBO-prep, **REF** K2-9-Et-100-CE.
- DNA-sorb-B, **REF** K1-2-100-CE.
- DNA-sorb-C, **REF** K1-6-100-CE (for viscera biopsy material).

Extract DNA according to the manufacturer's instructions.

Transfer **100 µl** of **Negative Control** to the tube labeled C–. Transfer **90 µl** of **Negative Control** and **10 µl** of **Positive Control DNA *EBV / CMV / HHV6* and human DNA** to the tube labeled PCE.

### 8.2. Preparing the PCR

Total reaction volume is **25 µl**, the volume of DNA sample is **10 µl**.

#### 8.2.1 Preparing tubes for PCR

1. Prepare the mixture of **PCR-mix-2-FRT** and **polymerase (TaqF)**. For this purpose transfer the content of the tube with **polymerase (TaqF) (30 µl)** into the tube with **PCR-mix-2-FRT (300 µl)** and mix by vortexing without foam forming. Mark the tube by the date of mixture preparation.

The prepared mixture is intended for analysis of 60 samples. The mixture is to be stored at 2–8 ºC for 3 months. Use when needed.

If the mixture cannot be used up for 3 months, prepare the mixture for a smaller number of reactions. For example, mix **150 µl of PCR-mix-2-FRT** and **15 µl of polymerase (TaqF).** The obtained mixture is intended for 30 reactions.

2. Prepare the reaction mixture. Note that for analysis of even one test DNA sample in the qualitative format, it is necessary to run two controls of PCR amplification stage: positive control (KSG2) and negative control of amplification (RNA-buffer). For analysis of even one DNA sample in the quantitative format, it is necessary to run five controls of PCR stage: two DNA calibrators (KSG1 and KSG2) in two replicates and the negative control of amplification (RNA-buffer). In addition, reagents should be taken for one extra reaction.
3. Mix **PCR-mix-1-FRT *EBV* / *CMV* / *HHV6* / Glob** and the mixture of **PCR-mix-2-FRT** and **polymerase (TaqF)** prepared before in an individual tube in the following proportion:
   - **10 µl of PCR-mix-1-FRT *EBV* / *CMV* / *HHV6* / Glob,**
   - **5 µl of PCR-mix-2-FRT and polymerase (TaqF).**

   To calculate the required number of reaction including test and control samples, see Appendix 1.
4. Take the required number of tubes for amplification of test and control DNA samples. Transfer **15 µl** of the prepared mixture to each tube.
5. Add **10 µl** of **DNA** obtained from clinical or control samples to the tubes with the reaction mixture.
6. <u>For qualitative analysis:</u>

**NCA** - Add **10 µl** of **RNA-buffer** to the tube labeled NCA (Negative Control of Amplification).

**C+** - Add **10 µl** of DNA calibrator **KSG2** to the tube labeled C+ (Positive Control of Amplification).

<u>For quantitative analysis:</u>

**NCA** - Add **10 µl** of **RNA-buffer** to the tube labeled NCA (Negative Control of Amplification).

**Calibrators KSG1 and KSG2** - Add **10 µl** of **KSG1** to two tubes and add **10 µl** of **KSG2** to other two tubes

### 8.2.2. Amplification

1. Program the thermocycler according to **Manufacturer's manual**, **Guidelines,** and Tables 1 and 2.
2. Create a temperature profile on your instrument as follows:

Table 1

**AmpliSens-1 program[1] for rotor-type instruments**

| *Step* | *Temperature, °C* | *Time* | *Fluorescence detection* | *Cycles* |
|---|---|---|---|---|
| Hold | 95 | 15 min | – | 1 |
| Cycling 1 | 95 | 5 s | – | 5 |
| | 60 | 20 s | – | |
| | 72 | 15 s | – | |
| Cycling 2 | 95 | 5 s | – | 40 |
| | 60 | 20 s | FAM/Green, JOE/Yellow, ROX/Orange, Cy5/Red | |
| | 72 | 15 s | – | |

Table 2

**AmpliSens-1 program[2] for plate-type instruments**

| *Step* | *Temperature, °C* | *Time* | *Fluorescence detection* | *Cycles* |
|---|---|---|---|---|
| 1 | 95 | 15 min | – | 1 |
| 2 | 95 | 5 s | – | 5 |
| | 60 | 20 s | – | |
| | 72 | 15 s | – | |
| 3 | 95 | 5 s | – | 40 |
| | 60 | 30 s | FAM, JOE, ROX, Cy5 | |
| | 72 | 15 s | – | |

Fluorescence is detected at the 2nd step **(60°C)** in FAM/Green, JOE/Yellow, ROX/Orange, and Cy5/Red fluorometer channels.

## 9. DATA ANALYSIS

β-Globin gene DNA (IC Glob) is detected in the FAM/Green channel, *EBV* DNA is detected in the JOE/HEX/Yellow channel, *CMV* DNA is detected in the ROX/Orange channel, and *HHV6* DNA is detected in the Cy5/Red channel.

### Interpretation of results

The results are interpreted by the software of the used Instrument by the crossing (or not) of the fluorescence curve with the threshold line.

1. The sample is considered to be **positive** for *EBV* DNA if its Ct value in the results grid in the JOE/HEX/Yellow channel is detected and does not exceed the threshold value of positive result.
2. The sample is considered to be **positive** for *CMV* DNA if its Ct value in the results grid in the ROX/Orange channel is defined and does not exceed the threshold value of positive result.
3. The sample is considered to be **positive** for *HHV6* DNA if its Ct value in the results grid in the Cy5/Red channel is defined and does not exceed the threshold value of positive result.

[1] For example, Rotor-Gene 3000 and Rotor-Gene 6000 (Corbett Research, Australia) or equivalent
[2] For example, iCycler iQ, iQ5 (Bio-Rad, USA), Mx3000P (Stratagene, USA) or equivalent.

4. For qualitative analysis, the sample is considered to be **negative** for *EBV* DNA if its Ct value is not detected in the results grid (the fluorescence curve does not cross the threshold line) in the JOE/Yellow/HEX channel; the sample is considered to be **negative** for *CMV* DNA if its Ct value is not detected in the results grid (the fluorescence curve does not cross the threshold line) in the ROX/Orange channel; and the sample is considered to be **negative** for *HHV6* DNA if its Ct value is not detected in the results grid (the fluorescence curve does not cross the threshold line) in Cy5/Red channel provided that the Ct value in the results grid in the FAM/Green channel does not exceed the Ct value indicated in the **Important Product Information Bulletin**. For quantitative analysis, the quantity of IC Glob DNA should be greater than 2000 copies per reaction for whole blood, white blood cells, viscera biopsy material or more than 500 copies per reaction for saliva and oropharyngeal swabs.

For cerebrospinal fluid (liquor), the Ct value can be greater than the Ct value indicated in the **Important Product Information Bulletin** in the results grid in the FAM/Green channel or the quantity of IC Glob DNA can be less than 500 copies per reaction in case of quantitative analysis because the cerebrospinal fluid samples may contain a very small number of cells.

5. For **qualitative** analysis, the result of analysis is considered to be **invalid** if the Ct value is not detected in the results grid (the fluorescence curve does not cross the threshold line) or if it is greater than the threshold value in the JOE/HEX/Yellow, ROX/Orange, or Cy5/Red channel and the Ct value in the results grid in the FAM/Green channel exceeds the Ct value indicated in the **Important product information bulletin**. For **quantitative** analysis, the analysis result is considered to be **invalid** if the Ct value is not detected in the results grid (the fluorescence curve does not cross the threshold line) or if it is greater than the boundary value in the JOE/Yellow/HEX, ROX/Orange, or Cy5/Red channel and the quantity of IC Glob DNA is less than 2000 copies per reaction for whole blood, white blood cells, viscera biopsy material or if it is less than 500 copies per reaction for saliva and oropharyngeal swabs. In such cases, PCR analysis of the sample should be repeated.

For **qualitative** analysis, if the Ct value in the FAM/Green channel exceeds the Ct value indicated in the **Important Product Information Bulletin,** the negative result is considered to be **invalid**.

For **quantitative** analysis, if the quantity of IC Glob DNA is less than 2000 copies per reaction for whole blood, white blood cells, and viscera biopsy material or if it is less than 500 copies per reaction for saliva and oropharyngeal swabs, the quantitative positive or negative result is considered to be **invalid**.

For qualitative analysis, results of analysis are considered reliable only if the results obtained for both Positive and Negative Controls of amplification as well as for the Negative Control of extraction are correct. For quantitative analysis, results on C+ should fall in range of

concentrations indicated in the **Important Product Information Bulletin.**

**Results for controls in qualitative analysis**

| Control | Stage for control | Ct in channel | | | | Interpre-tation |
|---|---|---|---|---|---|---|
| | | FAM/Green | JOE/HEX/ Yellow | ROX/Orange | Cy5/Red | |
| **C-** | DNA extraction, Amplification | Neg | Neg | Neg | Neg | OK |
| **PCE** | DNA extraction, Amplification | Ct value < threshold | Ct value < threshold | Ct value < threshold | Ct value < threshold | OK |
| **NCA** | Amplification | Neg | Neg | Neg | Neg | OK |
| **C+ (for qualitative analysis)** | Amplification | Ct value < threshold | Ct value < threshold | Ct value < threshold | Ct value < threshold | OK |

**Results for controls in quantitative analysis**

| Control | Stage for control | Ct in channel | | | | Interpre-tation |
|---|---|---|---|---|---|---|
| | | FAM/Green | JOE/HEX/ Yellow | ROX/Orange | Cy5/Red | |
| **C-** | DNA extraction, Amplification | Neg | Neg | Neg | Neg | OK |
| **PCE** | DNA extraction, Amplification | Ct value < threshold | Ct value is in the range indicated in the Bulletin | Ct value is in the range indicated in the Bulletin | Ct value is in the range indicated in the Bulletin | OK |
| **NCA** | Amplification | Neg | Neg | Neg | Neg | OK |
| **KSG1, KSG2** | Amplification | Ct value and calculated concentration are determined | Ct value and calculated concentration are determined | Ct value and calculated concentration are determined | Ct value and calculated concentration are determined | OK |

**In quantitative analysis, if total DNA is extracted from human whole blood, white blood cells, and viscera biopsy material, the concentration in log of DNA copies per standard cell quantity ($10^5$) in control and test samples is calculated by the following formula:**

**For *CMV*:**

$$\log\left\{\frac{\textit{CMV}\text{ DNA copies in PCR sample}}{\text{Glob DNA copies in PCR sample}} \times 2*10^5\right\} = \log\{\textit{CMV}\text{ DNA copies}/10^5\text{ of cells}\}.$$

**For *EBV*:**

$$\log\left\{\frac{\textit{EBV}\text{ DNA copies in PCR sample}}{\text{Glob DNA copies in PCR sample}} \times 2*10^5\right\} = \log\{\textit{EBV}\text{ DNA copies}/10^5\text{ of cells}\}.$$

**For *HHV6*:**

$$\log\left\{\frac{\textit{HHV6}\text{ DNA copies in PCR sample}}{\text{Glob DNA copies in PCR sample}} \times 2*10^5\right\} = \log\{\textit{HHV6}\text{ DNA copies}/10^5\text{ of cells}\}.$$

**If total DNA is extracted from saliva, oropharyngeal swabs, and cerebrospinal fluid (liquor), the concentration of DNA per ml of sample ($К_{P\ DNA}$) is calculated by the following formula:**

$$К_{P\ DNA} = К_{DNA} \times 100 \text{ (copies/ml)}$$

**$К_{DNA}$ is the number of *EBV* DNA copies, or the number of *CMV* DNA copies, or the number of *HHV6* DNA copies in DNA sample.**

## 10. TROUBLESHOOTING

Results of analysis are not taken into account in the following cases:

1. The presence of any Ct value in JOE/Yellow/HEX, FAM/Green, ROX/Orange and Cy5/Red channels in the results grid for the Negative Control of Amplification (NCA) and for the Negative Control of Extraction (C–) in the JOE/Yellow/HEX channel indicates contamination of reagents or samples. In this case, PCR analysis should be repeated for all samples in which pathogen DNA was detected starting from the DNA extraction stage.
2. If, for qualitative analysis, the Ct value in the results grid for the Positive Control of Amplification (KSG2) in the JOE/Yellow/HEX, FAM/Green, ROX/Orange, or Cy5/Red channels is absent, it is necessary to repeat amplification for all samples where pathogen DNA was not detected.
3. If the Ct value in the results grid for Positive Control of Extraction (Positive Control DNA *EBV* / *CMV* / *HHV6* and human DNA) in JOE/Yellow/HEX, FAM/Green, ROX/Orange, or Cy5/Red channels is absent, the results of analysis for all samples are considered to be **invalid**. It is necessary to repeat PCR analysis for such samples.
4. If the Ct value for the sample is not detected in JOE/Yellow/HEX, ROX/Orange, or Cy5/Red channel or it exceeds the boundary Ct value specified in the **Important product information bulletin** and the Ct value for the sample is greater than the maximum Ct value for IC in the FAM/Green channel, analysis should be repeated starting from the DNA extraction stage. This error may be foe to incorrect treatment of clinical material, which resulted in the loss of DNA, or to the presence of PCR inhibitors.
5. If the Ct value for the sample is detected in JOE/Yellow/HEX, ROX/Orange, or Cy5/Red channel and it is greater than the boundary Ct value specified in the **Important product information bulletin,** the result is considered to be **equivocal**. It is necessary to repeat analysis of such sample in duplicate. If a reproducible positive Ct value is obtained, the result is considered to be **positive;** otherwise, the result is considered to be **equivocal**.

If you have any further questions or if encounter problems, please contact our Authorized representative in the European Community.

## 11. TRANSPORTATION.

**AmpliSens® *EBV / CMV / HHV6*-screen-FRT** PCR kit should be transported at 2–8 ºC for no longer than 5 days.

## 12. STABILITY AND STORAGE

All components of the **AmpliSens® *EBV / CMV / HHV6*-screen-FRT** PCR kit (except for PCR-mix-1-FRT *EBV* / *CMV* / *HHV6* / Glob, PCR-mix-2-FRT, and Polymerase (TaqF)) are to be stored at 2–8 ºC when not in use. All components of the **AmpliSens® *EBV / CMV / HHV6*-screen-FRT** PCR kit are stable until the expiration date on the label. The shelf life of reagents before and after the first use is the same, unless otherwise stated.

PCR-mix-1-FRT *EBV* / *CMV* / *HHV6* / Glob, PCR-mix-2-FRT, and Polymerase (TaqF) are to be stored at temperature from minus 24 to minus 16 ºC when not in use.

PCR-mix-1-FRT *EBV* / *CMV* / *HHV6* / Glob is to be kept away from light.

## 13. SPECIFICATIONS

### 13.1. Sensitivity

The analytical sensitivity of **AmpliSens® *EBV / CMV / HHV6*-screen-FRT** PCR kit is specified in the table below.

| Type of clinical material | Nucleic acid extraction kit | Sensitivity |
|---|---|---|
| Cerebrospinal fluid (liquor), saliva, oropharyngeal swabs, and lavages | RIBO-prep | 400 copies/ml |
| Whole human blood, white blood cells, viscera biopsy material | RIBO-prep | 5 DNA copies per $10^5$ cells |

### 13.2. Specificity

**AmpliSens® *EBV / CMV / HHV6*-screen-FRT** PCR kit is intended for *Epstein-Barr virus* (*EBV*) DNA, *Human Herpes Virus* type 6 (*HHV6*) DNA and *human cytomegalovirus* (*CMV*) DNA detection. Specific activity of **AmpliSens® *EBV / CMV / HHV6*-screen-FRT** PCR kit was confirmed by analysis of reference *CMV* strain AD 169, QCMD panel for *Epstein-Barr virus,* as well as by analysis of clinical material with subsequent confirmation of results by sequencing the amplified fragments. The activity of the PCR kit components with respect to DNA of other viruses (herpes simplex virus types 1 and 2, human herpes virus type 8, Varicella Zoster Virus, Parvovirus B19, and others), bacterial pathogens (*Staphylococcus aureus, Streptococcus pyogenes, Streptococcus agalactiae,* and others) and human DNA was absent. The clinical specificity of **AmpliSens® *EBV / CMV / HHV6*-screen-FRT** PCR kit was confirmed in laboratory clinical trials.

## 14. REFERENCES


1. Handbook “Sampling, Transportation, and Storage of Clinical Material for PCR Diagnostics”, developed by Federal Budget Institute of Science “Central Research Institute for Epidemiology” of Federal Service for Surveillance on Consumers’ Rights Protection and Human Well-Being, Moscow, 2008.
2. Guidelines “Real-Time Fluorescence PCR Detection and Quantitation of *Epstein-Barr virus* (*EBV*) DNA, *Human Herpes Virus* type 6 (*HHV6*) DNA and *human cytomegalovirus* (*CMV*) DNA in Various Clinical Samples”.


## 15. QUALITY CONTROL

In compliance with Federal Budget Institute of Science “Central Research Institute for Epidemiology” ISO 13485-Certified Quality Management System, each lot of **AmpliSens®** ***EBV / CMV / HHV6*-screen-FRT** PCR kit has been tested against predetermined specifications to ensure consistent product quality.

## 16. KEY TO SYMBOLS USED

| | | | |
|---|---|---|---|
| REF | Catalogue number | Σ | Sufficient for |
| LOT | Batch code | | Expiration Date |
| IVD | *In vitro* diagnostic medical device | | Consult instructions for use |
| VER | Version | | Keep away from sunlight |
| | Temperature limitation | **NCA** | Negative control of amplification |
| | Manufacturer | **C–** | Negative control of extraction |
| | Date of manufacture | **C+** | Positive control of amplification |
| EC REP | Authorised representative in the European Community | **PCE** | Positive Control of Extraction |
| | Caution | | |

**List of Changes Made in the Instruction Manual**

| VER | Location of changes | Essence of changes |
|---|---|---|
| 23.06.11 RT | Cover page, text | The name of Institute was changed to Federal Budget Institute of Science “Central Research Institute for Epidemiology” |