Indications: Test system for the in vitro determination of antibodies against EBV-CA in human serum or plasma for the diagnosis of the following diseases: infectious mononucleosis, Burkitt's lymphoma, nasopharyngeal carcinoma.

Clinical significance: Epstein-Barr virus (EBV) is the causative agent of infectious mononucleosis, a febrile illness which is in most cases associated with pharyngitis and lymphadenopathy, frequently also with hepatosplenomegaly and more rarely with exanthema. EBV infections are also connected with the pathogenicity of Burkitt's lymphoma and nasopharyngeal carcinoma, as well as the occurrence of lymphomas in HIV infections or after organ transplants. In pregnancy Epstein-Barr virus can cause infection of the placenta with damage to the foetal heart, eyes and liver. In children, accompanying infections of the kidney have been observed with symptoms from microscopic haematuria to acute kidney failure.

The immune system reacts to an EBV infection by first producing antibodies of class IgM and then of class IgG against the EBV capsid antigen (EBV-CA). In more than 90% of patients with an acute EBV infection low-avidity IgG antibodies against EBV-CA can be found during the first 10 days after the onset of symptoms. After 30 days, 50% of patients still exhibit these antibodies. Antibodies against early EBV antigens (EBV-EA) occur in 70-80% of patients with infectious mononucleosis. High anti-EBV-EA titers indicate a chronic or reactivated infection. They are also found in association with Burkitt's lymphoma and nasopharyngeal carcinoma. The EBV nuclear antigens (EBNA-1 to -6) are synthesised earlier after infection than the other EBV antigens (EBV-CA and EBV-EA). However, they are presented to the immune system only after the destruction of B cells, so that, time-wise, antibodies against EBV-CA and EBV-EA are detectable before antibodies against EBNA. Antibodies against EBNA-1 are generally only detectable during the late phase of EBV infection.

Application of the Anti-EBV-CA ELISA: Infectious mononucleosis must be differentiated from cytomegalic inclusion body disease and toxoplasmosis and, in the case of atypical progress, also from HIV or other infections. Since direct evidence of the virus is difficult to obtain, serological parameters routinely serve as diagnostic markers. Parallel determination of antibodies against EBV-CA, EBV-EA, and EBNA-1 not only allows differentiation between acute and past EBV infections, but also provides evidence of chronicity or the presence of reactivation. For determination of antibodies against EBV-CA, EBV-EA, and EBNA-1, indirect immunofluorescence is considered the gold standard. If large groups of patients are being investigated, EUROIMMUN Anti-EBV-CA ELISA, Anti-EBV-EA-D, and Anti-EBNA-1 ELISA show a very good correlation with the indirect immunofluorescence test (IIFT). Serologically difficult patterns, such as persistent anti-EBV-CA IgM antibodies or the absence of specific anti-EBV-CA IgM antibodies in fresh infections, can be clarified by measuring the avidity of anti-EBV-CA IgG antibodies (e.g. by EUROIMMUN Anti-EBV-CA ELISA (IgG), order no. EI 2791-9601-1 G). EBV infections of the CNS can be diagnosed by detecting anti-EBV-CA antibodies of class IgG in the cerebrospinal fluid (CSF) (e.g. using the EUROIMMUN Anti-EBV-CA ELISA with CSF calibrators, order no. EI 2791-9601-L G).
Test Characteristics

**Anti-EBV-CA ELISA (IgG)**

**Linearity:** The linearity of the ELISA was determined by assaying serial dilutions of patient samples with high antibody concentrations. The anti-EBV-CA ELISA (IgG) is linear in the measurement range 2-200 RU/ml.

**Reproducibility:** The reproducibility of the test was investigated by determining the intra- and inter-assay coefficients of variation (CV) using three sera. The intra-assay CVs are based on 20 measurements for each serum and the inter-assay CVs on four measurements repeated on six different days.

**Reference range:** Levels of anti-EBV-CA antibodies were analysed in a group of 500 healthy blood donors using the EUROIMMUN ELISA. With a cut-off value of 20 RU/ml, 93.4% of the blood donors were anti-EBV-CA positive (IgG), in agreement with the known infection level in adults.

**Sensitivity and specificity:** 111 clinically and serologically precharacterised sera were analysed using the EUROIMMUN Anti-EBV-CA ELISA (IgG). The ELISA showed a sensitivity and specificity of 100% (borderline results were excluded).

**Technical data:**

- **Antigen:** The reagent wells were coated with a mixture of purified Epstein-Barr virus capsid antigens (EBV-CAs: gp22, gp33, gp40, gp41, gp42, gp65 and gp116) for high diagnostic sensitivity. The antigen source is a cell lysate of human B cells infected with Epstein-Barr virus strain P3HR1.

- **Calibration:** Quantitative, in relative units per ml (RU/ml).
  - Calibration serum 1: 200 RU/ml
  - Calibration serum 2: 20 RU/ml; cut-off value
  - Calibration serum 3: 2 RU/ml

- **Sample dilution:** Serum or plasma; 1:101 in sample buffer.

- **Reagents:** Ready to use, with the exception of the wash buffer (10x). Color-coded solutions, in most cases exchangeable with those in other EUROIMMUN ELISA kits.

- **Test procedure:** 30min/30min/15min. Room temperature. Fully automatizable.

- **Measurement:** 450 nm. Reference wavelength >620 nm.

- **Kit format:** 96 break-off wells.

- **Order no.:** EI 2791-9601 G

**EUROIMMUN Immunoassays**

**Autoantibody determination:**

- **EUROASSAY:**
  - flexible profiles of up to 10 antigens from: ENA and related antigens: nRNP/Sm, Sm, SS-A, SS-B, RNP/Scl, Jo-1, CENP B, Histones, nucleosomes, ENA B, PML/Scl, ribosomal ribonucleoproteins.
  - liver antigens: LKM-1, LPL, ANA Profile 1: nRNP/Sm, Sm, SS-A, Ro-52, SS-B, Scl-70, PM-Scl, Jo-1, CENP B, Histones, nucleosomes, ribosomal ribonucleoproteins, ANA M2.
  - Anti-ENA Profile 1: nRNP/Sm, Sm, SS-A, Ro-52, SS-B, Scl-70, Jo-1, CENP B, Histones, nucleosomes, ribosomal ribonucleoproteins, ANA M2.

- **EUROLINE-WB:**
  - ANCA Profiles: MPO, PR3, GBM, GD1a, GD1b, GT1b, GQ1b.
  - Anti-Ganglioside Profile 1: GM1, GD1b, GQ1b.
  - Anti-Ganglioside Profile 2: GM1, GM2, GM3.
  - ANCA Profiles: MPO, PR3, GBM.

- **EUROLINE:**
  - ANCA antigens: MPO, PR3, M2, M4, M9.
  - liver antigens: LKM-1, LC-1, SLA/LP, PM-Scl, ribosomal P-proteins, AMA M2.

- **EUROASSA Y:**
  - Inhalation Profile (IgE).
  - Food Profile (IgE).

- **EUROIMMUN Allergology:**
  - Treponema pallidum + cardiolipin.
  - Helicobacter pylori (VacA, Cag A; IgA, IgG).

- **EUROIMMUN Infection serology:**
  - EBV Profile (IgG).

- **EUROIMMUN Autoantibody determination:**
  - Radioimmunoassays.

- **Reagents Ready to use,** with the exception of the wash buffer (10x). Color-coded solutions, in most cases exchangeable with those in other EUROIMMUN ELISA kits.

- **Test procedure:** 30min/30min/15min. Room temperature. Fully automatizable.

- **Measurement:** 450 nm. Reference wavelength >620 nm.

- **Kit format:** 96 break-off wells.

- **Order no.:** EI 2791-9601 G

**Technical data:**

- **Antigen:** The reagent wells were coated with a mixture of purified Epstein-Barr virus capsid antigens (EBV-CAs: gp22, gp33, gp40, gp41, gp42, gp65 and gp116) for high diagnostic sensitivity. The antigen source is a cell lysate of human B cells infected with Epstein-Barr virus strain P3HR1.

- **Calibration:** Quantitative, in relative units per ml (RU/ml).
  - Calibration serum 1: 200 RU/ml
  - Calibration serum 2: 20 RU/ml; cut-off value
  - Calibration serum 3: 2 RU/ml

- **Sample dilution:** Serum or plasma; 1:101 in sample buffer.

- **Reagents:** Ready to use, with the exception of the wash buffer (10x). Color-coded solutions, in most cases exchangeable with those in other EUROIMMUN ELISA kits.

- **Test procedure:** 30min/30min/15min. Room temperature. Fully automatizable.

- **Measurement:** 450 nm. Reference wavelength >620 nm.

- **Kit format:** 96 break-off wells.

- **Order no.:** EI 2791-9601 G