Dengue Virus NS1 ELISA

- Important tool for the detection of acute dengue virus infections: reliable alternative to other direct pathogen detection methods such as RT-PCR
- Highly sensitive detection of all four dengue virus serotypes
- Highest specificity owing to neutralisation of HAMA (human anti-mouse antibodies) and other heterophilic antibodies

Technical data

**Antibody**
Monoclonal mouse anti-dengue virus NS1, specifically directed against dengue virus NS1 of serotypes 1 to 4

**Calibration**
Quantitative, in relative units per millilitre (RU/ml)
- Calibration serum 1: 100 RU/ml
- Calibration serum 2: 10 RU/ml
- Calibration serum 3: 1 RU/ml

Recommended upper threshold of the reference range for non-infected individuals (cut-off): 10 RU/ml

**Sample dilution**
Serum or plasma, 1:2 in sample buffer

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

**Test procedure**
60 min (37°C) / 60 min (37°C) / 15 min (room temperature), fully automatable

**Measurement**
450 nm, reference wavelength between 620 nm and 650 nm

**Test kit format**
96 break-off wells; kit includes all necessary reagents

**Order no.**
EQ 266a-9601-1

Clinical significance

Dengue viruses (DENV) belong to the flavivirus family. Dengue fever is the most frequent and the most rapidly spreading vector-borne viral infection in humans. Four different dengue virus serotypes exist (DENV1 to DENV4). Vectors of these viruses are mosquitoes of the Aedes species (A. aegypti, A. albopictus); reservoir hosts are primates and particularly humans. DENV are mainly found in Latin America, Central Africa, India, South East Asia and in some parts of the Pacific islands. The fever is also regularly introduced to Europe. Infections with dengue virus may cause a broad spectrum of diseases. The classic dengue fever is a self-limiting, short-term disease which is accompanied by high fever of over 40°C, severe headache, muscle and joint pains, exanthema and lymph node swellings. The symptoms usually persist for 2–7 days. There is no specific treatment with antiviral medication. Therefore, only the symptoms are treated. Primary infections usually have a mild course. Following an infection, life-long immunity exists against the respective serotype. Cross immunity against other serotypes is only partly present and is transient. In secondary infection with another virus serotype the risk of a severe disease course increases. This may result in dengue haemorrhagic fever (DHF) and/or dengue shock syndrome (DSS). DHF expresses itself in the form of distinct haemorrhagic symptoms such as petechiae, black and tar-like stool, nose and skin bleeds. Complications such as circulatory disturbances and even shock can occur. The lethality rate of DHF is on average 12%. 

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Time [days]</th>
</tr>
</thead>
<tbody>
<tr>
<td>NS1 IgM</td>
<td>0 10 20 30 40 50</td>
</tr>
<tr>
<td>IgG</td>
<td>0 10 20 30 40 50</td>
</tr>
</tbody>
</table>

**Primary infection**
- Symptoms

**Secondary infection**
- Symptoms

![Antibody titers](image)
Diagnostic application

The detection of the highly specific dengue NS1 antigen is possible in the serum of dengue virus-infected persons from the onset of clinical symptoms in primary as well as in secondary infections. Therefore, this antigen detection is an important tool for diagnosis of acute dengue virus infections. The parallel investigation of specific antibodies is recommended.

Reference range

A panel of 150 healthy blood donors was investigated with the Dengue Virus NS1 ELISA. With a cut-off of 10 RU/ml no blood donor was dengue virus NS1-positive.

Reproducibility

The reproducibility of the test was investigated by determining the intra- and inter-assay coefficients of variation using three samples. The intra-assay CVs are based on 20 determinations and the inter-assay CVs on three determinations performed in ten different test runs.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Intra-assay variation, n = 20</th>
<th>Inter-assay variation, n = 3 x 10</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean value (RU/ml)</td>
<td>CV (%)</td>
</tr>
<tr>
<td>1</td>
<td>9</td>
<td>3.1</td>
</tr>
<tr>
<td>2</td>
<td>29</td>
<td>3.2</td>
</tr>
<tr>
<td>3</td>
<td>37</td>
<td>2.8</td>
</tr>
</tbody>
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Quality assessment results

51 clinically precharacterised patient samples from a quality assessment institute (INSTAND e.V., Germany) were tested using the EUROIMMUN Dengue Virus NS1 ELISA. The results showed an agreement of 100% with the quality assessment results.

Sensitivity and specificity

413 precharacterised patient samples (reference method: commercially available ELISA from another manufacturer) were investigated using the EUROIMMUN Dengue Virus NS1 ELISA. The sensitivity was 99%, with a specificity of 98% (borderline sera excluded).

In order to evaluate the specificity of the Dengue Virus NS1 ELISA, another study with 69 patient samples was performed, which were seropositive for rheumatoid factors, heterophilic autoantibodies or HAMA (human anti-mouse antibodies). The specificity in this panel amounted to 99%.

Cross reactivity

The quality of the antibodies used guarantees a high specificity of the ELISA. Sera from patients with flavivirus infections or recent vaccinations against various flaviviruses were investigated with the EUROIMMUN Dengue Virus NS1 ELISA. Cross reactivity to other flaviviruses can be excluded in all likelihood.

<table>
<thead>
<tr>
<th>Antibodies against</th>
<th>n</th>
<th>Dengue Virus NS1 ELISA positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>TBE virus (TBEV)</td>
<td>10</td>
<td>0 %</td>
</tr>
<tr>
<td>Yellow fever virus (YFV)</td>
<td>10</td>
<td>0 %</td>
</tr>
<tr>
<td>Japanese encephalitis virus (JEV)</td>
<td>4</td>
<td>0 %</td>
</tr>
<tr>
<td>West Nile virus (WNV)</td>
<td>4</td>
<td>0 %</td>
</tr>
<tr>
<td>Zika virus (ZIKV)</td>
<td>5</td>
<td>0 %</td>
</tr>
</tbody>
</table>