CE-marked test systems for direct detection of the new coronavirus as well as for serological analysis following SARS-CoV-2 infection or COVID-19 vaccination

Differentiated analysis of the immune response to SARS-CoV-2 possible: quantification of IgG, detection of neutralising antibodies and determination of the activity of reactive T cells

ELISA-based Anti-SARS-CoV-2 IgG antibody diagnostics with serum or dried blood spots (DBS)

Suitable automation solutions for all laboratory sizes
SARS-CoV-2

SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) is the causative pathogen of COVID-19 (coronavirus disease 2019) and is mainly transmitted via virus-containing aerosols during speaking, breathing, coughing and sneezing. The incubation time of SARS-CoV-2 is three to seven, maximally 14 days. The infection can proceed asymptotically or cause symptoms of a febrile diseases with irregular lung infiltrates. Some patients, especially elderly or chronically ill patients, develop acute respiratory distress syndrome (ARDS).

COVID-19 diagnostics – the complete package from EUROIMMUN

Suitable methods for the diagnosis of acute SARS-CoV-2 infections are the detection of viral RNA by reverse transcriptase polymerase chain reaction (RT-PCR) or of virus protein by means of ELISA in sample material from the upper (naso- and oro-pharyngeal swabs) or lower respiratory tract (bronchoalveolar lavage fluid, tracheal secretion, sputum, etc.). The determination of antibodies enables confirmation of SARS-CoV-2 infection in patients with typical symptoms and in suspected cases. It also contributes to outbreak control. The detection of SARS-CoV-specific T cells also supports the identification of a past pathogen contact. Moreover, results from serological tests can provide answers to important epidemiological, clinical and virological questions concerning SARS-CoV-2, such as traceability of infection chains and the role of asymptomatic or pre-symptomatic transmission. Furthermore, they can be relevant for the development of vaccines against SARS-CoV-2 and for determination of the antibody status and assessment of the humoral and cellular immune response after COVID-19 vaccination.

EUROIMMUN has great expertise in the manufacturing of reagents and automation instruments for medical laboratory diagnostics. Thus, we were able to react quickly to the novel viral disease and brought the first CE-marked antibody tests to market within a few weeks. Meanwhile, a broad range of direct and indirect tests for SARS-CoV-2 has been established:

- In the acute phase of infection, the pathogen can be specifically detected using the PCR-based EURORealTime test systems as well as the SARS-CoV-2 Antigen ELISA.
- Our comprehensive product portfolio for serology enables detection of antibodies of the classes IgG, IgA and IgM against SARS-CoV-2 and of the activity of SARS-CoV-2-specific T cells. Alongside serum and plasma, dried blood spots (DBS) are also suitable as sample material for IgG detection.

EUROIMMUN test systems to use over the course of SARS-CoV-2 infection

* IgG seroconversion can take place at different time points after contact with the pathogen (Wölfel R, et al. Nature 581(7809):465-469 (2020) and Okba NMA, et al. Emerg Infect Dis 26(7):1478–1488 (2020)). In individual cases, antibodies are only detectable more than four weeks after onset of symptoms or not at all due to generally delayed or absent antibody secretion.
Direct detection of SARS-CoV-2

**Automation of the EURORealTime tests for detection of SARS-CoV-2**

1. **Nucleic acid extraction & preparation of EURORealTime PCR**
   - Inactivated swab sample
   - Extraction kit and test kit

2. **EURORealTime PCR**
   - Soon available!

3. **Data analysis**
   - EURORealTime Analysis software

Further automation solutions for nucleic acid extraction: chemagic Prepito-D and chemagic 360 (PerkinElmer chemagen).

**SARS-CoV-2 Antigen ELISA**

- Laboratory diagnostic assay for direct pathogen detection by semiquantitative determination of the SARS-CoV-2-specific nucleocapsid protein in swab samples of the upper respiratory tract
- Supporting acute diagnostics, especially during COVID-19 outbreaks
- Established ELISA method – suitable for any diagnostic laboratory and completely automatable

**EUROIMMUN SARS-CoV-2 Antigen ELISA Positive agreement**

<table>
<thead>
<tr>
<th><strong>EUROIMMUN</strong></th>
<th><strong>EUROIMMUN SARS-CoV-2 Antigen ELISA</strong></th>
<th><strong>Positive agreement</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EURORealTime</strong></td>
<td></td>
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</tr>
<tr>
<td><strong>positive at a Ct value up to</strong></td>
<td><strong>n</strong></td>
<td><strong>positive</strong></td>
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<tr>
<td>25</td>
<td>24</td>
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<td>32</td>
<td>54</td>
<td>49</td>
</tr>
<tr>
<td>34</td>
<td>63</td>
<td>52</td>
</tr>
</tbody>
</table>
Detection of antibodies against SARS-CoV-2

- With the EUROIMMUN test systems antibodies against S1 (incl. RBD), S2 or N can be detected. Vaccine development efforts are predominantly focusing on the S1 domain.
- The tests can support the determination of the antibody status and the evaluation of the immune response after infection or vaccination with S1/RBD-based vaccines.
- Parallel use of the spike and nucleocapsid protein-based ELISAs maximises the accuracy when assessing the anti-SARS-CoV-2 antibody status.

**Quantification of the IgG antibody concentration**

**Anti-SARS-CoV-2 QuantiVac ELISA (IgG)**

- Quantitative detection of IgG antibodies again S1 (incl. RBD) by means of a 6-point calibration curve.
- Allows exact determination of the course of the anti-S1 IgG antibody concentration.
- Excellent correlation with the WHO reference material "First WHO International Standard for anti-SARS-CoV-2 immunoglobulin" (NIBSC code: 20/136) – allows issuing of results in standardised units (BAU/ml).
- Very high agreement of results from different neutralisation tests.

**Anti-SARS-CoV-2 ELISA (IgG, IgA)**

- Semiquantitative determination of IgG and IgA antibodies against S1 (incl. RBD) of the spike protein.
- Excellent performance of the Anti-SARS-CoV-2 ELISA (IgG) and good correlation with neutralisation assays confirmed in external studies.
- Also available: Anti-SARS-CoV-2 Omicron ELISA (IgG); quantitative IgG detection (RU/ml) based on the S1 antigen of the Omicron variant.

**Anti-SARS-CoV-2 NCP ELISA (IgG, IgM)**

- Semiquantitative determination of IgG and IgM antibodies against the nucleocapsid protein.
- Optimised specificity of the ELISA due to the use of a modified nucleocapsid protein (NCP) that only contains diagnostically relevant epitopes.


**The test also detects antibodies against other SARS-CoV-2 variants.**
Detection of neutralising antibodies

SARS-CoV-2 NeutraLISA

- Surrogate virus neutralisation test (sVNT) for the detection of neutralising antibodies which inhibit the binding of SARS-CoV-2 S1/RBD to ACE2 receptors and thus prevent the virus from entering the host cell
- Very high agreement of results in comparison with a plaque reduction neutralisation test (PRNT<sub>50</sub>)
- Established ELISA method – suitable for the laboratory routine, no BSL-3 lab required, results available within 2 hours, automatable even for high throughput analysis
- Multispecies test – analysis of animal samples possible for research use

Anti-SARS-CoV-2-RBD-ChLIA (IgG)

- Chemiluminescence immunoassay for quantitative determination of IgG against the receptor binding domain (RBD) of SARS-CoV-2 with the possibility of conversion into standardised units (BAU/ml)
- For fully automated processing using the random access instruments IDS-i10 and IDS-iSYS Multi-Discipline Automated System (from software version 15.06a)
- Continuous loading of samples possible: maximum flexibility and results in a short time thanks to random access

EUROLINE Anti-SARS-CoV-2 Profile (IgG)

- Line blot for the detection of IgG against SARS-CoV-2 antigens and against the nucleocapsid protein of seasonal coronaviruses (HCoV)*
- Allows differentiated anti-SARS-CoV-2 antibody detection by separate antigen bands for the S1 and S2 domains of the spike protein and the nucleocapsid protein (NP)

*The determination of antibodies against the additional HCoV antigens is for information purposes only. Possible reactivities of the respective antigen bands do not affect the test result.
Determination of activity of SARS-CoV-2-reactive T cells

Both the humoral and the cellular immune response are involved in the development of immunity to SARS-CoV-2. In addition to IgG against the S1 domain of the SARS-CoV-2 spike protein, SARS-CoV-2-specific long-lasting T cells play a decisive role.

Quan-T-Cell SARS-CoV-2 and Quan-T-Cell ELISA

- Interferon-gamma (IFN-γ) release assay (IGRA) for quantitative determination of the IFN-γ release by SARS-CoV-2-specific T cells
- Supports the detection of a past contact with SARS-CoV-2 or of an immune response following COVID-19 vaccination
- Already well-established in research – high quality confirmed in numerous studies
- Quick and simple – only 1.5 ml whole blood required per analysis, no complicated sample preparation, results available within 24 hours
- Fully automated processing and evaluation of the Quan-T-Cell ELISA for IFN-γ quantification

Quan-T-Cell SARS-CoV-2: stimulation tube set

1. T-cell stimulation
   Heparinised whole blood is incubated in the three tubes of the stimulation tube set:
   - CoV-2 IGRA BLANK: no T-cell stimulation, for determination of the individual IFN-γ background
   - CoV-2 IGRA TUBE: specific T-cell stimulation using antigens based on the SARS-CoV-2 spike protein
   - CoV-2 IGRA STIM: unspecific T-cell stimulation by means of a mitogen, for control of the stimulation ability

2. IFN-γ detection
   The obtained plasma is analysed by ELISA, the SARS-CoV-2-specific IFN-γ-release is quantified fully automatically.

The Quan-T-Cell SARS-CoV-2 and the Quan-T-Cell ELISA are only to be used together!
Automation solutions for every lab

**Fully automated nucleic acid extraction and real-time PCR**

Pre-NAT II
- Nucleic acid extraction for up to 96 primary samples and pipetting of up to 288 PCRs per run
- Proven nucleic acid extraction system based on magnetic particles
- Integrated cooling for PCR reagents and plates
- Pipetting without carryover using disposable filter tips, and resource-friendly dispensing system

Eonis Q96
- Real-time PCR under ideal conditions: compact cycler for reliable analysis results
- Short protocol run times thanks to excellent heating and cooling times for 96-well blocks
- Six colour modules for reproducible quantification of nucleic acid amplicons
- Safe routine: bidirectional data transfer with the EURORealTime Analysis software

**Further automation solutions for nucleic acid extraction:** chemagic Prepito-D and chemagic 360 (PerkinElmer chemagen).

**Fully automated processing of the test systems for serology**

EUROLabWorkstation ELISA
- For high throughput: Up to 15 ELISA plates per run and more than 200 results per hour possible
- Integrated barcode reader for samples, reagents, dilution and ELISA plates
- Ideal for the use of DBS as sample material

EUROIMMUN Analyzer I-2P
- Random access instrument for up to 120 samples per hour and results after only 25 minutes

EUROIMMUN Analyzer I
- Up to seven ELISA plates per run and more than 57 results per hour possible

EUROBlotOne
- Up to 44 immunoblot strips per run with fully automated processing incl. image recording

Further automation solutions: EUROIMMUN Analyzer I-2P (ELISA), Sprinter XL (ELISA), IDS-i10 (ChLIA), EUROBlotMaster (blot)
<table>
<thead>
<tr>
<th>Product/Test system</th>
<th>Detection</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Sample material</th>
<th>Automation</th>
<th>Test kit stability (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EURORealTime SARS-CoV-2</td>
<td>SARS-CoV-2</td>
<td>98.2%</td>
<td>100%</td>
<td>Throat swabs, saliva</td>
<td>A, B, C, D</td>
<td>11</td>
</tr>
<tr>
<td>EURORealTime SARS-CoV-2 Fast</td>
<td>SARS-CoV-2</td>
<td>100%</td>
<td>100%</td>
<td>Throat swabs</td>
<td>A, C, D</td>
<td>6</td>
</tr>
<tr>
<td>EURORealTime SARS-CoV-2/Influenza A/B</td>
<td>SARS-CoV-2</td>
<td>97.8%</td>
<td>100%</td>
<td>Throat swabs</td>
<td>A, B, C, D</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Influenza A virus</td>
<td>93.0%</td>
<td>100%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Influenza B virus</td>
<td>100%</td>
<td>98.9%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SARS-CoV-2 Antigen ELISA</td>
<td>SARS-CoV-2</td>
<td>93.6%</td>
<td>100%</td>
<td>Nasopharyngeal swabs</td>
<td>E, F</td>
<td>12</td>
</tr>
<tr>
<td>Anti-SARS-CoV-2 ELISA (IgG)</td>
<td>IgG against S1</td>
<td>94.4%</td>
<td>(&gt; 10 days*)</td>
<td>Serum, plasma, DBS</td>
<td>E, F, G, H</td>
<td>12</td>
</tr>
<tr>
<td>Anti-SARS-CoV-2 ELISA (IgA)</td>
<td>IgA against S1</td>
<td>96.9%</td>
<td>(11 – 60 days*)</td>
<td>Serum, plasma, DBS</td>
<td>E, F, G, H</td>
<td>12</td>
</tr>
<tr>
<td>Anti-SARS-CoV-2 NCP ELISA (IgG)</td>
<td>IgG against NCP</td>
<td>94.6%</td>
<td>(&gt; 10 days*)</td>
<td>Serum, plasma, DBS</td>
<td>E, F, G, H</td>
<td>12</td>
</tr>
<tr>
<td>Anti-SARS-CoV-2 NCP ELISA (IgM)</td>
<td>IgM against NCP</td>
<td>88.2%</td>
<td>(&gt; 10 days*)</td>
<td>Serum, plasma</td>
<td>E, F, G, H</td>
<td>6</td>
</tr>
<tr>
<td>Anti-SARS-CoV-2 Omicron ELISA (IgG)</td>
<td>IgG against S1 of Omicron variant**</td>
<td>86.7%</td>
<td>(&gt; 21 days**)</td>
<td>Serum, plasma</td>
<td>E, F, G</td>
<td>12</td>
</tr>
<tr>
<td>Anti-SARS-CoV-2 QuantiVac ELISA (IgG)</td>
<td>IgG against S1 (quantitative)</td>
<td>90.3%</td>
<td>(&gt; 10 days*)</td>
<td>Serum, plasma, DBS</td>
<td>E, F, G, H</td>
<td>12</td>
</tr>
<tr>
<td>SARS-CoV-2 NeutralISA</td>
<td>Neutalisng antibodies against S1/RBD</td>
<td>95.9%</td>
<td>99.7%</td>
<td>Serum, plasma</td>
<td>E, F, G</td>
<td>12</td>
</tr>
<tr>
<td>Quan-T-Cell SARS-CoV-2 together with Quan-T-Cell ELISA</td>
<td>IFN-γ from SARS-CoV-2-reactive T cells</td>
<td>93.8%</td>
<td>96.7%</td>
<td>Heparinised whole blood</td>
<td>E, F, G</td>
<td>12</td>
</tr>
<tr>
<td>Anti-SARS-CoV-2 RBD ChLIA (IgG)</td>
<td>IgG against RBD</td>
<td>94.6%</td>
<td>(&gt; 21 days*)</td>
<td>Serum, plasma</td>
<td>I, J</td>
<td>12</td>
</tr>
<tr>
<td>EUROLINE Anti-SARS-CoV-2 Profile (IgG)</td>
<td>IgG against S1, S2, NP (SARS-CoV-2) and NP (HCoV)</td>
<td>100%</td>
<td>100%</td>
<td>Serum, plasma</td>
<td>K, L</td>
<td>18</td>
</tr>
</tbody>
</table>

* after symptom onset or positive direct detection  
** The test also detects antibodies against other SARS-CoV-2 variants.

** Order information **

** Direct detection **

- EURORealTime SARS-CoV-2: CE-IVD, FDA EUA***; Order number: MP 2606-0###
- EURORealTime SARS-CoV-2 Fast: CE-IVD; Order number: MP 2606-####-8
- EURORealTime SARS-CoV-2/Influenza A/B: CE-IVD; Order number: MP 2606-####-20
- SARS-CoV-2 Antigen ELISA: CE-IVD; Order number: EQ 2606-9601

** Serology **

- Anti-SARS-CoV-2 ELISA (IgG): CE-IVD, FDA EUA***; Order number: EI 2606-9601 G
- Anti-SARS-CoV-2 ELISA (IgA): CE-IVD; Order number: EI 2606-9601 A
- Anti-SARS-CoV-2 NCP ELISA (IgG): CE-IVD; Order number: EI 2606-9601-2 G
- Anti-SARS-CoV-2 NCP ELISA (IgM): CE-IVD; Order number: EI 2606-9601-30 G
- Anti-SARS-CoV-2 Omicron ELISA (IgG): CE-IVD; Order number: EI 2606-9601-10 G
- SARS-CoV-2 NeutraLISA: CE-IVD; Order number: EI 2606-9601-4
- Quan-T-Cell SARS-CoV-2 (stimulation tube set for 30 analyses) Quan-T-Cell ELISA (IFN-γ ELISA): CE-IVD; Order number: ET 2606-3003 EQ 6841-9601
- Anti-SARS-CoV-2 RBD ChLIA (IgG): CE-IVD; Order number: LI 2606-10010-1 G
- Control Set Anti-SARS-CoV-2 RBD ChLIA (IgG): CE-IVD; Order number: LR 2606-20210-1 G
- EUROLINE Anti-SARS-CoV-2 Profile (IgG): CE-IVD; Order number: DN 2606-####-1 G

**DBS analysis: Blood collection set and blood collection card**

Your EUROMMUN contact will be happy to advise you!

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**Notes:**

- Strong trio for analysis of the immune response

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**Order information**

**Category**

- Direct detection
- Serology

**Test system/instrument**

- EURORealTime SARS-CoV-2
- EURORealTime SARS-CoV-2 Fast
- EURORealTime SARS-CoV-2/Influenza A/B
- SARS-CoV-2 Antigen ELISA
- Anti-SARS-CoV-2 ELISA (IgG)
- Anti-SARS-CoV-2 ELISA (IgA)
- Anti-SARS-CoV-2 NCP ELISA (IgG)
- Anti-SARS-CoV-2 NCP ELISA (IgM)
- Anti-SARS-CoV-2 Omicron ELISA (IgG)
- SARS-CoV-2 NeutraLISA
- Quan-T-Cell SARS-CoV-2 together with Quan-T-Cell ELISA
- Anti-SARS-CoV-2 RBD ChLIA (IgG)
- EUROLINE Anti-SARS-CoV-2 Profile (IgG)
- Quan-T-Cell SARS-CoV-2 (stimulation tube set for 30 analyses)
- Quan-T-Cell ELISA (IFN-γ ELISA)
- Anti-SARS-CoV-2 RBD ChLIA (IgG)
- Control Set Anti-SARS-CoV-2 RBD ChLIA (IgG)
- EUROLINE Anti-SARS-CoV-2 Profile (IgG)
- DBS analysis: Blood collection set and blood collection card

**Status**

- CE-IVD
- FDA EUA***
- Only to be used together

**Order number**

- MP 2606-0###
- MP 2606-####-8
- MP 2606-####-20
- EQ 2606-9601
- EI 2606-9601 G
- EI 2606-9601 A
- EI 2606-9601-2 G
- EI 2606-9601-30 G
- EI 2606-9601-10 G
- EI 2606-9601-4
- ET 2606-3003 EQ 6841-9601
- LI 2606-10010-1 G
- LR 2606-20210-1 G
- DN 2606-####-1 G

*** FDA EUA: Validity of the FDA EUA according to the current US-specific instructions for use

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