COVID-19 diagnostics
Comprehensive test and automation portfolio for direct and indirect detection of SARS-CoV-2 infections

- 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 oropharyngeal 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.
- 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.

*EURORline Anti-SARS-CoV-2 Profile (IgG)
Direct detection of SARS-CoV-2

**EURORealTime SARS-CoV-2**

- Fast direct detection of SARS-CoV-2 by means of reverse transcription and real-time PCR in one step
- High sensitivity due to detection of two target sequences in the SARS-CoV-2 genome (ORF1ab gene and N gene)
- Limit of detection: 1 cp/µl eluate
- **NEW!** EURORealTime SARS-CoV-2 Fast: RT-PCR in only 45 minutes, presentation of the target sequences in two different channels

**EURORealTime SARS-CoV-2/Influenza A/B**

- PCR combination test for direct detection of SARS-CoV-2 and influenza viruses (types A and B)
- For differential diagnostic clarification of symptoms that can be associated with COVID-19 as well as influenza
- Limit of detection: 1.5 cp/µl (SARS-CoV-2, influenza virus A subtypes H3N2 and H1N1) and 3 cp/µl (influenza virus type B) eluate

- Automated workflow from sample to result
- No detectable cross reactivity with different pathogens that can occur in the respiratory tract or are closely related with SARS-CoV-2 or influenza viruses
- Only one reaction per sample

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

1. Nucleic acid extraction & preparation of EURORealTime PCR  
2. EURORealTime PCR  
3. Data analysis

Detection of antibodies against SARS-CoV-2

- 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.

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

BAU: Binding Antibody Units


** 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 (PRNT50)
- 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

Modelled upon nature: Neutralising antibodies in the sample compete with the host-cell receptor (ACE2) for the binding to S1/RBD in the first incubation step – no preadsorption required

The more neutralising antibodies inhibit the binding of the biotinylated ACE2 to S1/RBD, the weaker is the colour reaction of the sample

In contrast to classic antibody detection, only immunoglobulins with inhibitory effect on the ACE2-S1/RBD binding, but no other antibodies are detected

Antibody detection by blot

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)

Seasonal coronaviruses*  |  SARS-CoV-2
---|---
Control  | IGA  | HCoV-NP  | HCoV-Z596E NP  | HCoV-NL63 NP  | HCoV-OC43 NP  | HCoV-HKU1 NP  | NP  | S2  | S1

*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.
Determining activity of SARS-CoV-2-reactive T cells

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

Automated Workstation 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 and resource-friendly dispensing system for extraction reagents
- Use of disposable filter tips for precise pipetting
- Integrated cooling for PCR reagents and plates

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

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

Further automation solutions: EUROIMMUN Analyzer I-2P (ELISA), Sprinter XL (ELISA), IDS-i10 (ChLIA), EUROBlotMaster (blot)

<table>
<thead>
<tr>
<th>Category/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>Direct detection</td>
<td><strong>EURORealTime SARS-CoV-2</strong></td>
<td>SARS-CoV-2</td>
<td>98.2%</td>
<td>100%</td>
<td>Throat swabs, saliva</td>
<td>A, B, C, D</td>
</tr>
<tr>
<td>Direct detection</td>
<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>
</tr>
<tr>
<td>Direct detection</td>
<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>B, C, D</td>
</tr>
<tr>
<td>Direct detection</td>
<td>Anti-SARS-CoV-2 ELISA (IgG)</td>
<td>IgG against S1</td>
<td>94.4% (&gt; 10 days*)</td>
<td>99.6%</td>
<td>Serum, plasma, DBS</td>
<td>E, F, G, H</td>
</tr>
<tr>
<td>Direct detection</td>
<td>Anti-SARS-CoV-2 ELISA (IgA)</td>
<td>IgA against S1</td>
<td>96.9% (11 – 60 days*)</td>
<td>98.3%</td>
<td>Serum, plasma</td>
<td>E, F, G, H</td>
</tr>
<tr>
<td>Direct detection</td>
<td>Anti-SARS-CoV-2 NCP ELISA (IgG)</td>
<td>IgG against NCP</td>
<td>94.6% (&gt; 10 days*)</td>
<td>99.8%</td>
<td>Serum, plasma, DBS</td>
<td>E, F, G, H</td>
</tr>
<tr>
<td>Direct detection</td>
<td>Anti-SARS-CoV-2 NCP ELISA (IgM)</td>
<td>IgM against NCP</td>
<td>88.2% (&lt; 10 days*)</td>
<td>98.6%</td>
<td>Serum, plasma</td>
<td>E, F, G, H</td>
</tr>
<tr>
<td>Direct detection</td>
<td>Anti-SARS-CoV-2 Omicron ELISA (IgG)</td>
<td>IgG against S1 of Omicron variant**</td>
<td>86.7% (&gt; 21 days***)</td>
<td>99.8%</td>
<td>Serum, plasma</td>
<td>E, F, G</td>
</tr>
<tr>
<td>Direct detection</td>
<td>Anti-SARS-CoV-2 QuantiVac ELISA (IgG)</td>
<td>IgG against S1 (quantitative)</td>
<td>90.3% (&gt; 10 days*)</td>
<td>99.8%</td>
<td>Serum, plasma, DBS</td>
<td>E, F, G, H</td>
</tr>
<tr>
<td>Direct detection</td>
<td>SARS-CoV-2 NeutralISA</td>
<td>Neutralising antibodies against S1/RBD</td>
<td>95.9%</td>
<td>99.7%</td>
<td>Serum, plasma</td>
<td>E, F, G</td>
</tr>
<tr>
<td>Direct detection</td>
<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>
</tr>
<tr>
<td>Direct detection</td>
<td>Anti-SARS-CoV-2 RBD ChLIA (IgG)</td>
<td>IgG against RBD</td>
<td>94.8% (&gt; 21 days*)</td>
<td>99.5%</td>
<td>Serum, plasma</td>
<td>I, J</td>
</tr>
<tr>
<td>Direct detection</td>
<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>
</tr>
</tbody>
</table>

* after symptom onset or positive direct detection
** The test also detects antibodies against other SARS-CoV-2 variants.
A: Automated Workstation Pre-NAT II; B: chemagic Prepito-D; C: chemagic 360-D (PerkinElmer chemagen); D: Eonis Q96; E: EUROIMMUN Analyzer I; F: EUROIMMUN Analyzer I-2P; G: EUROIMMUN Analyzer I-2P; H: EUROIMMUN Analyzer I-2P; I: IDS-i10; J: IDS-iSYS Multi-Discipline Automated System; K: EUROBlotOne; L: EUROBlotMaster

Order information

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

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**Strong trio for analysis of the immune response**

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EUROIMMUN contact will be happy to advise you!