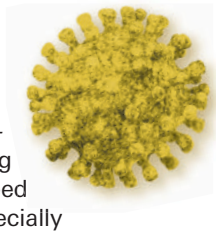
EUROIMMUN Medizinische Labordiagnostika AG

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 SARS-CoV-2 and 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 and determination of reactive-T-cell activity
- 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 asymptomatically 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).

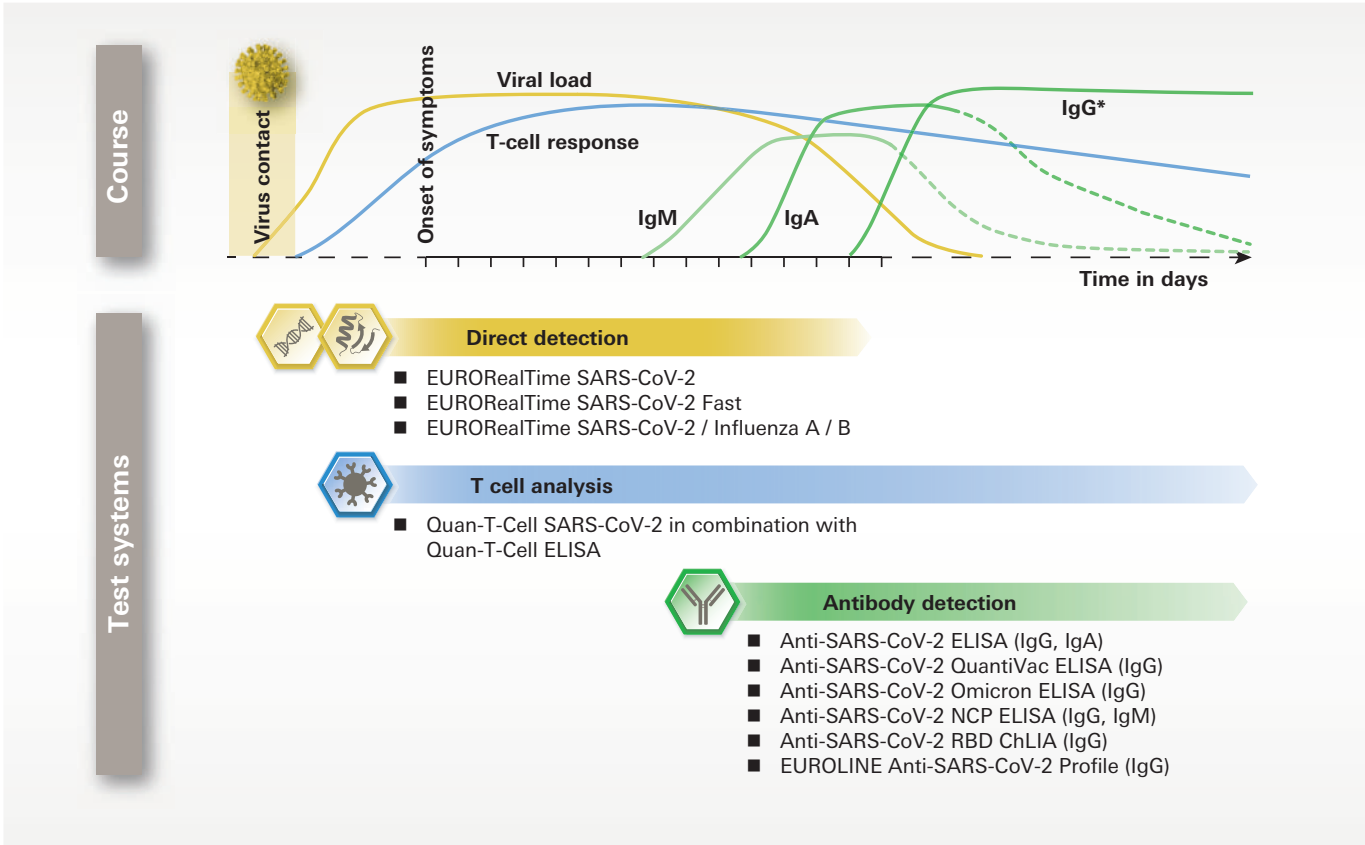
COVID-19 diagnostics – the complete package from EUROIMMUN

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 presymptomatic 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:

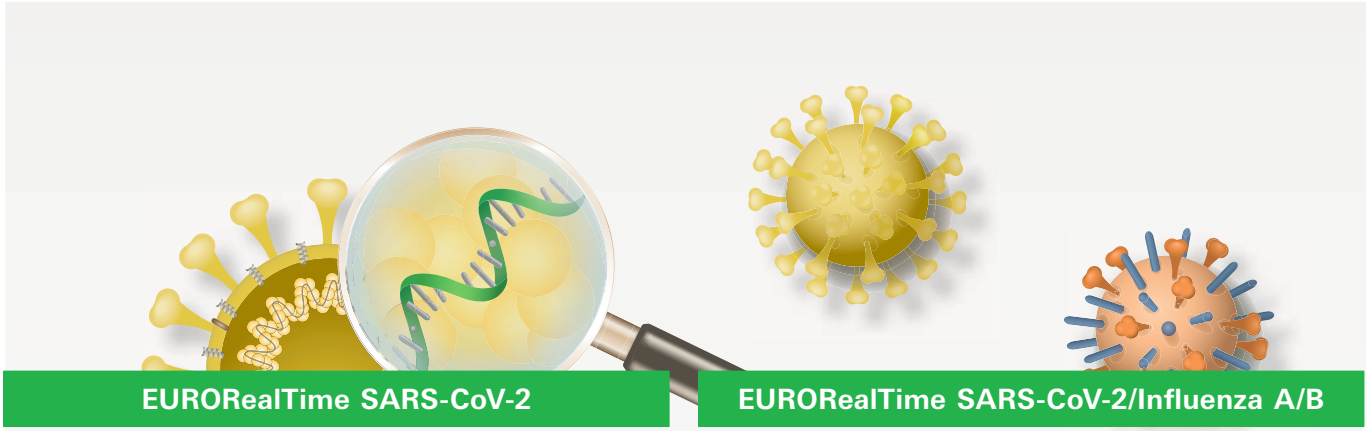
- In the acute phase of infection, the pathogen can be specifically detected using the PCR-based EURORealTime test systems.
- Our comprehensive product portfolio for serology enables detection of antibodies of the classes IgG, IgA and IgM against SARS-CoV-2 and of the activity of SARS-CoV-2-specific 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.

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
- EURORealTime SARS-CoV-2 Fast: RT-PCR in only 45 minutes, presentation of the target sequences in two different channels

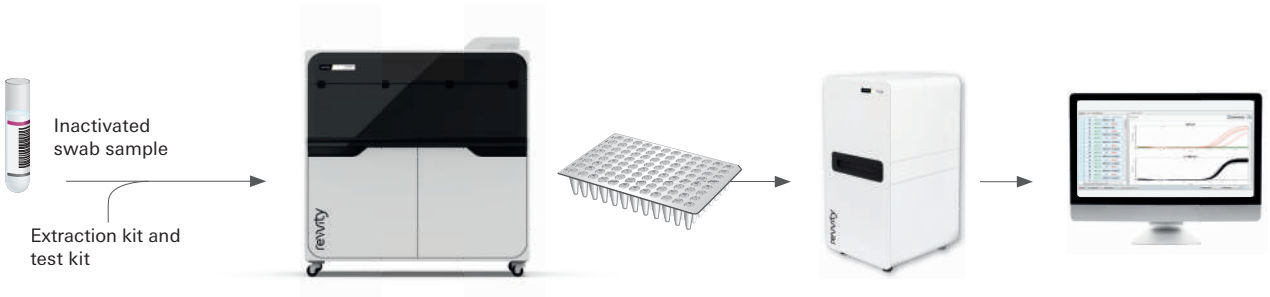
EURORealTime SARS-CoV-2/Influenza A/B

- 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**



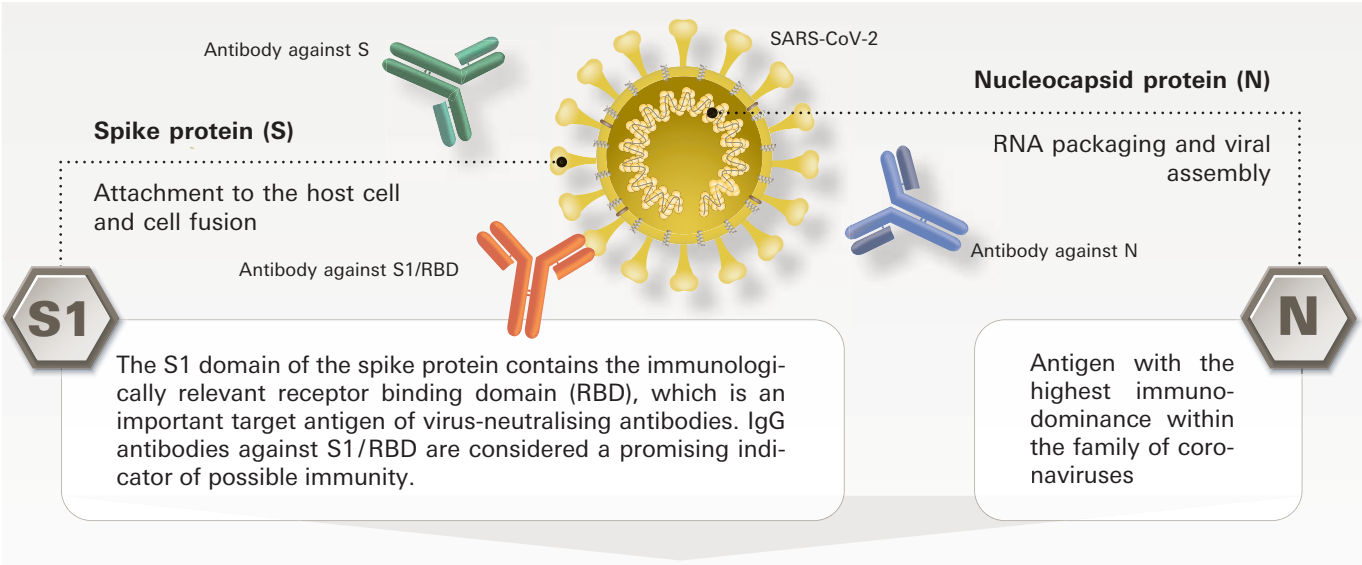
Automated Workstation Pre-NAT II

Eonis Q96

EURORealTime Analysis software

Further automation solutions for nucleic acid extraction: chemagic Prepito-D and chemagic 360-D (Revvity chemagen).
More information at https://chemagen.com.

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

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**

* Patent applications BR102021003012-7, CN202180001126.9, EP21158065.9, EP20158626.0, IL295754, IN202117059700, MX/a/2022/010234, SG11202112544X, US17/180616, ZA2021/09064 and ZA2023/00650 are pending. Utility models DE202020105116.4, DE202020105117.2 and DE202021100842.3 have been registered. Patents AU2021223701, CA3109607, EP3869199, EP3855186, JP7022969, KR102570713 have been granted.
** The test also detects antibodies against other SARS-CoV-2 variants.

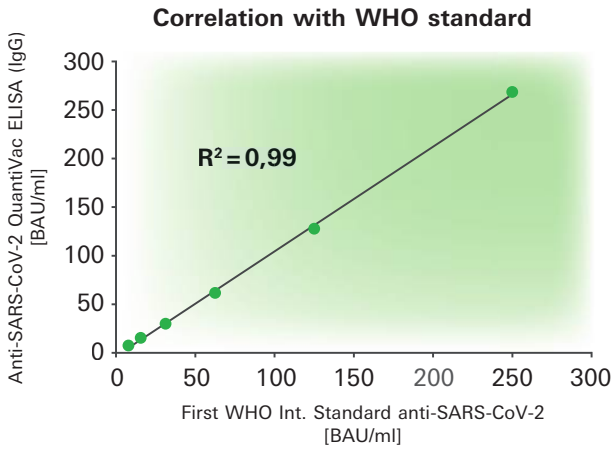
Anti-SARS-CoV-2-NCP ELISA (IgG, IgM)

- 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

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

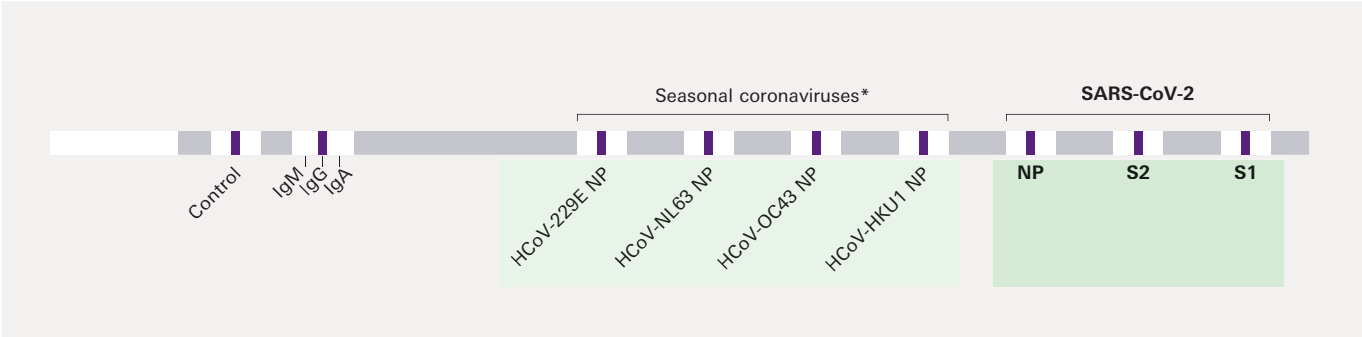
Anti-SARS-CoV-2-RBD ChLIA (IgG)

- 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

Antibody detection by blot

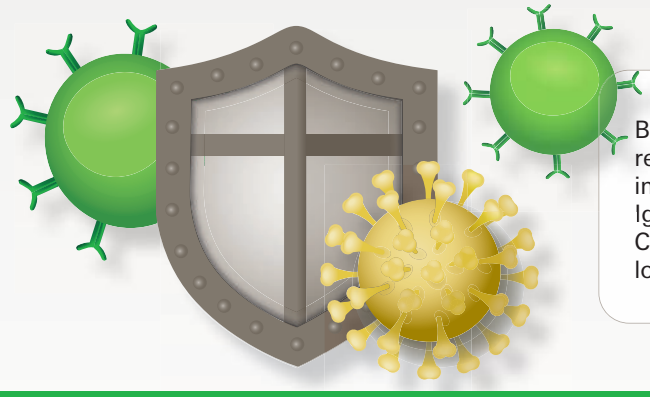
EUROLINE Anti-SARS-CoV-2 Profile (IgG)

- 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)



* 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

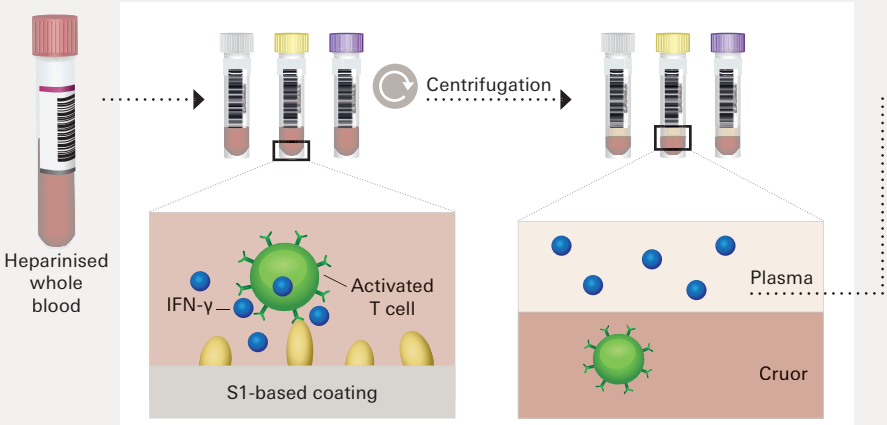


Both the humoral and the cellular immune response are involved in the development of immunity to SARS-CoV-2. In addition to IgG against the S1 domain of the SARS-CoV-2 spike protein, SARS-CoV-2-specific long-lasting T cells play a decisive role.

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 a vailable 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

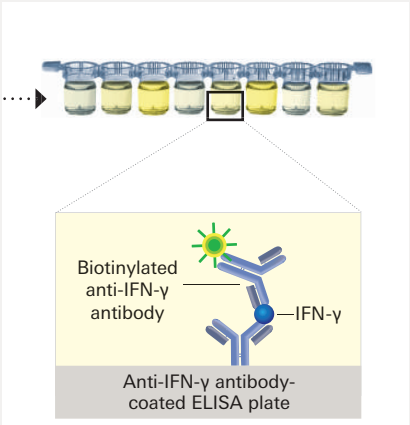


1 T-cell stimulation

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

Quan-T-Cell ELISA



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

Further automation solutions for nucleic acid extraction: chemagic Prepito-D and chemagic 360-D (Revvity chemagen).
Further information at https://chemagen.com.

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

IDS-iSYS Multi-Discipline Automated System

- 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 44 (blot)

At a glance: Product features of EUROIMMUN test systems for COVID-19 diagnostics

Product/Test system	Detection	Sensitivity	Specificity	Sample material	Automation	Test kit stability (months)
EURORealTime SARS-CoV-2	SARS-CoV-2	98.2%	100%	Throat swabs, saliva	A, B, C, D	11
EURORealTime SARS-CoV-2 Fast	SARS-CoV-2	100%	100%	Throat swabs	A, C, D	6
EURORealTime SARS-CoV-2/ Influenza A/B	SARS-CoV-2	97.8%	100%	Throat swabs	B, C, D	12
	Influenza A virus	93.0%	100%			
	Influenza B virus	100%	98.9%			
Anti-SARS-CoV-2 ELISA (IgG)	IgG against S1	94.4% (>10 days*)	99.6%	Serum, plasma, DBS	E, F, G, H	12
Anti-SARS-CoV-2 ELISA (IgA)	IgA against S1	96.9% (11–60 days*)	98.3%	Serum, plasma,	E, F, G, H	12
Anti-SARS-CoV-2 NCP ELISA (IgG)	IgG against NCP	94.6% (>10 days*)	99.8%	Serum, plasma, DBS	E, F, G, H	12
Anti-SARS-CoV-2 NCP ELISA (IgM)	IgM against NCP	88.2% (<10 days*)	98.6%	Serum, plasma	E, F, G, H	6
Anti-SARS-CoV-2 Omicron ELISA (IgG)	IgG against S1 of Omicron variant**	86.7 % (>21 days**)	99.8 %	Serum, plasma	E, F, G	12
Anti-SARS-CoV-2 QuantiVac ELISA (IgG)	IgG against S1 (quantitative)	90.3% (>10 days*)	99.8%	Serum, plasma, DBS	E, F, G, H	12
Quan-T-Cell SARS-CoV-2 together with Quan-T-Cell ELISA	IFN-γ from SARS-CoV-2-reactive T cells	93.8%	96.7%	Heparinised whole blood	E, F, G	12
Anti-SARS-CoV-2 RBD ChLIA (IgG)	IgG against RBD	94.6% (>21 days*)	99.5%	Serum, plasma	I, J	12
EUROLINE Anti-SARS-CoV-2 Profile (IgG)	IgG against S1, S2, NP (SARS-CoV-2) and NP (HCoV)	100%	100%	Serum, plasma	K, L	18

* 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 (Revvity chemagen); **D:** Eonis Q96; **E:** EUROIMMUN Analyzer I; **F:** EUROIMMUN Analyzer I-2P; **G:** EUROLabWorkstation ELISA; **H:** Sprinter XL; **I:** IDS-i10; **J:** IDS-iSYS Multi-Discipline Automated System; **K:** EUROBlotOne; **L:** EUROBlotMaster 44

Order information

Category	Test system/instrument	Status	Order number	
Direct detection	EURORealTime SARS-CoV-2	CE-IVD, FDA EUA***	MP 2606-0###	Not available in China
	EURORealTime SARS-CoV-2 Fast	CE-IVD	MP 2606-####-8	
	EURORealTime SARS-CoV-2/Influenza A/B	CE-IVD	MP 2606-####-20	Not available in the USA and China
Serology	Anti-SARS-CoV-2 ELISA (IgG)	CE-IVD, FDA EUA***	EI 2606-9601 G	
	Anti-SARS-CoV-2 ELISA (IgA)	CE-IVD	EI 2606-9601 A	
	Anti-SARS-CoV-2 NCP ELISA (IgG)	CE-IVD	EI 2606-9601-2 G	
	Anti-SARS-CoV-2 NCP ELISA (IgM)	CE-IVD	EI 2606-9601-2 M	
	Anti-SARS-CoV-2 Omicron ELISA (IgG)	CE-IVD	EI 2606-9601-30 G	
	Anti-SARS-CoV-2 QuantiVac ELISA (IgG)	CE-IVD	EI 2606-9601-10 G	
	Quan-T-Cell SARS-CoV-2 (stimulation tube set for 30 analyses) Quan-T-Cell ELISA (IFN-γ ELISA)	CE-IVD	ET 2606-3003 EQ 6841-9601	Only to be used together!
	Anti-SARS-CoV-2 RBD ChLIA (IgG) Control Set Anti-SARS-CoV-2 RBD ChLIA (IgG)	CE-IVD	LI 2606-10010-1 G LR 2606-20210-1 G	
	EUROLINE Anti-SARS-CoV-2 Profile (IgG)	CE-IVD	DN 2606-####-1 G	

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