BioVendor Group CLIA

COVID-19

SARS-CoV-2
Antibody determination

RBD IgA, IgG, IgM
NP IgA, IgG, IgM

Diagnostic panels:
COVID-19
Vaccination monitoring
Respiratory diseases

CE IVD

The kits are CE-IVD certified and intended for professional use.

CLIA kits are optimized and validated for the determination of antibodies in human serum and plasma

Designed for the platform

Kleeya®


Kleeya

Introduction

The SARS-CoV-2 virus belongs to the group coronaviruses, enveloped RNA viruses that cause respiratory and digestive tract diseases in humans and animals. The clinical picture can differ among various viruses, from the common cold up to severe respiratory syndromes (MERS, SARS, and Covid-19). A total of 7 species of human coronaviruses are known so far - 229E, NL63, OC43, HKU1, MERS, SARS, SARS-CoV-2.

Covid-19 is an acute infectious disease caused by the SARS-CoV-2 virus. Its incubation period ranges from 2 to 14 days after exposure, on average it is 5-6 days. Infection can occur asymptomatically in a significant percentage of infected individuals. SARS-CoV-2 is a respiratory virus, transmitted to humans via infectious droplets after close contact with the infected person. Transmission is also possible from objects contaminated with secretions of infected persons. Infected persons may transmit the virus 1–3 days before the onset of symptoms. In the acute phase of the disease, respiratory tract damage may be caused as a result of the infection, or by an exaggerated response of the adaptive immune system, the so-called „cytokine storm“. Aside from serious acute manifestations of the disease, there might be long-term disease-related issues, such as “long-covid” or “post-covid syndrome”. The most severe clinical manifestations are post-inflammatory lung fibrillation, neuropathy, myopathy, carditis or cardiomyopathy.

SARS-CoV-2 has mutated during the pandemic. Its infectivity and the course of the disease shift significantly with each variant, therefore the need for an immunity status check arises, as spike mutations can affect the effectiveness of both post-infection and post-vaccination antibodies.

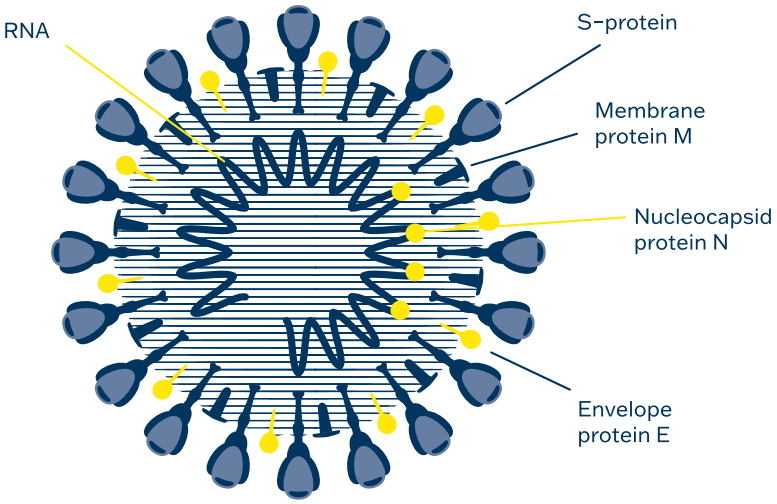
Diagnosis of the disease

The diagnosis of COVID-19 is based on the clinical picture, epidemiological history, and laboratory tests. Molecular biology methods, such as PCR and LAMP are used to prove the acute infection, Immunochemical tests for the detection of viral antigens are suitable for screening; positive findings may be confirmed with PCR. Serological tests only take on a supporting role as recommended by the WHO.

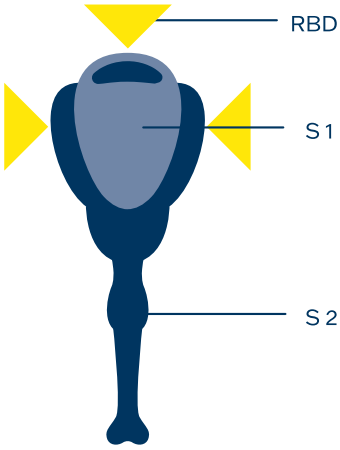
Antibody determination

The SARS-CoV-2 virus consists of four structural proteins: spike (S), nucleocapsid (N), envelope (E) and membrane (M) protein. Two of them are highly antigenic and therefore have important diagnostic value. The nucleocapsid protein (NP) encapsulates the viral genomic RNA and forms a major part of the virion. NP is highly antigenic and is associated with several virus-host interactions. The receptor-binding domain (RBD), a subunit of the Spike S1 protein, binds specifically to angiotensin-converting enzyme 2 (ACE2) receptor on the host cell surface. This link is highly correlated with the formation of neutralizing antibodies.

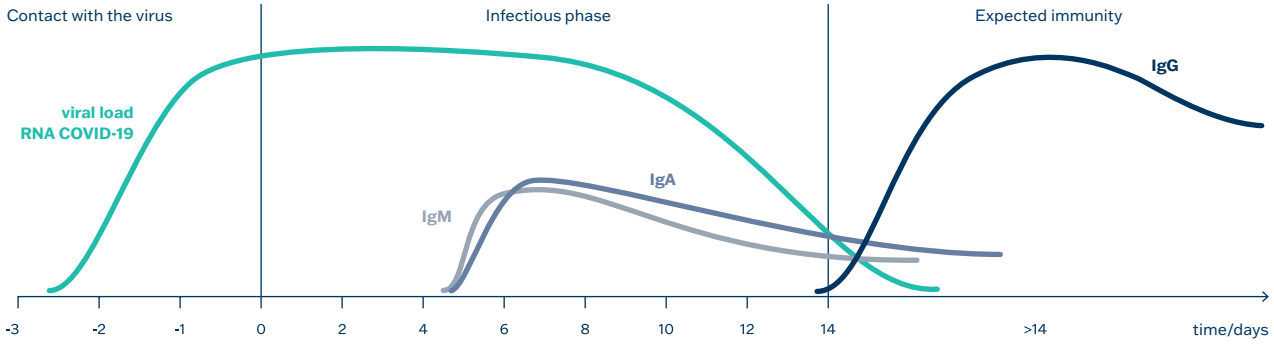
SARS-CoV-2

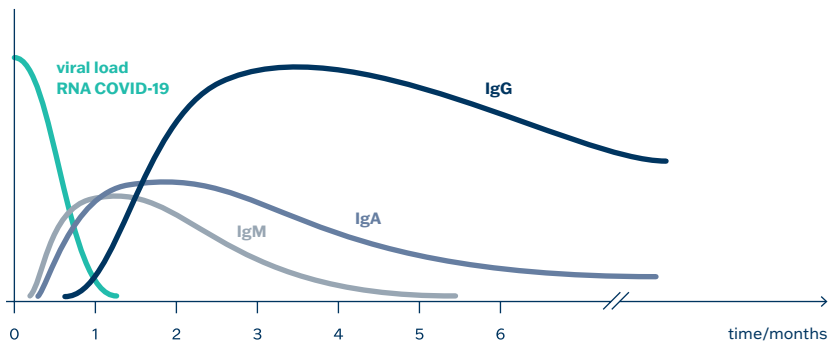


SPIKE



Serological tests for COVID-19 are not routinely performed to detect an acute infection. Antibodies to SARS-CoV-2 appear after 1 - 3 weeks after the onset of symptoms. IgA and IgM class antibodies are usually detected in the first week, IgG antibodies are present after 2 - 3 weeks. In COVID-19, however, IgM, IgA and IgG antibodies can also form simultaneously. Exceptionally, some people with asymptomatic infection or mild symptoms do not develop antibodies at all.





Why it is important to test SARS-CoV-2 antibodies

Antibody detection provides a substantial part of a comprehensive assessment of the state of immunity after illness or vaccination. The examination of cellular immunity is more complex and time consuming, and is performed at specialised laboratories.

Detection of antibodies to SARS-CoV-2 may help to confirm or refute a previous infection and to determine whether the subject is susceptible to the infection or has developed some defense, especially against a serious course of illness requiring hospitalization. It is also irreplaceable for screening and identifying convalescent plasma donors. Antibody testing is included in many ongoing or planned epidemiological studies. Depending on the class of antibodies, it is possible to distinguish what stage a person is in after an infection. It is important to monitor the dynamics of antibodies, reaching maximum values and when and how quickly they decrease; whether in the individual or in the population. These findings can result in a better understanding of the immune system's response to the disease.

Infectious and vaccine immunity can be distinguished by the specificity of antibodies to protein S (RBD) or NP.

RBD IgG

They have the largest representation in the serum of people who have been infected or vaccinated against COVID-19 and reach the highest concentrations there. Anti-RBD (or Spike) IgG persists for several months at high levels and performs a neutralizing function in the blood, similar to IgA on the mucous membranes. RBD IgG values measured with CLIA correlate with virus neutralizing antibody titers in the VNT (virus neutralisation test).

NP IgG

They occur in a high percentage of people who have had a COVID-19 infection. NP antibodies are a specific marker of disease, they do not form after vaccination. Vaccinated persons who have not undergone COVID-19 produce antibodies only against the S-protein. It can also serve to distinguish persons who had the natural infection before or after vaccination, in particular, if a health complication is suspected associated with the post-covid syndrome.

RBD IgA

They are a marker of mucosal immunity against COVID-19 and an indication of a recent infection. RBD IgA antibody levels usually rise after reinfection.

NP IgA

Similar in importance to RBD IgA antibodies, but the prevalence is significantly lower.

RBD IgM

They are a marker of a recent infection with short-term persistence in the circulation.

NP IgM

Similar to RBD IgM antibodies, but the prevalence is significantly lower.

It is necessary to take into consideration that antibody response shows high variability among the population and there are exceptions to the general interpretations above.

Clinical applications

- Disease diagnosis (complementary)
- Prevalence studies
- Post-vaccination antibody detection (RBD)
- Waning immunity monitoring, recommendation for a booster dose, especially in elderly and immunocompromised patients
- Identification of asymptomatic infection
- Detection of antibodies against the Omicron variant

Characteristics

Antigens

CLIA COVID-19 NP IgA, IgG a IgM	CLIA COVID-19 RBD IgA, IgG a IgM
Recombinant nucleocapside protein (NP)	Recombinant RBD domain of Spike S1 protein

Test characteristics

Kit	Calibration range	Diagnostic sensitivity	Diagnostic specificity
CLIA COVID-19 NP IgA	5–100 U/ml	92,86 %	99,99 %
CLIA COVID-19 NP IgG	5–320 U/ml	99,99 %	99,99 %
CLIA COVID-19 NP IgM	5–100 U/ml	99,99 %	99,99 %
CLIA COVID-19 RBD IgA	5–100 U/ml	92,86 %	99,99 %
CLIA COVID-19 RBD IgG	5–1000 U/ml	99,99 %	99,99 %
CLIA COVID-19 RBD IgM	5–100 U/ml	96,55 %	99,99 %

The compliance with the international WHO standard

All BioVendor Group CLIA kits for the determination of anti-SARS-CoV-2 antibodies were standardized using the international standard WHO 20/136. For CLIA COVID-19 RBD IgG, 1 U / ml = 1 BAU / ml applies.

Correlation of methods

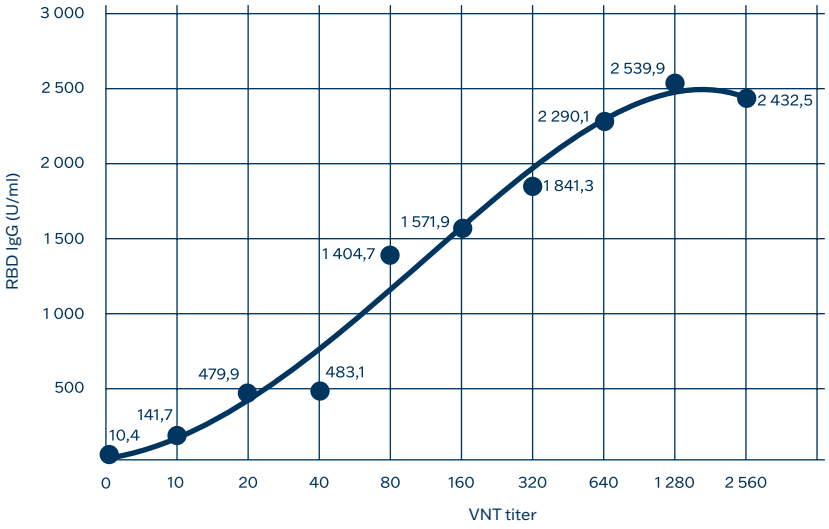
Correlation with VNT

CLIA COVID-19 RBD diagnostic kits were compared with the VNT method. Significant agreement was found for the CLIA COVID-19 RBD IgG kit.

		CLIA RBD IgG	
		pos	neg
VNT	pos	77	0
	neg	5	28
Agreement		95 %	

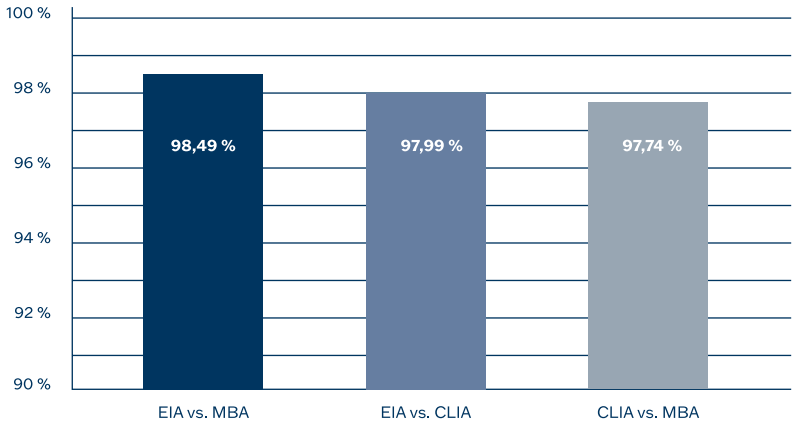
Comparison of CLIA COVID-19 RBD IgG and the VNT titer

RBD IgG antibody concentrations measured with the CLIA COVID-19 RBD IgG kit correspond very well with the virus-neutralizing titers detected by the VNT.



The agreement with ELISA and Microblot-array

CLIA has also been correlated with well established enzyme immunoassay (EIA) and microblot-array (MBA). The comparison showed a very good agreement and correlation of results.

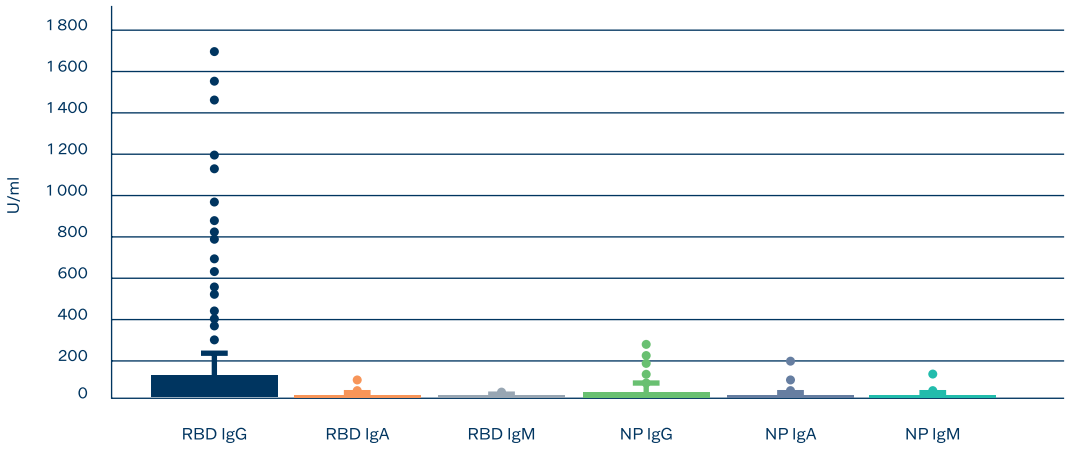


Application examples

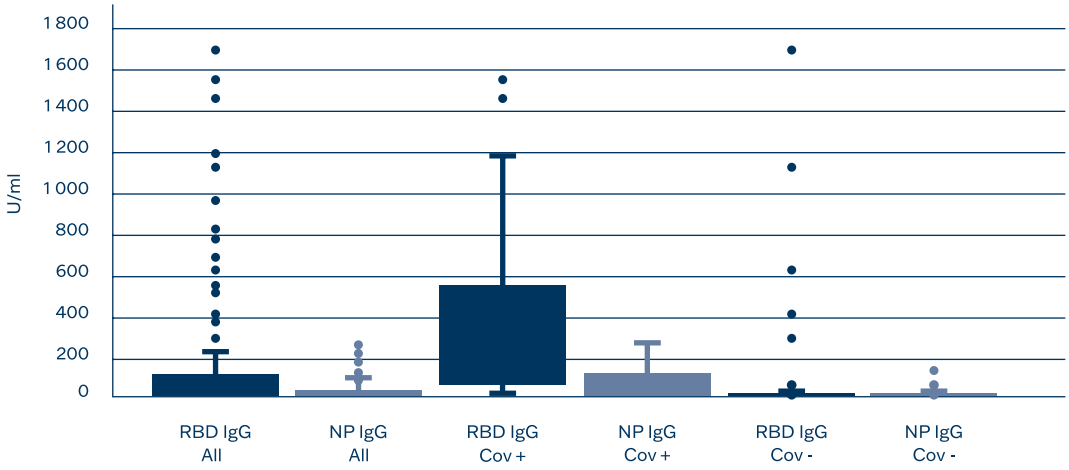
Antibody levels – Unvaccinated persons

179 unvaccinated individuals were examined using CLIA kits. 80 of them underwent COVID-19 in the range of 4-10 months before collection.

Complex antibody examination



RBD IgG and NP IgG vs. diagnosis



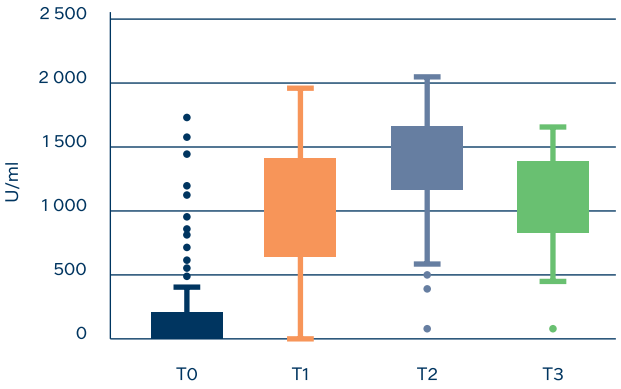
Of the 80 people diagnosed with the disease, 70 had positive RBD IgG antibodies; 51 had positive NP IgG antibodies.

Of the 99 people without diagnosed disease, 18 had positive RBD IgG antibodies (max. 1708 U/ml); 5 of them had NP IgG in addition to RBD (max. 156 U/ml); only one person had positive NP IgG and no RBD IgG. It can be concluded that the the NP IgG and RBD IgG positive persons without a confirmed diagnosis also underwent COVID-19.

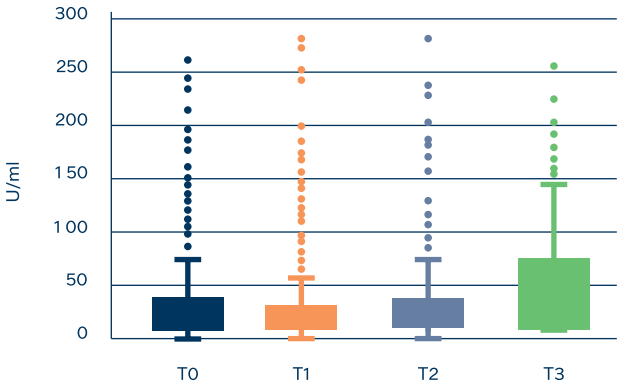
Antibody response dynamics after vaccination

Sera obtained from 167 subjects (73 underwent COVID-19) vaccinated with two doses of Comirnaty vaccine (Pfizer / BioNTech) were tested for the presence of anti-RBD (IgA, IgG) and anti-NP (IgA, IgG) antibodies with specific CLIA COVID-19 kits. Samples were taken 4 times over a period of 12 weeks:

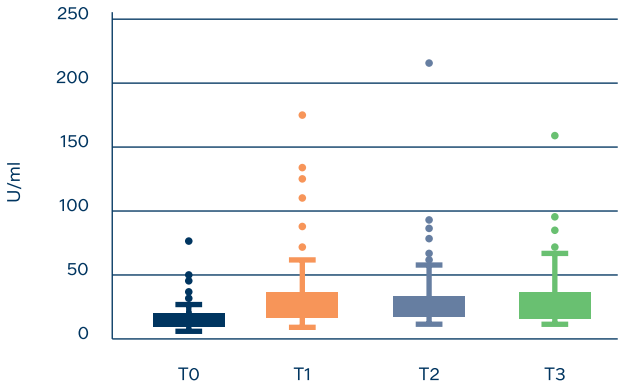
RBD IgG



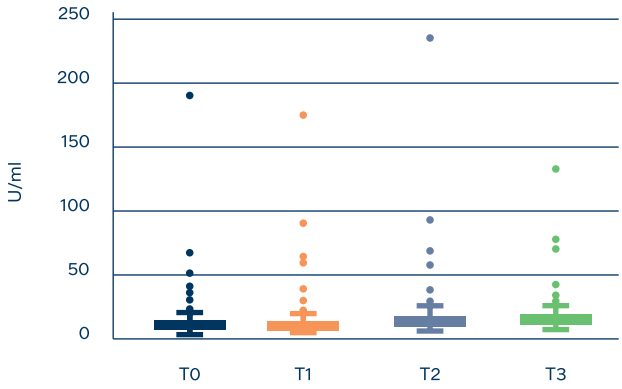
NP IgG



RBD IgA



NP IgA



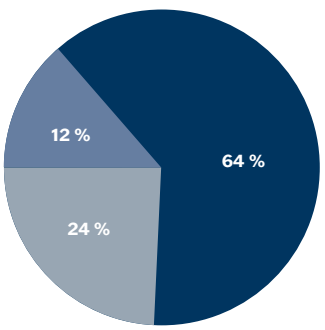
T0: 1st dose / **T1**: T0 + 3 weeks (2nd dose) / **T2**: T1 + 3 weeks / **T3**: T2 + 6 weeks.

High levels of RBD IgG were found in individuals with past COVID-19 infection and the increase was especially large after vaccination. Also, NP IgG levels in COVID-19 subjects were high. Unlike RBD IgG antibodies, the production of NP antibodies is not affected by vaccination.

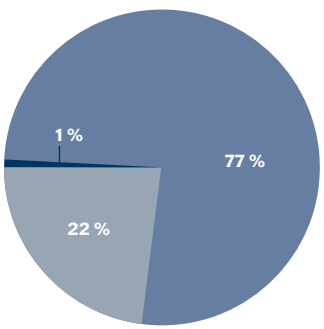
Antibody stability in the elderly

Anti-RBD antibodies (IgG and IgA) were tested in 201 seniors ~ 8 months after vaccination. In 88 % of them, RBD IgG antibodies were positive; for RBD IgA, it was 23%.

RBD IgG



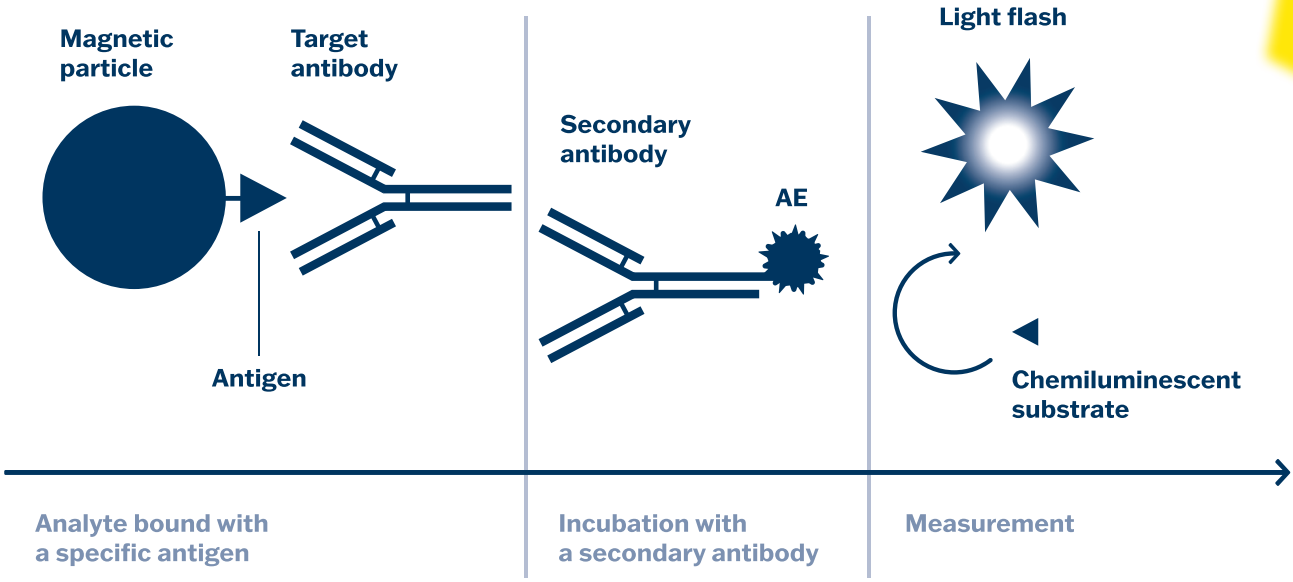
RBD IgA



● >200 U/ml ● 22–200 U/ml ● <22 U/ml

How does CLIA method work?

CLIA is a fully automated, fast, specific and sensitive method. It combines magnetic particle-mediated antigen / antibody immunocomplex separation and flash chemiluminescence to achieve sensitive detection. The use of magnetic particle suspension facilitates automation, significantly shortens reaction times and improves the specificity of the determination. Flash chemiluminescence of acridinium ester provides an intense light signal even at very low concentrations and its intensity is measured in relative units of light (RLU). CLIA kits are designed for use on the KleeYa® automated platform.



CLIA kits

Diagnostic CLIA kits are used to determine specific antibodies against SARS-CoV-2 in human serum or plasma on a KleeYa® analyzer. The results are reported in U/ml.

Control set CLIA

Control sera verify the accuracy of results obtained by the CLIA kits.

Ease of use

- Fully automated method
- Kits include all necessary reagents, incl. calibrators
- Ready-to-use reagents in the reaction cartridges
- Control sera available as independent sets
- Quantitative determination (U/ml) - equivalent to the BAU/ml units (CLIA COVID-19 RBD IgG)

Advantages

- High diagnostic sensitivity and specificity
- Low sample (10 µl) and reagent consumption
- Short test time (30 min)
- Wide measuring range
- Full traceability of reagent consumption and number of tests available using RFID tags
- LIS connectivity available
- Superior customer service
- Complex diagnostics involving all classes of antibody

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Ordering information

CLIA kits

CLIA diagnostic kits are used to determine specific antibodies in human serum or plasma on a KleeYa® analyzer.

Kit	Catalogue number	Number of tests
CLIA COVID-19 NP IgA	CL-CoNA100	100
CLIA COVID-19 NP IgG	CL-CoNG100	100
CLIA COVID-19 NP IgM	CL-CoNM100	100
CLIA COVID-19 RBD IgA	CL-CoRA100	100
CLIA COVID-19 RBD IgG	CL-CoRG100	100
CLIA COVID-19 RBD IgM	CL-CoRM100	100

Control sets

Each set contains two vials of positive and two vials of negative control serum with the predetermined level of specific antibodies. They are designed to verify the accuracy of results obtained with CLIA kits.

Control set	Catalogue number	Number of tests
Control set CLIA COVID-19 NP IgA	CL-CoNACON	2 x 20
Control set CLIA COVID-19 NP IgG	CL-CoNGCON	2 x 20
Control set CLIA COVID-19 NP IgM	CL-CoNMCON	2 x 20
Control set CLIA COVID-19 RBD IgA	CL-CoRACON	2 x 20
Control set CLIA COVID-19 RBD IgG	CL-CoRGCON	2 x 20
Control set CLIA COVID-19 RBD IgM	CL-CoRMCON	2 x 20

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