Elecsys® Anti-SARS-CoV-2

Immunoassay for the qualitative detection of antibodies against SARS-CoV-2

Summary

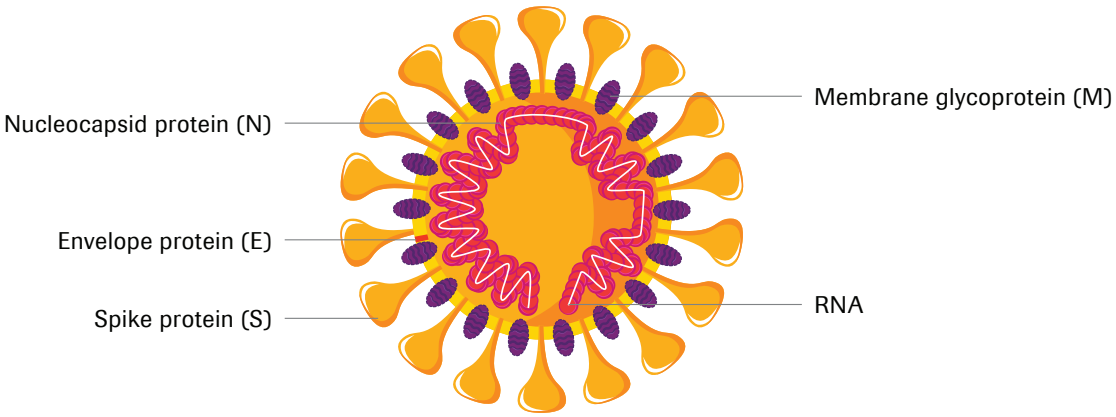
Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is an enveloped, single-stranded RNA virus of the family Coronaviridae. Coronaviruses share structural similarities and are composed of 16 nonstructural proteins and 4 structural proteins: spike (S), envelope (E), membrane (M), and nucleocapsid (N). Coronaviruses cause diseases with symptoms ranging from those of a mild common cold to more severe ones such as Coronavirus Disease 2019 (COVID-19) caused by SARS-CoV-2 [1,2].

SARS-CoV-2 is transmitted from person-to-person primarily via respiratory droplets, while indirect transmission through contaminated surfaces is also possible[3-6]. The virus accesses host cells via the angiotensin-converting enzyme 2 (ACE2), which is most abundant in the lungs[7-9].

The incubation period for COVID-19 ranges from 2 – 14 days following exposure, with most cases showing symptoms approximately 4 – 5 days after exposure[3,10]. The spectrum of symptomatic infection ranges from mild (fever, cough, fatigue, loss of smell, shortness of breath) to critical[11,12]. While most symptomatic cases are not severe, severe illness occurs predominantly in adults with advanced age or underlying medical comorbidities and requires intensive care. Acute respiratory distress syndrome (ARDS) is a major complication in patients with severe disease. Critical cases are characterized by e.g., respiratory failure, shock and/or multiple organ dysfunction, or failure[11,13,14].

Definitive COVID-19 diagnosis entails direct SARS-CoV-2 detection by nucleic acid amplification technology (NAAT)[15-17]. Serological assays can contribute to the identification of individuals exposed to the virus and assess the extent of exposure of a population, and might thereby help to decide on application, enforcement or relaxation of containment measures[18].

Structure of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)



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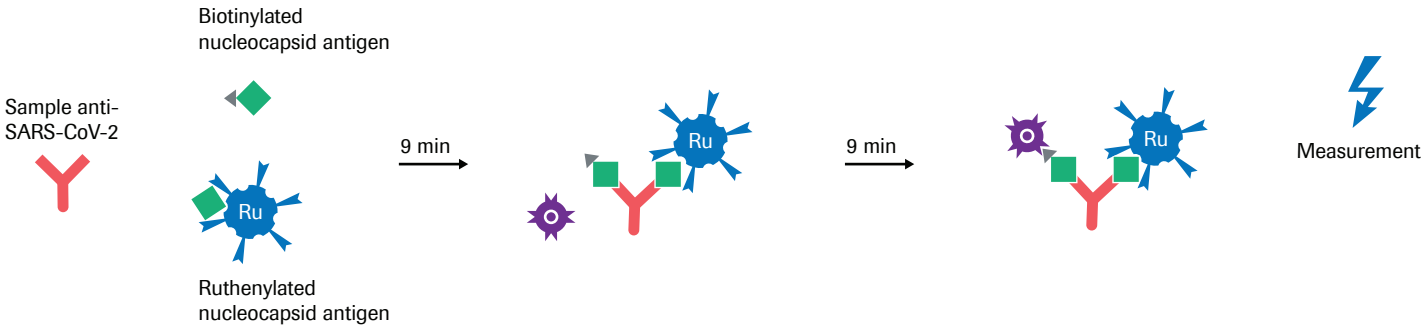
Depending on the applied method, seroconversion is observed after a median of 10 – 13 days after symptom onset for IgM and 12 – 14 days for IgG[19-21]. According to current knowledge, maximum seroconversion occurs at 2 – 3 weeks for IgM, at 3 – 6 weeks for IgG, and at two weeks for total antibodies[19,21-26]. Whereas IgM seems to vanish around week 6 – 7, high IgG seropositivity is seen at that time[22,24,27]. Levels and chronological order of IgM and IgG antibody appearance are highly variable, supporting detection of both antibodies simultaneously[21,23,25,28]. Neutralizing antibodies targeting the spike and nucleocapsid proteins are formed as early as day 9 onwards, showing strong neutralizing response, thus seroconversion may lead to protection at least for a limited time[26,29-32].

Elecsys® Anti-SARS-CoV-2 is an immunoassay intended for the qualitative detection of antibodies to SARS-CoV-2 in human serum and plasma. The assay uses a recombinant protein representing the nucleocapsid (N) antigen for the determination of antibodies against SARS-CoV-2. The test is intended for use as an aid in identifying individuals with an adaptive immune response to SARS-CoV-2, indicating recent or prior infection.[33]

Electro-chemiluminescence immunoassay (ECLIA)

Test principle: double-antigen sandwich assay (testing time: 18 minutes) [33]



Step 1 (9 minutes)
20 µL* / 12 µL** of the patient sample are incubated with a mix of biotinylated and ruthenylated nucleocapsid (N) antigen. Double-antigen sandwich immune complexes are formed in the presence of corresponding antibodies.

* **cobas e** 411 analyzer and **cobas e** 601/602 modules
** **cobas e** 801 module

Step 2 (9 minutes)
After addition of streptavidin-coated microparticles, the DAGS complexes bind to the solid phase via interaction of biotin and streptavidin.

Step 3 (measurement)
The reagent mixture is transferred to the measuring cell, where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are subsequently removed. Electrochemiluminescence is then induced by applying a voltage and measured with a photomultiplier. The signal yield increases with the antibody titer.

Elecsys® Anti-SARS-CoV-2 assay characteristics

Systems	**cobas e** 411 analyzer **cobas e** 601 / **cobas e** 602 modules	**cobas e** 801 module
Testing time	18 minutes	
Calibration	2-point	
Result interpretation	COI* <1.0 = non-reactive COI ≥1.0 = reactive	
Sample material	Serum collected using standard sampling tubes. Li-heparin, K_2-EDTA and K_3-EDTA plasma.	
Sample volume	20 µL	12 µL
Onboard stability	72 hours	

* cutoff index

Clinical sensitivity[33]

A total of 204 samples from 69 symptomatic patients with a PCR confirmed SARS-CoV-2 infection were tested with the Elecsys® Anti-SARS-CoV-2 assay. One or more consecutive specimens from these patients were collected after PCR confirmation at various time points.

Days post PCR confirmation	N	Sensitivity (95 % CI*)
0 – 6 days	116	65.5 % (56.1 – 74.1 %)
7 – 13 days	59	88.1 % (77.1 – 95.1 %)
≥14 days	29	100 % (88.1 – 100 %)

* confidence intervall

Clinical specificity[33]

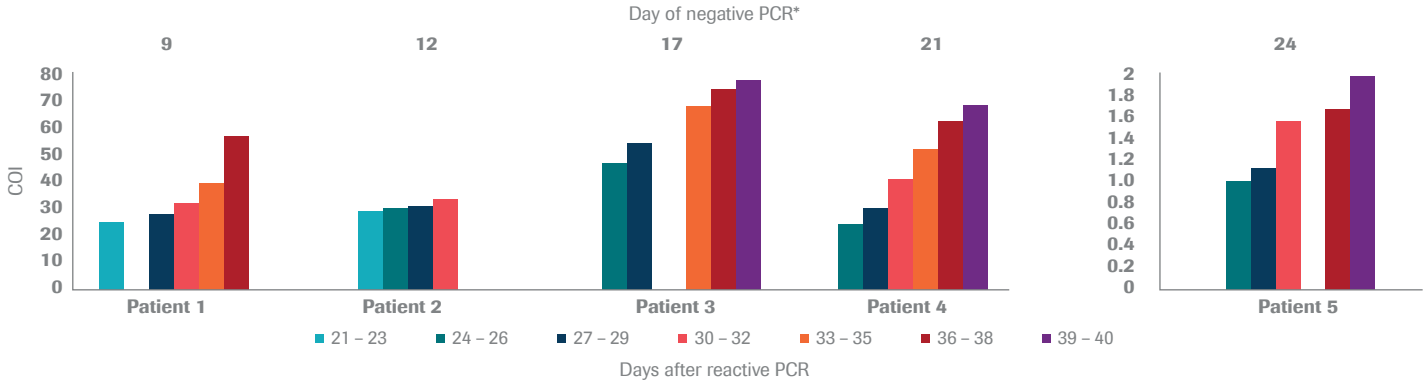
A total of 5,272 samples (from diagnostic routine, blood donors, a common cold panel, and a coronavirus panel*) obtained before December 2019 were tested with the Elecsys® Anti-SARS-CoV-2 assay.

Cohort	N	Reactive	Specificity % (95 % CI)
Diagnostic routine	3,420	7	99.80 % (99.58 – 99.92 %)
Blood donors	1,772	3	99.83 % (99.51 – 99.97 %)
Common cold panel	40	0	100 % (91.19 – 100 %)
Coronavirus panel	40	0	100 % (91.19 – 100 %)
Overall	**5,272**	**10**	**99.81 % (99.65 – 99.91 %)**

* 40 potentially cross-reactive samples from individuals with past infection with coronavirus HKU1, NL63, 229E, or OC43, confirmed by PCR.

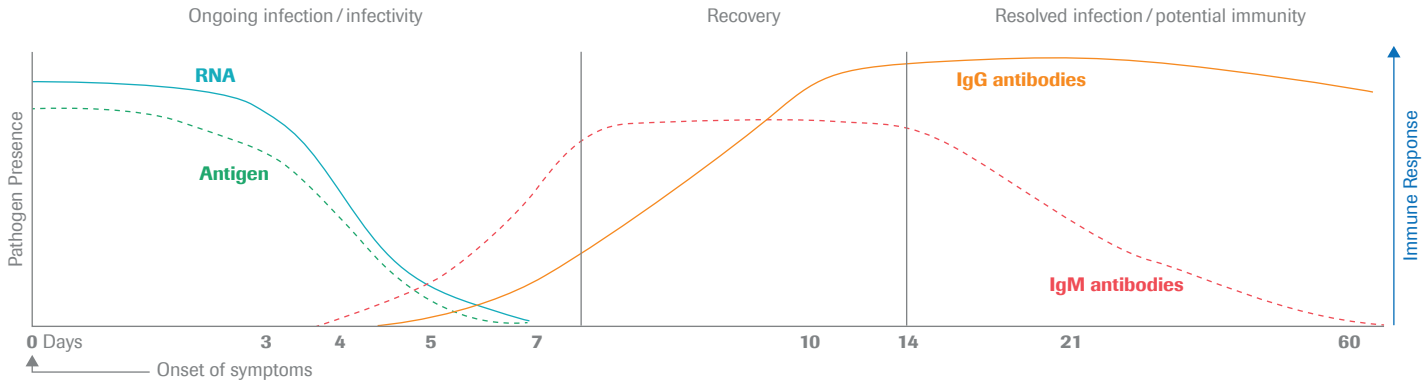
Seroconversion sensitivity[33]

After recovery from infection, confirmed by a negative PCR result, 26 consecutive samples from 5 individuals were tested with the Elecsys® Anti-SARS-CoV-2 assay.



* Day 0 represents initial positive PCR

Illustrative course of markers in SARS-CoV-2 infection[19-27]



Ordering information

Product	Material configuration	Material number
Elecsys® Anti-SARS-CoV-2 a)	200 tests	09 203 095 190
Elecsys® Anti-SARS-CoV-2 b)	300 tests	09 203 079 190
Diluent MultiAssay* a)	2 × 16 mL	03 609 987 190
Diluent MultiAssay* b)	45.2 mL	07 299 010 190

* optionally required for the preparation of positive control material from positive sample

a) for use on the **cobas e** 411 analyzer and the **cobas e** 601 / 602 modules; b) for use on the **cobas e** 801 module

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33 *Elecsys® Anti-SARS-CoV-2. Package Insert 2020-04, V1.0; Material Numbers 09203095190 and 09203079190.*

- Not for screening of donated blood
- This test has not been FDA cleared or approved
- This test has been authorized by FDA under an EUA for use by authorized laboratories
- This test has been authorized only for detecting the presence of antibodies against SARS-CoV-2, not for any other viruses or pathogens
- This test is only authorized for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of in vitro diagnostic tests for detection and/or diagnosis of COVID-19 under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb- 3(b)(1), unless the authorization is terminated or revoked sooner

Roche Diagnostics
9115 Hague Road,
Indianapolis, IN 46256

diagnostics.roche.com