FACT SHEET FOR RECIPIENTS

Roche Diagnostics, Inc.
Elecsys Anti-SARS-CoV-2 S

November 25, 2020

Coronavirus Disease 2019 (COVID-19)

You are being given this Fact Sheet because your sample(s) is being tested or was tested for antibodies to the virus that causes Coronavirus Disease 2019 (COVID-19) using the Elecsys Anti-SARS-CoV-2 S.

You should not interpret the results of this test as an indication or degree of immunity or protection from reinfection.

This Fact Sheet contains information to help you understand the risks and benefits of using this test to evaluate your adaptive immune response to SARS-CoV-2, the virus that causes COVID-19. After reading this Fact Sheet, if you have questions or would like to discuss the information provided, please talk to your healthcare provider. You have the option to refuse use of this test. However, your doctor may be recommending this test because they believe it could help with your care.

For the most up to date information on COVID-19 please visit the CDC Coronavirus Disease 2019 (COVID-19) webpage: https://www.cdc.gov/COVID19

What is COVID-19?
COVID-19 is caused by the SARS-CoV-2 virus which is a new virus in humans causing a contagious respiratory illness. COVID-19 can present with a mild to severe illness, although some people infected with COVID-19 may have no symptoms at all. Older adults and people of any age who have underlying medical conditions have a higher risk of severe illness from COVID-19. Serious outcomes of COVID-19 include hospitalization and death. The SARS-CoV-2 virus can be spread to others not just while one is sick, but even before a person shows signs or symptoms of being sick (e.g., fever, coughing, difficulty breathing, etc.). A full list of symptoms of COVID-19 can be found at the following link: https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html.

How are people tested for COVID-19?
Two kinds of tests are currently available for COVID-19: diagnostic tests and antibody tests.

- A diagnostic test tells you if you have a current infection.
- An antibody test tells you if you had a previous infection

What is the Elecsys Anti-SARS-CoV-2 S?
This test is an antibody test. It will help assess if you have antibodies to the virus that causes COVID-19. An antibody test may not be able to show if you have a current infection, because it can take 1-3 weeks after infection to make antibodies.

What are the known and potential risks and benefits of the test?

Potential risks include:

- Possible discomfort or other complications that can happen during sample collection.
- Possible incorrect test result (see below for more information).

Potential benefits include:

- The results, along with other information, can help your healthcare provider make informed recommendations about your care.

What does it mean if I have a positive test result?
If you have a positive test result, it is possible that you have or previously had COVID-19 and that you have developed an antibody response to the virus. Your healthcare provider will work with you to determine how best to care for you based on the test results along with other factors of your medical history, your symptoms, possible exposures, and geographic location of places

- **Where can I go for updates and more information?** The most up-to-date information on COVID-19 is available at the CDC General webpage: **https://www.cdc.gov/COVID19.** In addition, please also contact your healthcare provider with any questions/concerns.

you have recently traveled. There is also a chance that this test can give a positive result that is wrong (a false positive result). Even a high-performing antibody test when used in a population without many cases of COVID-19 infection may produce as many or more false results as true results because the likelihood of finding someone who has been infected is very small.

Your healthcare provider will work with you to determine the likelihood of false result.

This test may give you a numerical result, but you should not interpret the number to mean that having any measurement of antibodies to SARS-CoV-2 will protect you from getting infected again or help reduce the severity or duration of a future COVID-19 infection. This topic is being studied, but the information is unknown. It is also not known how long antibodies to SARS-CoV-2 will remain present in the body after infection.

Regardless of your test result, you should continue to follow CDC guidelines to reduce the risk of infection, including social distancing and wearing masks.

What does it mean if I have a negative test result?
A negative test result means that antibodies to the virus that causes COVID-19 were not found in your sample. However, it is possible for this test to give a negative result that is incorrect (false negative) in some people with COVID-19. Additionally, a negative result may occur if you are tested early in your illness and your body hasn't had time to produce antibodies to infection. This means that you could possibly still have COVID-19 even though the test is negative. If this is the case, your healthcare provider will consider the test result together with all other aspects of your medical history (such as symptoms, possible exposures, and geographical location of places you have recently traveled) in deciding how to care for you.

It is important that you work with your healthcare provider to help you understand the next steps you should take.

Is this test FDA-approved or cleared?
No. This test is not yet approved or cleared by the United States FDA. When there are no FDA-approved or cleared tests available, and other criteria are met, FDA can make tests available under an emergency access mechanism called an Emergency Use Authorization (EUA). The EUA for this test is supported by the Secretary of Health and Human Service's (HHS's) declaration that circumstances exist to justify the emergency use of in vitro diagnostics for the detection and/or diagnosis of the virus that causes COVID-19. This EUA will remain in effect (meaning this test can be used) for the duration of the COVID-19 declaration justifying emergency of IVDs, unless it is terminated or revoked by FDA (after which the test may no longer be used).

What are the approved alternatives?

There are no approved available alternative tests. FDA has issued EUAs for other tests that can be found at: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization.

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Updated: October 23, 2020

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It is not known how long antibodies to SARS-CoV-2 will remain present in the body after infection. It is not known whether having antibodies to SARS-CoV-2 will protect you from getting infected again or help reduce the severity or duration of a future COVID-19 infection. Regardless of your test result, you should continue to follow CDC guidelines to reduce the risk of infection, including social distancing and wearing masks.

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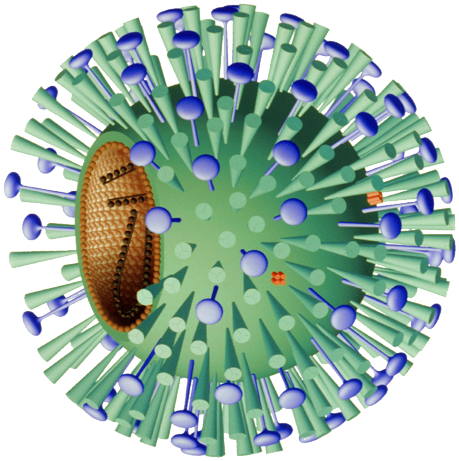
A clinical overview of Roche SARS-CoV-2 antibody tests

Elecsys® Anti-SARS-CoV-2 (qualitative) Assay
Elecsys® Anti-SARS-CoV-2 S (semi-quantitative) Assay

Targeting high affinity antibodies is important for detecting previous exposure to SARS-CoV-2



When determining individual exposure and community prevalence of COVID-19, it is important to select tests that minimize the risk of false-positive results, which could infer a level of immune response or protection that is not actually present.

When COVID-19 prevalence is low, CDC guidance is to consider employing two independent tests in sequence when the first test yields a positive result in order to minimize false-positive test results and improve positive predictive value.[1] Additionally, the FDA suggests a second test using a different viral protein to make an informed decision on whether or not an individual has had a prior infection or truly has antibodies to the virus.[2]

The Roche **Elecsys® Anti-SARS-CoV-2 S (semi-quantitative)** and **Anti-SARS-CoV-2 (qualitative)** immunoassays detect high affinity antibodies against the spike and nucleocapsid proteins, respectively, to provide high specificity—delivering results you can trust to inform clinical decisions and support patient care.

Elecsys® Anti-SARS-CoV-2 Assays: Performance by Design

Using a unique double-antigen sandwich assay format, Roche Elecsys® Anti-SARS-CoV-2 assays provide you with the flexibility to detect the relevant antibodies to achieve high specificity: high affinity, mature antibodies — predominantly immunoglobulin G (IgG), avoiding the drawbacks of immunoglobulin M (IgM)-only tests.

Factors contributing to high Negative Percent Agreement

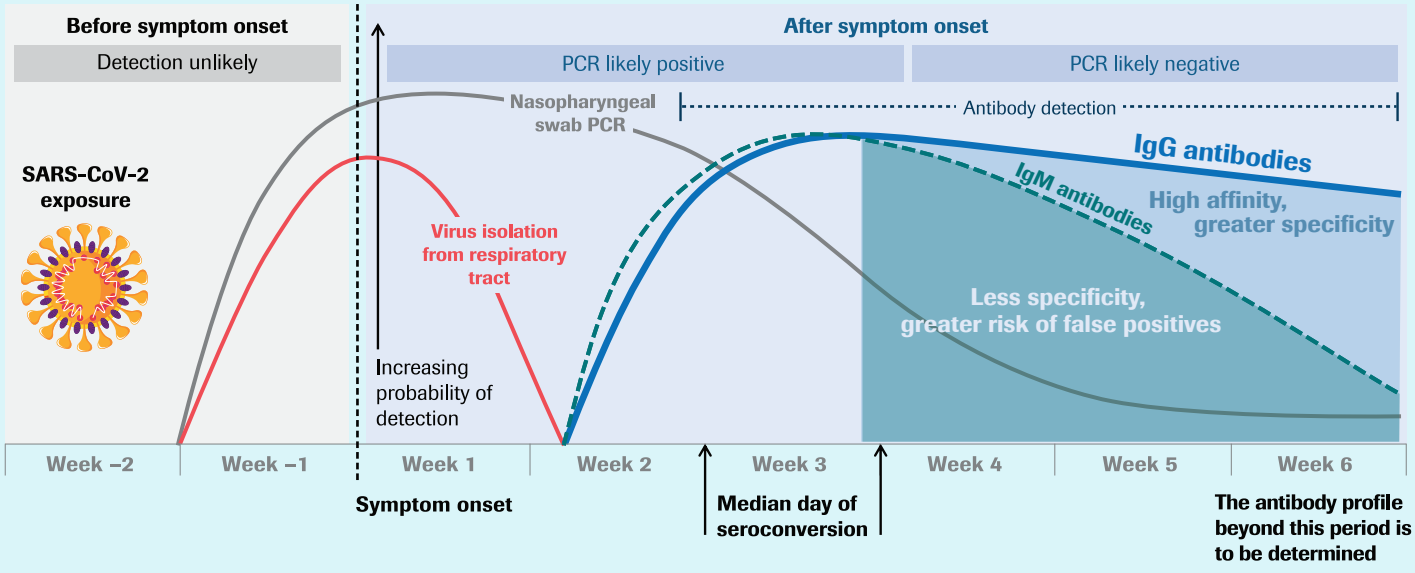
Low cross-reactivity[3]

Detecting high affinity antibodies[3,4,5]

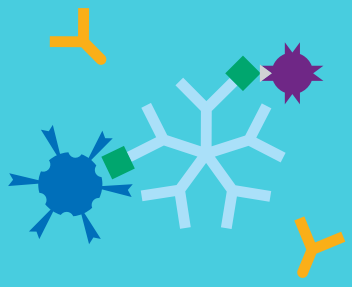
Elecsys® Anti-SARS-CoV-2 S (semi-quantitative) Assay
99.98% Negative Percent Agreement
(N=5,991) [6]

Elecsys® Anti-SARS-CoV-2 (qualitative) Assay
99.80% Negative Percent Agreement
(N=10,453) [7]

Estimated course of markers in SARS-CoV-2 infection[8]



It's clear that SARS-CoV-2 is no ordinary disease, and it doesn't behave like one either. While **IgM** antibodies often appear before **IgG** in other diseases, research shows that **IgG and IgM largely appear at the same time in SARS-CoV-2**. Since **IgM antibodies decline earlier than IgG** antibodies, are **less specific**, have a **high risk of false positives**, and are **not suitable to diagnose acute infection**, there is limited value in detecting class specific antibodies for SARS-CoV-2. This makes **IgG**, total, or high affinity antibodies **better suited for the use cases of SARS-CoV-2 antibody testing**.



Test Principle

Elecsys® Anti-SARS-CoV-2 immunoassays utilize an in-solution double-antigen sandwich (DAGS) format, which requires the simultaneous binding of two differently labeled antigens via high affinity interactions to generate a signal. This reduces the probability of non-specific reactions with low affinity antibodies and cross-reaction with antibodies from other coronaviruses.

Elecsys® Anti-SARS-CoV-2 S (semi-quantitative) Assay

*Immunoassay for the **semi-quantitative** determination of antibodies against the SARS-CoV-2 **spike (S) protein***

Intended Use

Elecsys® Anti-SARS-CoV-2 S for use on the **cobas e** analyzers is an electrochemiluminescence immunoassay intended for the qualitative and semi-quantitative detection of antibodies to SARS CoV 2 spike (S) protein receptor binding domain (RBD) in human serum and plasma (lithium heparin, dipotassium-EDTA, tripotassium-EDTA, and sodium citrate). The Elecsys® Anti-SARS-CoV-2 S assay is intended as an aid in identifying individuals with an adaptive immune response to SARS-CoV-2, indicating recent or prior infection.[6]

Elecsys® Anti-SARS-CoV-2 (qualitative) Assay

*Immunoassay for the **qualitative** detection of antibodies against SARS-CoV-2 **nucleocapsid (N) protein***

Intended Use

Elecsys® Anti-SARS-CoV-2 for use on the **cobas e** analyzers is an electrochemiluminescence 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.[7]

Why use Elecsys® SARS-CoV-2 antibody tests?

	Elecsys® Anti-SARS-CoV-2 S (semi-quantitative) Assay	Elecsys® Anti-SARS-CoV-2 (qualitative) Assay
Measure adaptive immune response ▪ Indicate recent or prior infection	✔	✔
Determine seroprevalence in a given population in high, moderate and low prevalence settings	✔	✔
Determine seroprevalence in a given population in very low to moderate seroprevalence settings ▪ Perform sequential testing to improve specificity in low prevalence settings	✔ +	✔
Increase sensitivity by combining Anti-S and Anti-N ▪ Identify S-only AND N-only responders	✔ +	✔
Determine antibody levels in convalescent plasma donations ▪ Assist with preparation of therapeutic Ig formulations	✔	✔
Evaluate vaccine-induced immune response* ▪ Support vaccine evaluation studies ▪ Semi-quantitatively measure the immune response to RBD-containing vaccines ▪ Determine pre-vaccination immune status in order to administer vaccine to sero-naïve individuals	✔	

** Subject to vaccine emergency use authorization and CDC guidelines.*

Assay Characteristics	Elecsys® Anti-SARS-CoV-2 S Assay	Elecsys® Anti-SARS-CoV-2 Assay
Specimen type	Serum collected using standard sampling tubes or tubes containing separating gel; Li-heparin, K2-EDTA-, K3-EDTA-, and sodium citrate plasma; plasma tubes containing separating gel can be used.	Serum collected using standard sampling tubes or tubes containing separating gel. Li-heparin, K-EDTA and K-EDTA plasma as well as plasma tubes containing separating gel.
Sample volume	12 to 20 µL, depending on system used	
Testing time	18 minutes	
Traceability	Internal Roche standard for anti-SARS-CoV-2-S consisting of monoclonal antibodies. 1 nM of these antibodies correspond to 20 U/mL of the Elecsys® Anti-SARS-CoV-2 S assay.	Internal positive and negative samples
Linear range	0.4 to 250 U/mL	(qualitative)
Result interpretation	<0.8 U/mL = negative, ≥0.8 U/mL = positive	COI (cutoff index) <1.0 = non-reactive, COI ≥1.0 = reactive
Positive Percent Agreement (PPA)	**1,485 samples** from 331 symptomatic patients with a PCR confirmed SARS-CoV-2 infection were tested. 233 samples ≥15 days after diagnosis with PCR. 225 of these 233 samples ≥ 0.8 U/mL considered positive, PPA of **96.6%** (95% confidence interval: 93.35 – 98.51%) in this sample cohort.	**496 samples** from 102 symptomatic patients with a PCR confirmed SARS-CoV-2 infection were tested. One or more sequential specimens were collected after PCR confirmation at various time points. PPA of **99.5%** (95% confidence interval: 97.0 – 100%) in this sample cohort.
Negative Percent Agreement (NPA)	**5,991 samples** drawn before Oct. 2019 were tested. Overall NPA in this cohort of potentially cross-reactive samples was **99.98%** (95% confidence interval: 99.91 – 100%).	**10,453 samples** drawn before Dec. 2019 were tested. Overall NPA in this cohort of potentially cross-reactive samples was **99.80%** (95% confidence interval: 99.69 – 99.88%).
Cross-reactivity (analytical specificity)	Showed **no cross-reactivity** in **1,100** potentially cross-reactive samples including 7 samples from patients with MERS-CoV, 21 samples from patients with symptoms of common cold, 94 samples from other coronaviruses, and 978 pre-pandemic samples with reactivity for various other indications.	Out of **792** potentially cross-reacting samples, **4 samples** showed reactivity in the Elecsys® Anti-SARS-CoV-2 assay resulting in an overall specificity in this cohort of **99.5%** (95% confidence interval: 98.63-99.85 %).

REFERENCES

1. https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antibody-tests-guidelines.html. Accessed 12/08/2020.
2. https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/eua-authorized-serology-test-performance. Accessed 12/08/2020.
3. Roche Diagnostics. SARS-CoV-2 antibody specificity white paper. June 29, 2020.
4. Callaway E. The race for coronavirus vaccines: a graphical guide. *Nature*. 2020;580:576-7.
5. Zhou G, Zhao Q. Perspectives on therapeutic neutralizing antibodies against the Novel Coronavirus SARS-CoV-2. *Int J Biol Sci.* 2020;16:1718-23.
6. Elecsys® Anti-SARS-CoV-2 S Assay. Package Insert 2020-12, V1.0; Material Numbers 09289267190 and 09289275190. Roche Diagnostics.
7. Elecsys® Anti-SARS-CoV-2 Assay. Package Insert 2020-07, V3.0; Material Numbers 09203095190 and 092030. Roche Diagnostics.
8. Adapted from Sethuraman et al. Estimated time intervals and rates of viral detection are based on data from several published reports. Because of variability in values among studies, estimated time intervals should be considered approximations and the probability of detection of SARS-CoV-2 infection is presented qualitatively. Sethuraman N, Jeremiah SS, Ryo A. Interpreting diagnostic tests for SARS-CoV-2. *JAMA*. Published online May 06, 2020. doi:10.1001/jama.2020.8259.
9. CDC, Interim Guidelines for COVID-19 Antibody Testing: https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antibody-tests-guidelines.html.
10. Deeks JJ, et al. Antibody tests for identification of current and past infection with SARS-CoV-2 (Review). Cochrane Database of Systematic Reviews 2020, Issue 6. Art. No.: CD013652. doi: 10.1002/14651858.CD013652.
11. Cheng MP, et al. Serodiagnostics for severe acute respiratory syndrome–related coronavirus-2: a narrative review. *Ann Intern Med.* 2020. doi:10.7326/M20-2854.
12. Sethuraman N, et al. Interpreting diagnostic tests for SARS-CoV-2. *JAMA*. 2020;323:2249–51.
13. To K, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infections by SARS-CoV-2: an observational cohort study. *The Lancet.* 2020;20(5):P565-74. https://doi.org/10.1016/S1473-3099(20)30196-1.
14. Long Q, et al. Antibody responses to SARS-CoV-2 in COVID-19 patients: the perspective application of serological tests in clinical practice. medRxiv 2020. https://www.medrxiv.org/content/10.1101/2020.03.18.20038018v1.
15. Xiang F, et al. Antibody detection and dynamic characteristics in patients with coronavirus disease 2019. *Clin Infect Dis.* 2020;71(8):1930-34. https://doi.org/10.1093/cid/ciaa461.
16. Hou H, et al., Detection of IgM and IgG antibodies in patients with coronavirus disease 2019. *Clin Transl Immunology.* 2020;9(5): e01136. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7202656/pdf/

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.

For more information, contact your sales representative or visit go.roche.com/cobas-SARS-CoV-2

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