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*Published in:*  
Clinical Chemistry

*DOI:*  
[10.1093/clinchem/hvaa131](https://doi.org/10.1093/clinchem/hvaa131)

*Publication date:*  
2020

*Document Version*  
Peer reviewed version

[Link to publication](#)

*Citation for published version (HARVARD):*  
Favresse, J, Eucher, C, Elsen, M, Marie, T-H, Dogné, J-M & Douxfils, J 2020, 'Clinical performance of the Elecsys electrochemiluminescent immunoassay for the detection of SARS-CoV-2 total antibodies', *Clinical Chemistry*, vol. 66, no. 8, hvaa131, pp. 1104-1106. <https://doi.org/10.1093/clinchem/hvaa131>

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**Clinical performance of the Elecsys electrochemiluminescent immunoassay for the  
detection of SARS-CoV-2 total antibodies**

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**Running title:** Elecsys anti-SARS-CoV-2 evaluation.

**Keywords:** COVID-19, SARS-CoV-2, serology, kinetic.

**Words (manuscript):** 743 (excluding references, figure, and legend).

**Number of figures:** 1

To the Editor

In the context of COVID-19, a wide range of serology immunoassays with different SARS-CoV-2 antigen recognition and antibody specificity have been developed to complement RT-PCR assays [1]. Serological testing is useful for diagnosis and characterization of the course of the disease, identification of convalescent plasma donors, for epidemiology studies, lockdown exit programs and COVID-19 vaccine development [2, 3]. Due to the widespread dissemination of these new methods and the limited experience with these assays, it is crucial for laboratories to rigorously validate these methods before broad introduction into routine clinical practice. Independent validations are also needed to assure the assays are in line with expected analytical and clinical performance specifications [1-4].

This study is the first to report the external validation of a new electrochemiluminescent immunoassay (ECLIA) test, the Elecsys anti-SARS-CoV-2 from Roche Diagnostics®. This test allows the detection of total antibodies (including IgG) specifically directed against SARS-CoV-2 nucleocapsid and is performed on the cobas® e801 module. The test result is given as a cut-off index (COI). According to the manufacturer, a result <1.0 is considered negative while a result ≥1.0 is considered positive [5]. The within-run and between-run imprecision (CV) on 5 patient pools (COI means of 0.081, 1.0, 8.7, 24, and 54) varied from 0.8% to 3.3%, and from 1.2% to 3.6%, respectively. Sample storage complied with the conditions listed in the package insert.

This retrospective study was conducted from May 6 to 12, 2020 at the clinical biology laboratory of the Clinique Saint-Luc Bouge (SLBO, Namur, Belgium). Serum samples (n=140) obtained from 97 patients with a confirmed RT-PCR SARS-CoV-2 diagnosis were used to determine the clinical sensitivity of the assay. RT-PCR on respiratory samples (nasopharyngeal swab samples) was performed on the LightCycler® 480 Instrument II using the LightMix® Modular SARS-CoV-2 E-gene set (Roche Diagnostics®). Serum samples were subdivided into

different categories based on the number of days after a positive RT-PCR test as follows: 0-6 days: 45 sera; 7-13 days: 35 sera; 14-20 days: 24 sera; 21-27 days: 15 sera; 28 days or more: 21 sera. Among the 60 samples collected 14 or more days after the RT-PCR positive detection, and using the manufacturer's cut-off, the Elecsys anti-SARS-CoV-2 immunoassay identified 55 true positive and 5 false negative samples. The diagnostic sensitivity was 91.7% (95%CI: 81.6-97.2%). Using the optimal cut-off provided by ROC curve analyses (i.e.>0.165) improved the performance of the test to give a sensitivity of 100% (95%CI: 94.0-100%) (**Figure 1**).

A sensitivity analysis was also performed considering the date of symptom onset. Among the 97 patients, data about time of symptom onset were available for 92 patients. The collected samples (n=129) were subdivided into different categories according to the number of days after the onset of symptoms as follows: 0-6 days: 22 sera; 7-13 days: 28 sera; 14-20 days: 26 sera; 21-27 days: 23 sera; 28 days or more: 30 sera. Among the 79 samples evaluated 14 or more days after the onset of symptoms, and using the manufacturer's cut-off, the Elecsys anti-SARS-CoV-2 assay identified 72 true positive and 7 false negative samples. The diagnostic sensitivity was 91.1% (95%CI: 82.6-96.4%). Using the ROC curve cut-off (i.e.>0.165) improved the performance of the tests with a sensitivity of 95.1% (95%CI: 88.0-98.7%). Analyses of serum samples obtained 28 days or more after symptom onset provided a sensitivity of 96.7% (95%CI: 82.8-99.9%) and 100% (95%CI: 88.9-100%) with the manufacturer and the optimized cut-off, respectively (**Figure 1**).

Considering samples obtained before 14 days (from RT-PCR + or symptoms onset), sensitivities were not sufficient to be reliable in clinical practice (**Figure 1**).

Non-SARS-CoV-2 sera (n=79) collected prior to the COVID-19 pandemic (between January 2019 and December 2019) with potential cross-reactions (cross-reactivity test group) were also analyzed. Samples in this group included positive antinuclear antibodies (n=5), anti-thyroglobulin antibody (n=1), anti-*Treponema pallidum* antibodies (n=2), antistreptolysin O

(n=1), anti-thyroid peroxidase antibodies (n=4), chikungunya antibody (n=1), direct Coombs (n=1), hepatitis B Ag (n=4), hepatitis C antibodies (n=7), hepatitis E antibodies (n=4), human immunodeficiency virus antibodies (n=2), IgA *Chlamydia pneumoniae* (n=1), IgG *Chlamydia trachomatis* (n=1), IgG *Coxiella burnetii* (n=2), IgM *Borrelia* (n=1), IgM *Coxiella burnetii* (n=1), IgM cytomegalovirus (n=5), IgM Epstein Barr virus viral capsid (n=5), IgM *Mycoplasma pneumoniae* (n=6), IgM parvovirus B19 (n=7), IgM *Toxoplasma gondii* (n=5), influenza antibodies (n=6), RAI (search for irregular agglutinins) (n=2), and rheumatoid factor (n=5). The calculated specificity was 100% (95%CI: 95.44-100.0%). Using the ROC curve cut-off (i.e.>0.165) had no effect on the measured diagnostic specificity (**Figure 1**).

The optimal ROC cut-off showed excellent clinical performance 14 days or more following RT-PCR positivity or following the onset of COVID-19 symptoms. Additional studies are needed to further confirm the best cut-off. Expert societies are also urged to provide guidance on the best time after RT-PCR positivity or symptom onset to perform serological investigations, since this is an important determinant of the true positivity rate.

### **Acknowledgment**

We wish to thank the personnel of the Saint-Luc Bouge laboratory for its technical assistance.

**Author Contributions:** *All authors confirmed they have contributed to the intellectual content of this paper and have met the following 4 requirements: (a) significant contributions to the conception and design, acquisition of data, or analysis and interpretation of data; (b) drafting or revising the article for intellectual content; (c) final approval of the published article; and (d) agreement to be accountable for all aspects of the article thus ensuring that questions related to the accuracy or integrity of any part of the article are appropriately investigated and resolved.*

J. Favresse, statistical analysis, administrative support, provision of study material or patients; C. Eucher, administrative support, provision of study material or patients; M. Elsen, administrative support, provision of study material or patients; J. Douxfils, statistical analysis.

**Authors' Disclosures or Potential Conflicts of Interest:** *Upon manuscript submission, all authors completed the author disclosure form. Disclosures and/or potential conflicts of interest:*

**Employment or Leadership:** J. Douxfils, chief executive officer and founder of QUALIblood sa.

**Consultant or Advisory Role:** None declared.

**Stock Ownership:** None declared.

**Honoraria:** None declared.

**Research Funding:** Roche Diagnostics provided the kits for the validation.

**Expert Testimony:** None declared.

**Patents:** None declared.

**Other Remuneration:** J. Douxfils, personal fees from Diagnostica Stago, Roche, Roche Diagnostics, Daiichi-Sankyo, and Portola, outside the submitted work.

## References

1. Vashist SK. In Vitro Diagnostic Assays for COVID-19: Recent Advances and Emerging Trends. *Diagnostics (Basel)* 2020;10:202.
2. Winter AK, Hegde ST. The important role of serology for COVID-19 control. [epub ahead of print] *Lancet Infect Dis* 2020 Apr 21 as doi: 10.1016/S1473-3099(20)30322-4.
3. Farnsworth CW, Anderson NW. SARS-CoV-2 Serology: Much Hype, Little Data. *Clin* [epub ahead of print] *Chem* 2020 Apr 28 as doi: 10.1093/clinchem/hvaa107.
4. Kirkcaldy RD, King BA, Brooks JT. COVID-19 and Postinfection Immunity: Limited Evidence, Many Remaining Questions. [epub ahead of print] *JAMA* 2020 May 11 as doi: 10.1001/jama.2020.7869.
5. Roche Diagnostics. Elecsys Anti-SARS-CoV-2, insert sheet REF 09203079190, 2020-04, V 1.0.

**Figure legend**

**Figure 1:** Clinical performance of the Elecsys anti-SARS-CoV-2 assay subdivided by time since the RT-PCR positivity or since the onset of symptoms. Cross-reactivity refers to the cross-reactivity test group described in the text. \* = unaffected by the cut-off used ( $\geq 1.0$  or  $>0.165$ ). The dotted lines indicate the manufacturer’s cut-off (in black) and the optimized cut-off (in grey).

