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Specificity of an automated Anti-SARS-CoV-2 immunoassay in COVID-19 pre-pandemic cohorts

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Introduction

- The COVID-19 pandemic has prompted the launch of several different serological assays. Reliable information regarding the relative performance of these assays in a wide range of settings is urgently needed.
- Research into antibody responses against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) – the infectious agent responsible for COVID-19 – has revealed information about the timing of seroconversion, a critical consideration in serological testing.
  - Evidence suggests that immunoglobulin M (IgM) antibodies are detectable within 5 days of symptom onset, immunoglobulin G (IgG) antibodies within 5–14 days,[1–3] and immunoglobulin A (IgA) antibodies after approximately 3–6 days.[2,4] The chronological order in which IgM and IgG antibodies develop appears to be highly variable, as are antibody levels.[3,5–7]
  - This supports the need for accurate serological tests for the detection of high-affinity (i.e. late-onset/mature) antibodies to identify previous SARS-CoV-2 infection.
- The Elecsys® Anti-SARS-CoV-2 immunoassay (Roche Diagnostics International Ltd) was developed to provide an accurate and reliable method for detecting antibodies to SARS-CoV-2.
- This in vitro qualitative electrochemiluminescence assay detects various antibodies (including IgG) to SARS-CoV-2 in human serum and plasma and is intended for use on cobas e immunoassay analysers.[8,9]
- The immunoassay uses an in-solution double-antigen sandwich test principle, with a recombinant protein representing the nucleocapsid antigen of SARS-CoV-2.[8,9]

Objectives

- **To evaluate the specificity of the Elecsys Anti-SARS-CoV-2 immunoassay using pre-pandemic samples collected from five sites across Germany, Austria and Switzerland.**

Methods

- This retrospective, non-interventional study was conducted at five sites: one site (Innsbruck [Austria]) provided serum samples and four sites (Augsburg, Hagen, Heidelberg [Germany] and Bern [Switzerland]) provided serum and/or plasma samples and performed testing using the cobas e 801 analyser (Roche Diagnostics International Ltd).
- Samples were anonymised, frozen, residual serum and/or plasma specimens from blood donors or routine diagnostic testing obtained prior to September 2019, and were therefore assumed negative for SARS-CoV-2-specific antibodies. Specimens included pregnancy screening and paediatric samples.
- Specificity of the Elecsys Anti-SARS-CoV-2 immunoassay was assessed using the cobas e 801 analyser, which compared the electrochemiluminescence signal obtained from the reaction product of the sample with the signal of the cut-off value, previously obtained by calibration.
- Point estimates and 95% confidence intervals were calculated.

Results

- A total of 9575 samples presumed negative for SARS-CoV-2 antibodies were analysed.
- Specificity of the Elecsys Anti-SARS-CoV-2 immunoassay for the overall sample cohort and by analysis group are shown in **Table 1**.
- Using an assay COI of ≥1 resulted in an overall specificity of 99.85% in samples obtained across all five sites.
- Among 6714 serum and/or plasma samples from blood donors and 2861 serum and/or plasma samples from routine diagnostic samples, specificity was 99.82% and 99.93%, respectively.
- Among 2256 samples from pregnant women, specificity was 99.91% and among 205 paediatric samples, specificity was 100%.
- Across Groups A (blood donors) and B (routine diagnostic specimens), a total of 14 reactive samples were detected (Group A, n=12; Group B, n=2).
- The COI distribution across samples is shown in **Figure 1**. Only 14 samples had a COI ≥1 (pre-specified cut-off for reactivity).

Figure 1. Cut-off index (COI) distribution of patient samples (n=9575)

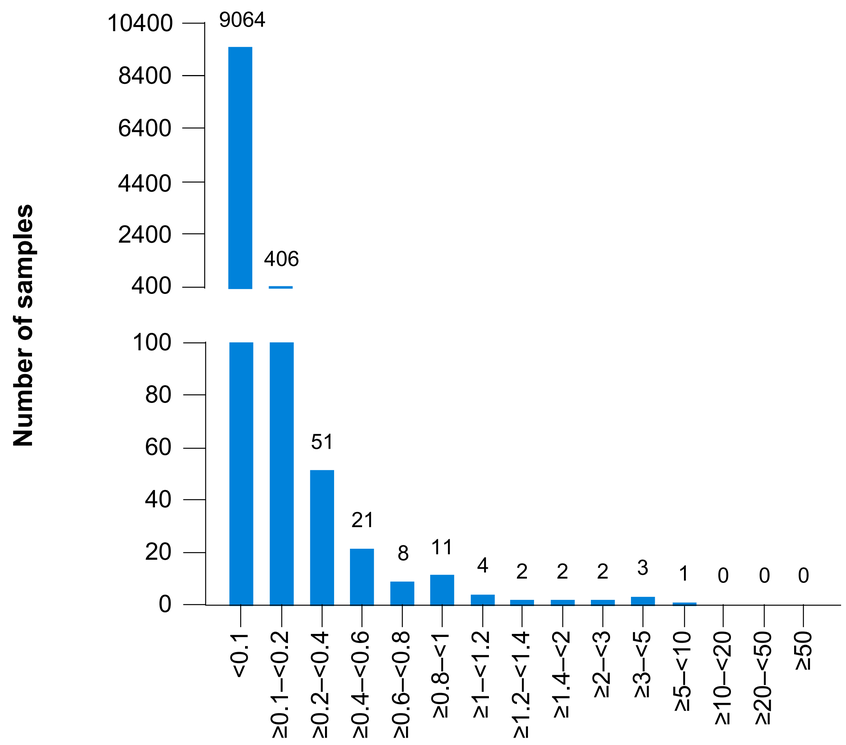

Table 1. Summary of specificity results for the Elecsys Anti-SARS-CoV-2 immunoassay in blood donor samples and routine diagnostic specimens

Group	Sample cohort	No. samples tested	No. samples reactive	No. samples non-reactive	Specificity, % (95% CI)
Groups A and B	**All**	**9575**	**14**	**9561**	**99.85 (99.75–99.92)**
	Austria (Innsbruck), flu season*	**1048**	**5**	**1043**	**99.52 (98.89–99.84)**
	Germany (Hagen)	**2625**	**2**	**2623**	**99.92 (99.73–99.99)**
Group A	**Switzerland (Bern)**	**3041**	**5**	**3036**	**99.84 (99.62–99.95)**
Blood donors	*Switzerland (Bern), no flu season*	*2003*	*2*	*2001*	*99.90 (99.64–99.99)*
	Switzerland (Bern), flu season	*1038*	*3*	*1035*	*99.71 (99.16–99.94)*
	All	**6714**	**12**	**6702**	**99.82 (99.69–99.91)**
	Germany (Augsburg), diagnostic routine	**400**	**0**	**400**	**100 (99.08–100)**
	Germany (Augsburg and Heidelberg), pregnancy	**2256**	**2**	**2254**	**99.91 (99.68–99.99)**
Group B	*Germany (Augsburg), pregnancy*	*1498*	*2*	*1496*	*99.87 (99.52–99.98)*
Routine diagnostic testing	*Germany (Heidelberg), pregnancy*	*758*	*0*	*758*	*100 (99.51–100)*
	Germany (Heidelberg), paediatrics	**205**	**0**	**205**	**100 (98.22–100)**
	All	**2861**	**2**	**2859**	**99.93 (99.75–99.99)**

*Samples from Innsbruck were analysed at Augsburg.

CI, confidence interval; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Conclusions

- **The performance of SARS-CoV-2 antibody assays in general is of high importance for public health and may affect political decision-making in pandemic management.**
- **This study generated additional data on the performance of the Elecsys Anti-SARS-CoV-2 immunoassay and provided broader evidence on the very high specificity of the assay across various pre-pandemic cohort samples, including blood donors, pregnant women and paediatric populations.**
- **Our findings support the use of the Elecsys Anti-SARS-CoV-2 immunoassay as a potential tool for determination of a mature immune response following previous exposure to SARS-CoV-2 in the general population.**

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Disclosures

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