Overview
SARS-CoV-2, the causative agent of Coronavirus Disease 2019 (COVID-19), is an enveloped, single-stranded RNA Beta-coronavirus. Seven coronaviruses have been identified as agents of human infection, causing disease ranging from mild common cold to severe respiratory failure. SARS-CoV-2 is transmitted primarily from person-to-person through respiratory droplets and aerosols. The incubation period from infection to detectable viral load in the host commonly ranges from two to 14 days. Detection of viral load can be associated with the onset of clinical signs and symptoms, although a considerable proportion of individuals remain asymptomatic or mildly symptomatic. The interval during which an individual with COVID-19 is infectious has not yet been clearly established; however, transmission from symptomatic, asymptomatic, and pre-symptomatic individuals has been well described.\(^{1,3}\) Coronavirus genomes encode 4 main structural proteins: spike (S), envelope (E), membrane (M), and nucleocapsid (N). The S protein is a very large transmembrane protein that assembles into trimers to form the distinctive surface spike of SARS-CoV-2. Each S protein consists of an S1 subunit and a membrane-proximal S2 subunit. The S1 subunit is involved in virus entry into the host cell through binding of the S protein to the angiotensin-converting enzyme 2 (ACE2) receptor, which is present on the surface of numerous cell types including the absorptive type II cell of the lung and epithelial cell of the oral mucosa.\(^{1,3}\) Mechanically, ACE2 is engaged by the receptor-binding domain of the S2 subunit.\(^{1,3}\)

Upon infection with SARS-CoV-2, the host usually mounts an immune response against the virus, typically including production of specific antibodies against viral antigens. IgM and IgG antibodies against SARS-CoV-2 appear to arise nearly simultaneously in blood. There is significant inter-individual difference in the levels and chronological appearance of antibodies in COVID-19 patients, but median monoclonality has been observed in approximately two weeks.\(^{1,3}\) The presence of antibodies against the receptor-binding domain of the S protein is associated with protection from COVID-19.\(^{1,3}\)

Elecys® Anti-SARS-CoV-2 S
Immunooassay for the quantitative determination of antibodies to the SARS-CoV-2 spike protein

Structure of the SARS-CoV-2 spike protein and binding to host receptor

<table>
<thead>
<tr>
<th>Product</th>
<th>Material configuration</th>
<th>Material number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elecsys® Anti-SARS-CoV-2 S</td>
<td>3 x 1.0 mL</td>
<td>120 206 275 188</td>
</tr>
<tr>
<td>Precicontrol Anti-SARS-CoV-2 S</td>
<td>9 x 1.1 mL</td>
<td>120 206 281 192</td>
</tr>
<tr>
<td>TrueSet Anti-SARS-CoV-2</td>
<td>2 x 1.0 mL</td>
<td>120 206 313 180</td>
</tr>
</tbody>
</table>

References
\(^{1}\) Zhao, J. et al. (2020).
\(^{2}\) Zhang, L. et al. (2020).
\(^{3}\) Zhong, N.K. et al. (2020).
\(^{4}\) Chan, J.F.-W. et al. (2020).
\(^{5}\) Lauer, S.A. et al. (2020).
\(^{6}\) He, X. et al. (2020).
\(^{7}\) Mizumoto, K. et al. (2020).
\(^{8}\) Wu, F. et al. (2020).
\(^{9}\) Jeanmougin, F. et al. (2020).
\(^{10}\) Liu, Z. et al. (2020).
\(^{11}\) Yu, P. et al. (2020).
\(^{12}\) Letko, M. et al. (2020).
\(^{13}\) Xu, H. et al. (2020).
\(^{14}\) Wrapp, D. et al. (2020).
\(^{15}\) Xu, X. et al. (2020).

Infection with SARS-CoV-2, the host usually mounts an immune response against the virus, typically including production of specific antibodies against viral antigens. IgM and IgG antibodies against SARS-CoV-2 appear to arise nearly simultaneously in blood. There is significant inter-individual difference in the levels and chronological appearance of antibodies in COVID-19 patients, but median monoclonality has been observed in approximately two weeks.\(^{1,3}\)
Electro-chemiluminescence immunoassay (ECLI) Test principle: double-antigen sandwich assay (testing time: 18 minutes)®

Electrolyte Anti-SARS-CoV-2 S is an immunoassay for the in vitro quantitative determination of antibodies (including IgG) to the SARS-CoV-2 spike (S) protein receptor binding domain (RBD) in human serum. It is intended for detection of anti-SARS-CoV-2 antibodies in samples collected using standard sampling tubes; Li-heparin, K3 EDTA, K3 EDTA, and sodium citrate plasma. The test is intended as an aid to assess the adaptive humoral immune response to the SARS-CoV-2 S protein.®

Clinical sensitivity®
A total of 5,991 samples from diagnostic routine and blood donors drawn before October 2019 were tested with the Electrolyte Anti-SARS-CoV-2 S assay. Overall specificity in this cohort of pre-pandemic samples was 99.96% (99.79 – 100 %). 1,423 of the tested samples had a sampling date of 14 days or later after diagnosis with PCR. 1,406 of these 1,423 samples were determined with ≥0.8 U/mL in the Electrolyte Anti-SARS-CoV-2 S assay and hence considered positive, resulting in a sensitivity of 98.8% (95% CI: 98.1 – 99.3 %) in this sample cohort.

<table>
<thead>
<tr>
<th>Days post PCR confirmation</th>
<th>N</th>
<th>Non-reactive</th>
<th>Sensitivity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–8 Days</td>
<td>15</td>
<td></td>
<td>99.9% (73–86 %)</td>
</tr>
<tr>
<td>9–15 Days</td>
<td>15</td>
<td></td>
<td>99.9% (73–86 %)</td>
</tr>
<tr>
<td>16–20 Days</td>
<td>15</td>
<td></td>
<td>99.9% (73–86 %)</td>
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<tr>
<td>21–27 Days</td>
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<tr>
<td>28–34 Days</td>
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<td></td>
<td>99.9% (73–86 %)</td>
</tr>
<tr>
<td>35–41 Days</td>
<td>15</td>
<td></td>
<td>99.9% (73–86 %)</td>
</tr>
<tr>
<td>≥42 Days</td>
<td>15</td>
<td></td>
<td>99.9% (73–86 %)</td>
</tr>
</tbody>
</table>

Days post PCR confirmation = 0 (time from symptom onset) to ≥42 (days post PCR confirmation) ± 2 days.

Estimated course of markers in SARS-CoV-2 infection®

Correlation to serosurveillance®
The Electrolyte Anti-SARS-CoV-2 S assay was compared to a VSE-based pseudo-neutralization assay in 15 clinical samples from individual patients.