

Elecsys Anti-SARS-CoV-2 **cobas**[®]

REF			SYSTEM
09289267190	09289267501	200	cobas e 411 cobas e 601 cobas e 602
09289275190	09289275501	300	cobas e 801

For use in the USA only

System information

For **cobas e 411** analyzer: test number 2550

For **cobas e 601** and **cobas e 602** analyzers: Application Code Number 71

For **cobas e 801** analyzer: Application Code Number 10230

Warning

- For use under Emergency Use Authorization only.
- For prescription use only.
- For in vitro diagnostic use.
- The results of this semi-quantitative test should not be interpreted as an indication or degree of immunity or protection from reinfection.

Intended use

Elecsys Anti-SARS-CoV-2 S for use on the **cobas e** analyzers is an electrochemiluminescence immunoassay intended for qualitative and semi-quantitative detection of antibodies to SARS-CoV-2 in human serum and plasma (lithium heparin, dipotassium-EDTA, tripotassium-EDTA, and sodium citrate). The Elecsys Anti-SARS-CoV-2 S assay is intended for use as an aid in identifying individuals with an adaptive immune response to SARS-CoV-2, indicating recent or prior infection. At this time, it is unknown for how long antibodies persist following infection and if the presence of antibodies confers protective immunity. The Elecsys Anti-SARS-CoV-2 S assay should not be used to diagnose or exclude acute SARS-CoV-2 infection. Testing is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. 263a, that meet requirements to perform moderate or high complexity tests. Results are for the detection of SARS-CoV-2 antibodies. Antibodies to SARS-CoV-2 are generally detectable in blood several days after initial infection, although the duration of time antibodies are present post-infection is not well characterized. Individuals may have detectable virus present for several weeks following seroconversion.

Laboratories within the United States and its territories are required to report all results to the appropriate public health authorities. The sensitivity of the Elecsys Anti-SARS-CoV-2 S assay early after infection is unknown. Negative results do not preclude acute SARS-CoV-2 infection. If acute infection is suspected, direct testing for SARS-CoV-2 is necessary.

False positive results for Elecsys Anti-SARS-CoV-2 S assay may occur due to cross-reactivity from pre-existing antibodies or other possible causes.

The Elecsys Anti-SARS-CoV-2 S assay is only for use under the Food and Drug Administration's Emergency Use Authorization.

The electrochemiluminescence immunoassay "ECLIA" is intended for use on **cobas e** immunoassay analyzers.

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Summary

SARS-CoV-2, the causative agent of Coronavirus Disease 2019 (COVID-19), is an enveloped, single-stranded RNA Betacoronavirus. 7 coronaviruses have been identified as agents of human infection, causing disease ranging from mild common cold to severe respiratory failure.¹

SARS-CoV-2 is transmitted primarily from person-to-person through respiratory droplets and aerosols.^{2,3} The incubation period from infection to detectable viral load in the host commonly ranges from 2 to 14 days.^{4,5}

Detection of viral load can be associated with the onset of clinical signs and symptoms, although a considerable proportion of individuals remains asymptomatic or mildly symptomatic.^{6,7,8} 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.^{9,10,11}

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 spikes of coronaviruses. Each S monomer consists of an N-terminal S1 domain and a membrane-proximal S2 domain. The virus gains entry to the host cell through binding of the S protein to the angiotensin-converting enzyme 2 (ACE2), which is enzymatically active on the surface of numerous cell types including the alveolar type II cells of the lung and epithelial cells of the oral mucosa.^{12,13}

Mechanistically, ACE2 is engaged by the receptor-binding domain (RBD) on the S1 subunit.^{14,15}

Upon infection with SARS-CoV-2, the host mounts an immune response against the virus, typically including production of specific antibodies against viral antigens. IgM and IgG antibodies to SARS-CoV-2 appear to arise nearly simultaneously in blood.¹⁶ There is significant inter-individual difference in the levels and chronological appearance of antibodies in COVID-19 patients, but median seroconversion has been observed at approximately 2 weeks.^{17,18,19,20}

Serologic assays can play an important role in understanding viral epidemiology in the general population. The Elecsys Anti-SARS-CoV-2 S assay uses a recombinant protein representing the RBD of the spike antigen in a double-antigen sandwich assay format. The Elecsys Anti-SARS-CoV-2 S assay detects antibodies to SARS-CoV-2 spike protein RBD.

Test principle

Double-antigen sandwich principle. The antigens within the reagent capture predominantly anti-SARS-CoV-2 IgG, but also anti-SARS-CoV-2 IgA and IgM. Total duration of assay: 18 minutes.

- 1st incubation: 20 µL of sample (**cobas e 411**, **cobas e 601**, and **cobas e 602** analyzers) or 12 µL of sample (**cobas e 801** analyzer), biotinylated SARS-CoV-2 S-RBD-specific recombinant antigen and SARS-CoV-2 S-RBD-specific recombinant antigen labeled with a ruthenium complex^{a)} form a sandwich complex.
- 2nd incubation: After addition of streptavidin-coated microparticles, the complex becomes bound to the solid phase via interaction of biotin and streptavidin.
- The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with ProCell/ProCell M/ProCell II M. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier.
- Results are determined via a calibration curve which is instrument-specifically generated by 2-point calibration and a master curve provided via the reagent barcode or e-barcode.

a) Tris(2,2'-bipyridyl)ruthenium(II)-complex (Ru(bpy)₃²⁺)

Reagents - working solutions

cobas e 411, **cobas e 601**, and **cobas e 602** analyzers:

The reagent rackpack is labeled as ACOV2S.

M Streptavidin-coated microparticles (transparent cap), 1 bottle, 12.0 mL:

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Streptavidin-coated microparticles 0.72 mg/mL; preservative.

- R1 SARS-CoV-2 S-Ag~biotin (gray cap), 1 bottle, 16 mL:
Biotinylated RBD domain of SARS-CoV-2 S as recombinant antigen < 0.4 mg/L; HEPES^{b)} buffer 50 mmol/L, pH 7.4; preservative.
- R2 SARS-CoV-2 S-Ag~Ru(bpy)₃²⁺ (black cap), 1 bottle, 16 mL:
RBD domain of SARS-CoV-2 S as recombinant antigen labeled with ruthenium complex < 0.4 mg/L; HEPES^{b)} buffer 50 mmol/L, pH 7.4; preservative.

b) HEPES = [4-(2-hydroxyethyl)-piperazine]-ethane sulfonic acid

cobas e 801 analyzer:

The **cobas e** pack is labeled as ACOV2S.

- M Streptavidin-coated microparticles, 1 bottle, 16 mL:
Streptavidin-coated microparticles 0.72 mg/mL; preservative.
- R1 SARS-CoV-2 S-Ag~biotin, 1 bottle, 18.8 mL:
Biotinylated RBD domain of SARS-CoV-2 S as recombinant antigen < 0.4 mg/L; HEPES^{b)} buffer 50 mmol/L, pH 7.4; preservative.
- R2 SARS-CoV-2 S-Ag~Ru(bpy)₃²⁺, 1 bottle, 18.8 mL:
RBD domain of SARS-CoV-2 S as recombinant antigen labeled with ruthenium complex < 0.4 mg/L; HEPES^{b)} buffer 50 mmol/L, pH 7.4; preservative.

Calibrators are available separately. See Materials required (but not provided) section of this Method Sheet.

Precautions and warnings

For use under Emergency Use Authorization only.

This test has not been FDA-cleared or -approved; this test has been authorized by FDA under an Emergency Use Authorization (EUA) for use by authorized laboratories; by laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. 263a, that meet requirements to perform high complexity tests.

This test has been authorized only for detecting 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 emergency use of in vitro diagnostic tests for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

For in vitro diagnostic use.

Do not use reagents beyond the labeled expiration date.

Exercise the normal precautions required for handling all laboratory reagents.

Disposal of all waste material should be in accordance with local guidelines.

Safety data sheet available for professional user on request.

For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:



Warning

H317 May cause an allergic skin reaction.

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Prevention:

- P261 Avoid breathing dust/fume/gas/mist/vapours/spray.
- P272 Contaminated work clothing should not be allowed out of the workplace.
- P280 Wear protective gloves.

Response:

- P333 + P313 If skin irritation or rash occurs: Get medical advice/attention.
- P362 + P364 Take off contaminated clothing and wash it before reuse.

Disposal:

- P501 Dispose of contents/container to an approved waste disposal plant.
- Product safety labeling follows EU GHS guidance.
- Contact phone: 1-800-428-2336
- Avoid foam formation in all reagents and sample types (specimens, calibrators and controls).

Reagent handling

- The reagents in the kit have been assembled into a ready-for-use unit that cannot be separated.
- cobas e 411**, **cobas e 601**, and **cobas e 602** analyzers:
- All information required for correct operation is read in from the respective reagent barcodes.
- cobas e 801** analyzer:
- All information required for correct operation is available via the **cobas** link.

Storage and stability

- Store at 2-8 °C.
- Do not freeze.
- Store the Elecsys reagent kit / **cobas e** pack **upright** in order to ensure complete availability of the microparticles during automatic mixing prior to use.

Stability of the reagent rackpack:	
unopened at 2-8 °C	up to the stated expiration date
after opening at 2-8 °C	12 weeks
on the cobas e 411 , cobas e 601 and cobas e 602 analyzers	28 days

Stability of the cobas e pack:	
unopened at 2-8 °C	up to the stated expiration date
on the cobas e 801 analyzer	16 weeks

Specimen collection and preparation

Only the specimens listed below were tested and found acceptable.

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Serum collected using standard sampling tubes or tubes containing separating gel.

Li-heparin, dipotassium EDTA (K₂-EDTA), tripotassium EDTA (K₃-EDTA), and sodium citrate plasma.

Plasma tubes containing separating gel can be used.

Criterion: Slope 1.00 ± 0.10 + bias at $0.8 \text{ U/mL} \pm 20 \%$.

For native samples collected in sodium citrated plasma: Slope 0.84 ± 0.10 .

Results with sample materials other than serum were compared to serum results. Linear regression was performed for results obtained with the different sample materials, comparison of slope and bias verified comparability to serum results.

Sampling devices containing liquid anticoagulants have a dilution effect resulting in lower values (U/mL) for individual patient specimens. In order to minimize dilution effects it is essential that respective sampling devices are filled completely according to manufacturer's instructions. For citrated plasma (1 part citrate solution + 9 parts blood), the dilution effect must be taken into account.

Stable for 14 days at 15-25 °C, 14 days at 2-8 °C, 3 months at -20 °C (± 5 °C). The samples may be frozen 3 times.

The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube manufacturer.

Specimens should not be subsequently altered with additives (e.g. biocides, anti-oxidants or substances that could possibly change the pH or ionic strength of the sample) in order to avoid erroneous findings.

Centrifuge samples containing precipitates and thawed samples before performing the assay.

Do not use heat-inactivated samples.

Ensure the samples and calibrators are at 20-25 °C prior to measurement.

Due to possible evaporation effects, samples and calibrators on the analyzers should be analyzed/measured within 2 hours.

Sample stability claims were established by experimental data by the manufacturer or based on reference literature and only for the temperatures/time frames as stated in the method sheet. It is the responsibility of the individual laboratory to use all available references and/or its own studies to determine specific stability criteria for its laboratory.

Materials provided

See "Reagents – working solutions" section for reagents.

Materials required (but not provided)

- [REF] 09289291190, CalSet Anti-SARS-CoV-2 S, for 4 x 1.0 mL
- [REF] 09289313190, PreciControl Anti-SARS-CoV-2 S, 4 x 1.0 mL
- [REF] 03183971122, Diluent Universal, 2 x 36 mL sample diluent (**cobas e 411**, **cobas e 601**, and **cobas e 602** analyzers) or
- [REF] 05192943190, Diluent Universal 2, 2 x 36 mL sample diluent (**cobas e 411**, **cobas e 601**, and **cobas e 602** analyzers) or
- [REF] 07299001190, Diluent Universal, 36 mL sample diluent (**cobas e 801** analyzer)
- General laboratory equipment
- **cobas e** analyzer

Additional materials for the **cobas e 411** analyzer:

- [REF] 11662988122, ProCell, 6 x 380 mL system buffer
- [REF] 11662970122, CleanCell, 6 x 380 mL measuring cell cleaning solution
- [REF] 11930346122, Elecsys SysWash, 1 x 500 mL washwater additive

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- [REF] 11933159001, Adapter for SysClean
- [REF] 11706802001, AssayCup, 60 x 60 reaction cups
- [REF] 11706799001, AssayTip, 30 x 120 pipette tips
- [REF] 11800507001, Clean-Liner

Additional materials for **cobas e 601** and **cobas e 602** analyzers:

- [REF] 04880340190, ProCell M, 2 x 2 L system buffer
- [REF] 04880293190, CleanCell M, 2 x 2 L measuring cell cleaning solution
- [REF] 03023141001, PC/CC-Cups, 12 cups to prewarm ProCell M and CleanCell M before use
- [REF] 03005712190, ProbeWash M, 12 x 70 mL cleaning solution for run finalization and rinsing during reagent change
- [REF] 12102137001, AssayTip/AssayCup, 48 magazines x 84 reaction cups or pipette tips, waste bags
- [REF] 03023150001, WasteLiner, waste bags
- [REF] 03027651001, SysClean Adapter M

Additional materials for the **cobas e 801** analyzer:

- [REF] 06908799190, ProCell II M, 2 x 2 L system solution
- [REF] 04880293190, CleanCell M, 2 x 2 L measuring cell cleaning solution
- [REF] 07485409001, Reservoir Cup, 8 cups to supply ProCell II M and CleanCell M
- [REF] 06908853190, PreClean II M, 2 x 2 L wash solution
- [REF] 05694302001, Assay Tip/Assay Cup tray, 6 magazines x 6 magazine stacks x 105 assay tips and 105 assay cups, 3 wasteliners
- [REF] 07485425001, Liquid Flow Cleaning Cup, 2 adaptor cups to supply ISE Cleaning Solution/Elecsys SysClean for Liquid Flow Cleaning Detection Unit
- [REF] 07485433001, PreWash Liquid Flow Cleaning Cup, 1 adaptor cup to supply ISE Cleaning Solution/Elecsys SysClean for Liquid Flow Cleaning PreWash Unit

Additional material for all analyzers:

- [REF] 11298500160, ISE Cleaning Solution/Elecsys SysClean, 5 x 100 mL system cleaning solution

Assay

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator's manual for analyzer-specific assay instructions.

Resuspension of the microparticles takes place automatically prior to use.

cobas e 411, **cobas e 601**, and **cobas e 602** analyzers:

Read in the test-specific parameters via the reagent barcode. If in exceptional cases the barcode cannot be read, enter the 15-digit sequence of numbers. Bring the cooled reagents to approximately 20 °C and place on the reagent disk (20 °C) of the analyzer.

cobas e 801 analyzer:

Place the cooled (stored at 2-8 °C) **cobas e** pack on the reagent manager.

All analyzers: Avoid foam formation. The system automatically regulates the temperature of the reagents and the opening/closing of the bottles/ **cobas e** pack.

Calibration

Traceability: This method has been standardized against the internal Roche standard for anti-SARS-CoV-2-S. This standard consists of an equimolar mixture of 2 monoclonal antibodies that bind Spike-1 RBD at 2 different epitopes. 1 nM of these antibodies correspond to 20 U/mL of the Elecsys Anti-SARS-CoV-2 S assay. No international standard is currently available for anti-SARS-CoV-2-S.

Note: The defined unit is specific for the Elecsys Anti-SARS-CoV-2 S assay and must not be used interchangeably with units of other assays.

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Every Elecsys reagent set has a barcoded label containing specific information for calibration of the particular reagent lot. The predefined master curve is adapted to the analyzer using the relevant CalSet.

Calibration frequency: Calibration must be performed once per reagent lot using fresh reagent (i.e. not more than 24 hours since the same reagent kit was registered on the analyzer).

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

Renewed calibration is recommended as follows:

- after 31 days when using the same reagent lot on the **cobas e 411**, **cobas e 601** and **cobas e 602** analyzers
- after 42 days when using the same reagent lot on the **cobas e 801** analyzer
- after 14 days when using the same reagent kit or **cobas e** pack on the analyzer
- as required: e.g. quality control findings outside the defined limits

Quality control

For quality control, use PreciControl Anti-SARS-CoV-2 S. Please refer to the PreciControl Method Sheet for instructions for use, including description of the controls and the expected results.

In addition, other commercially available quality control material can be used that covers at least two levels of analyte.

Controls for the various concentration ranges should be run individually at least once every 24 hours when the test is in use, once per reagent kit / **cobas e** pack, and following each calibration.

The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined limits. Follow your laboratory's quality control procedures if the results obtained do not fall within the acceptable limits. Please refer to PreciControl instructions for use. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

If necessary, repeat the measurement of the samples concerned.

Follow the applicable government regulations and local and accrediting group guidelines for quality control.

Calculation

The analyzer automatically calculates the analyte concentration of each sample in U/mL.

Interpretation of the patient results

Result	Interpretation
< 0.80 U/mL	Negative for anti-SARS-CoV-2-S
≥ 0.80 U/mL - ≤ 250 U/mL	Positive for anti-SARS-CoV-2-S, numeric value within the measuring interval
> 250 U/mL	Positive for anti-SARS-CoV-2-S, numeric value as "> 250 U/mL"

Note: Due to the diversity of the antibodies, the measured anti-SARS-CoV-2-S value can vary depending on the testing procedure used and the applied standard. Results obtained from a single sample using tests from different manufacturers can therefore differ. If there is a change in the assay procedure used to test the same patient then the anti-SARS-CoV-2-S values obtained upon changing over to the new procedure must be confirmed by parallel measurements with both methods. For citrated plasma (1 part citrate solution + 9 parts blood), the dilution effect must be taken into account.

Limitations

- Drug interferences are measured based on recommendations given in CLSI (Clinical and Laboratory Standards Institute) guidelines EP07 and EP37 and other published literature. Effects of concentrations exceeding these recommendations have not been characterized.

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- In rare cases, interference due to extremely high titers of antibodies to analyte-specific antibodies, streptavidin or ruthenium can occur. These effects are minimized by suitable test design.
- Results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.
- This device should not be used to diagnose or exclude acute SARS-CoV-2 infection. Direct testing for SARS-CoV-2 with a molecular assay should be performed to evaluate acute infection in symptomatic individuals.
- The clinical applicability of semi-quantitative results is currently unknown and cannot be interpreted as an indication or degree of immunity nor protection from reinfection, nor compared to other SARS-CoV-2 antibody assays.
- Results obtained with this assay may not be used interchangeably with values obtained with different manufacturers' test methods.
- A positive result may not indicate previous SARS-CoV-2 infection. Consider other information including clinical history and local disease prevalence, in assessing the need for a second but different serology test to confirm an immune response.
- A negative result for an individual subject indicates the absence of detectable anti-SARS-CoV-2 antibodies. Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions. A negative result can occur if the quantity of the anti-SARS-CoV-2 antibodies that are detected and are not present in the specimen is below the detection limits of the assay, or the antibodies that are detected are not present during the stage of disease in which a sample is collected.
- It is not known at this time if the presence of antibodies to SARS-CoV-2 confers immunity to re-infection.
- Not to be used to determine SARS-CoV-2 infection in donated blood units. This test should not be used for blood donor screening.
- The performance of this test has not been established in individuals that have received a COVID-19 vaccine. The clinical significance of a positive or negative antibody result following COVID-19 vaccination has not been established, and the result from this test should not be interpreted as an indication or degree of protection from infection after vaccination.
- The performance of this test was established based on the evaluation of a limited number of clinical specimens. Samples used to establish positive clinical agreement were collected between March and July 2020 in Switzerland, Germany, and Ukraine. The clinical performance has not been established in all circulating variants but is anticipated to be reflective of the prevalent variants in circulation at the time and location of the clinical evaluation. Performance at the time of testing may vary depending on the variants circulating, including newly emerging strains of SARS-CoV-2 and their prevalence, which change over time.

Conditions of Authorization for the Laboratory

The Elecsys Anti-SARS-CoV-2 S assay Letter of Authorization, along with the authorized Fact Sheet for Healthcare Providers, the authorized Fact Sheet for Patients, and authorized labeling are available on the FDA website: <https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas>. However, to assist clinical laboratories using the Elecsys Anti-SARS-CoV-2 S ("your product" in the conditions below), the relevant Conditions of Authorization are listed below:

- Authorized laboratories^{o)} using your product will include with test result reports, all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.
- Authorized laboratories using your product will use your product as outlined in the Instructions for Use. Deviations from the authorized procedures, including the authorized instruments, authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and authorized materials

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required to use your product are not permitted.

- Authorized laboratories that receive your product will notify the relevant public health authorities of their intent to run your product prior to initiating testing.
- Authorized laboratories using your product will have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
- Authorized laboratories will collect information on the performance of your product and report to DMD/OHT7-OIR/OPEQ/ CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov) and Roche (1-800-428-2336) any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of your product of which they become aware.
- All laboratory personnel using your product must be appropriately trained in automated immunoassay techniques and use appropriate laboratory and personal protective equipment when handling this kit, and use your product in accordance with the authorized labeling. All laboratory personnel using the assay must also be trained in and be familiar with the interpretation of results of the product.
- Roche, authorized distributors, and authorized laboratories using your product will ensure that any records associated with this EUA are maintained until otherwise notified by FDA. Such records will be made available to FDA for inspection upon request.

c) The letter of authorization refers to, "Laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet requirements to perform moderate or high complexity tests" as "authorized laboratories".

Limits and ranges

Analytical measuring interval

The analytical measuring interval is 0.40-250 U/mL. Numeric values are interpreted as "negative" (< 0.8 U/mL) and as "positive" (≥ 0.80 U/mL). Please see Interpretation of the results section. When sample results exceed the upper limit of the analytical measuring interval, refer to the Dilution section below. Values above the measuring range are reported as > 250 U/mL (or up to 2500 U/mL for 10-fold diluted samples).

Lower limits of measurement

Limit of Blank, Limit of Detection and Limit of Quantitation

Limit of Blank = 0.30 U/mL

Limit of Detection = 0.35 U/mL

Limit of Quantitation = 0.40 U/mL

The Limit of Blank, Limit of Detection and Limit of Quantitation were determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A2 requirements.

The Limit of Blank corresponds to the highest measurement result that is likely to be observed for analyte-free samples with a probability of 95 %. The Limit of Blank was estimated as the 95th percentile value from $n \geq 60$ measurements of analyte-free samples over several independent series. The Limit of Blank is 0.30 U/mL.

The Limit of Detection is the lowest concentration of antibodies to SARS-CoV-2 in a sample that can be detected with a probability of 95 %. The Limit of Detection was calculated based on the Limit of Blank and the standard deviation of low concentration samples. The Limit of Detection is 0.35 U/mL.

The Limit of Quantitation is defined as the lowest amount of analyte in a sample that can be accurately quantified with a $CV \leq 20$ %. It has been determined using low concentration of anti-SARS-CoV-2-S samples. The Limit of Quantitation is 0.40 U/mL.

Dilution

Samples with anti-SARS-CoV-2-S concentrations above the measuring range can be diluted with Diluent Universal or Diluent Universal 2. The recommended dilution is 1:10 up to 1:100.

After dilution by the analyzers, the software automatically takes the dilution into account when calculating the sample concentration.

Note: Antibodies to SARS-CoV-2 are heterogeneous. In some isolated cases, this may lead to non-linear dilution behavior.

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Specific performance data

Representative performance data on the analyzers are given below. Results obtained in individual laboratories may differ.

Precision

Precision was determined using Elecsys reagents, samples and controls in a protocol (EP05-A3) of the CLSI: 1 run per day with 5 replicates of each sample for 5 days. The following results were obtained:

Repeatability and Intermediate precision

cobas e 411 analyzer					
		Repeatability		Intermediate precision ^{d)}	
Sample N = 25	Mean U/mL	SD U/mL	CV %	SD U/mL	CV %
Human plasma 1	0.483	0.014	2.8	0.016	3.4
Human plasma 2	0.826	0.023	2.8	0.023	2.8
Human plasma 3	5.74	0.131	2.3	0.150	2.6
Human plasma 4	12.3	0.266	2.2	0.304	2.5
Human plasma 5	54.6	1.58	2.9	1.58	2.9
Human plasma 6	77.9	1.78	2.3	2.07	2.7
Human plasma 7	190	3.03	1.6	3.69	1.9
PC ^{e)} ACOV2S 1 ^{f)}	< 0.40	-	-	-	-
PC ACOV2S 2	10.8	0.207	1.9	0.230	2.1

d) Intermediate precision includes repeatability and between-day/run components.

e) PC = PreciControl

f) PC ACOV2S 1 is free of analyte and therefore consistently resulted below the measuring range (< 0.40 U/mL) throughout the experiment, standard deviation and coefficient of variance could therefore not be determined (-).

cobas e 601 and cobas e 602 analyzers					
		Repeatability		Intermediate precision ^{d)}	
Sample N = 25	Mean U/mL	SD U/mL	CV %	SD U/mL	CV %
Human plasma 1	0.441	0.007	1.6	0.016	3.7
Human plasma 2	0.933	0.014	1.5	0.022	2.3
Human plasma 3	5.60	0.102	1.8	0.181	3.2

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cobas e 601 and cobas e 602 analyzers					
		Repeatability		Intermediate precision ^{d)}	
Sample N = 25	Mean U/mL	SD U/mL	CV %	SD U/mL	CV %
Human plasma 4	12.0	0.189	1.6	0.334	2.8
Human plasma 5	53.2	0.761	1.4	1.46	2.7
Human plasma 6	75.5	1.55	2.1	2.70	3.6
Human plasma 7	183	3.31	1.8	5.13	2.8
PC ACOV2S 1 ^{g)}	< 0.40	-	-	-	-
PC ACOV2S 2	10.5	0.118	1.1	0.341	3.3

g) PC ACOV2S 1 is free of analyte and therefore consistently resulted below the measuring range (< 0.40 U/mL) throughout the experiment, standard deviation and coefficient of variance could therefore not be determined (-).

cobas e 801 analyzer					
		Repeatability		Intermediate precision ^{d)}	
Sample N = 25	Mean U/mL	SD U/mL	CV %	SD U/mL	CV %
Human plasma 1	0.483	0.014	2.9	0.014	2.9
Human plasma 2	0.826	0.015	1.9	0.015	1.9
Human plasma 3	5.69	0.121	2.1	0.136	2.4
Human plasma 4	12.0	0.159	1.3	0.191	1.6
Human plasma 5	54.8	0.743	1.4	0.770	1.4
Human plasma 6	77.3	1.23	1.6	1.54	2.0
Human plasma 7	184	1.69	0.90	2.63	1.4
PC ^{e)} ACOV2S 1 ^{g)}	< 0.40	-	-	-	-
PC ACOV2S 2	10.4	0.139	1.3	0.206	2.0

Precision study for evaluation of Lot-to-lot and Between-platform variability

An additional precision study for the estimation of lot-to-lot precision component was conducted with the design similar to the single-site precision study and with 2 additional lots.

Lot-to-lot precision

Lot-to-lot variability was evaluated for the **cobas e 801** analyzer with 3 lots.

Elecsys Anti-SARS-CoV-2

cobas e 801 analyzer					
		Repeatability		Between-day	
Sample N = 75	Mean U/mL	SD U/mL	CV %	SD U/mL	CV %
Human plasma 1	0.474	0.015	3.2	0.004	0.8
Human plasma 2a	0.824	0.018	2.2	0.003	0.4
Human plasma 2b	0.940	0.015	1.6	0.007	0.8
Human plasma 3	5.49	0.112	2.0	0.053	1.0
Human plasma 4	11.8	0.192	1.6	0.106	0.9
Human plasma 5	53.4	0.838	1.6	0.000	0.0
Human plasma 6	73.2	1.20	1.6	0.785	1.1
Human plasma 7	183	2.05	1.1	1.45	0.8
Human plasma 8	253	2.97	1.2	2.09	0.8

cobas e 801 analyzer					
		Between-lot		Reproducibility	
Sample N = 75	Mean U/mL	SD U/mL	CV %	SD U/mL	CV %
Human plasma 1	0.474	0.023	4.9	0.028	5.9
Human plasma 2a	0.824	0.052	6.3	0.055	6.7
Human plasma 2b	0.940	0.025	2.7	0.030	3.2
Human plasma 3	5.49	0.209	3.8	0.244	4.4
Human plasma 4	11.8	0.555	4.7	0.596	5.0
Human plasma 5	53.4	1.83	3.4	2.02	3.8
Human plasma 6	73.2	3.90	5.3	4.15	5.7
Human plasma 7	183	3.06	1.7	3.96	2.2
Human plasma 8	253	0.842	0.3	3.73	1.5

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Between-platform precision

Between-platform precision was evaluated as between different platform variability (1 **cobas e 411**, 1 **cobas e 601**, and 1 **cobas e 801** analyzer).

cobas e 411, cobas e 601 and cobas e 801 analyzers					
		Repeatability		Between-day	
Sample N = 75	Mean U/mL	SD U/mL	CV %	SD U/mL	CV %
Human plasma 1	0.469	0.012	2.6	0.010	2.1
Human plasma 2a	0.812	0.020	2.4	0.017	2.1
Human plasma 2b	0.960	0.019	2.0	0.013	1.3
Human plasma 3	5.68	0.119	2.1	0.103	1.8
Human plasma 4	12.1	0.229	1.9	0.183	1.5
Human plasma 5	54.2	1.10	2.0	0.673	1.2
Human plasma 6	76.9	1.54	2.0	1.51	2.0
Human plasma 7	186	3.03	1.6	3.04	1.6
Human plasma 8	256	4.73	1.8	0.220	1.6

cobas e 411, cobas e 601 and cobas e 801 analyzers					
		Between-platform		Reproducibility	
Sample N = 75	Mean U/mL	SD U/mL	CV %	SD U/mL	CV %
Human plasma 1	0.469	0.024	5.1	0.028	6.0
Human plasma 2a	0.812	0.025	3.1	0.036	4.4
Human plasma 2b	0.960	0.023	2.4	0.032	3.4
Human plasma 3	5.68	0.050	0.9	0.165	2.9
Human plasma 4	12.1	0.124	1.0	0.319	2.6
Human plasma 5	54.2	0.777	1.4	1.51	2.8
Human plasma 6	76.9	0.970	1.3	2.36	3.1
Human plasma 7	186	3.16	1.7	5.33	2.9
Human plasma 8	256	2.71	1.1	6.89	2.7

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Reproducibility including Lot-to-lot and Between-platform variability

cobas e 411, cobas e 601 and cobas e 801 analyzers							
		Repeatability		Between-day		Between-lot	
Sample N = 225	Mean U/mL	SD U/mL	CV %	SD U/mL	CV %	SD U/mL	CV %
Human plasma 1	0.465	0.014	3.0	0.015	3.2	0.013	2.9
Human plasma 2a	0.818	0.018	2.2	0.022	2.7	0.039	4.7
Human plasma 2b	0.940	0.018	1.9	0.017	1.7	0.014	1.5
Human plasma 3	5.57	0.106	1.9	0.110	2.0	0.178	3.2
Human plasma 4	12.0	0.249	2.1	0.229	1.9	0.539	4.5
Human plasma 5	53.6	1.11	2.1	0.846	1.6	1.83	3.4
Human plasma 6	73.9	1.55	2.1	1.62	2.2	3.36	4.5
Human plasma 7	186	3.00	1.6	3.09	1.7	5.15	2.8
Human plasma 8	257	4.72	1.8	4.67	1.8	2.12	0.8

cobas e 411, cobas e 601 and cobas e 801 analyzers					
		Between-platform		Reproducibility	
Sample N = 225	Mean U/mL	SD U/mL	CV %	SD U/mL	CV %
Human plasma 1	0.465	0.016	3.4	0.029	6.3
Human plasma 2a	0.818	0.018	2.1	0.051	6.3
Human plasma 2b	0.940	0.021	2.2	0.035	3.7
Human plasma 3	5.57	0.102	1.8	0.256	4.6
Human plasma 4	12.0	0.246	2.0	0.682	5.7
Human plasma 5	53.6	0.900	1.7	2.47	4.6
Human plasma 6	73.9	1.62	2.2	4.35	5.9
Human plasma 7	186	5.02	2.7	8.38	4.5
Human plasma 8	257	4.91	1.9	8.52	3.3

Elecsys Anti-SARS-CoV-2 scobas®

Analytical specificity

1468 samples containing potentially cross-reacting analytes were tested with the Elecsys Anti-SARS-CoV-2 S assay. All samples were obtained before October 2019. No cross-reactivity was found. The resulting overall specificity was 100 %. Results are shown in the following tables:
SARS-CoV-2 related

Indication	N	Reactive	Specificity %
MERS CoV (anti-S1 IgG+)	51	0	100
Common Coronavirus panel ^{h)}	151	0	100

h) pre-pandemic samples, which showed serologic reactivity to at least one of the endemic Coronavirus HKU1, NL63, 229E, or OC43.

Infectious respiratory diseases

Indication	N	Reactive	Specificity %
Bordetella pertussis	39	0	100
Chlamydia pneumoniae	36	0	100
Common cold panel ⁱ⁾	21	0	100
Enterovirus	35	0	100
Haemophilus influenzae B	75	0	100
Influenza A	40	0	100
Influenza B	45	0	100
Influenza vaccines	25	0	100
Mycoplasma pneumoniae	46	0	100
Parainfluenza	82	0	100
Respiratory syncytial virus	51	0	100

i) 21 potentially cross-reactive samples from individuals with common cold symptoms, collected before October 2019

Other infectious agents or disease states

Indication	N	Reactive	Specificity %
Adenovirus	25	0	100
Borrelia spp.	6	0	100
Candida albicans	13	0	100

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Indication	N	Reactive	Specificity %
Chlamydia trachomatis	12	0	100
CMV acute (IgM+, IgG+)	86	0	100
E. coli (anti-E. coli-reactive)	10	0	100
EBV acute (IgM+, VCA IgG+)	106	0	100
Gonorrhea	5	0	100
HAV acute (IgM+)	10	0	100
HAV late (IgG+)	15	0	100
HAV vaccines	15	0	100
HBV acute	12	0	100
HBV chronic	12	0	100
HBV vaccines	15	0	100
HCV	50	0	100
HEV	12	0	100
HIV	10	0	100
HSV acute (IgM+)	24	0	100
HTLV	6	0	100
Legionella (IgGAM+)	7	0	100
Listeria spp.	6	0	100
Measles	10	0	100
Mumps	14	0	100
Parvovirus B19	30	0	100
Plasmodium falciparum (malaria)	8	0	100
Rubella acute (IgM+, IgG+)	12	0	100
Toxoplasma gondii (IgM+, IgG+)	8	0	100
Treponema pallidum (syphilis)	62	0	100
VZV (varicella-zoster virus)	30	0	100

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Autoimmune diseases

Indication	N	Reactive	Specificity %
AMA (anti-mitochondrial antibodies)	30	0	100
ANA (anti-nuclear antibodies)	17	0	100
Hemophiliacs	15	0	100
RA (rheumatoid arthritis)	10	0	100
SLE (systemic lupus erythematosus)	10	0	100

Hepatic diseases

Indication	N	Reactive	Specificity %
Alcohol induced hepatitis/cirrhosis	13	0	100
Drug induced hepatitis/cirrhosis	10	0	100
Fatty liver	10	0	100
Liver cancer	10	0	100
Non-viral liver disease	15	0	100

Interfering substances

The effect of the following endogenous substances and pharmaceutical compounds on assay performance was tested. Interferences were tested up to the listed concentrations and no impact on results was observed.

Endogenous substances

Compound	Concentration tested	Interference (%)
Bilirubin	≤ 1129 µmol/L or ≤ 66 mg/dL	-1.4
Hemoglobin	≤ 1000 mg/dL or ≤ 10 g/L	-1.3
Intralipid	≤ 2000 mg/dL	2.9
Biotin	≤ 4912 nmol/L or ≤ 1200 ng/mL	-2.3
Rheumatoid factors	≤ 1200 IU/mL	1.6
IgG	≤ 6.4 g/dL or ≤ 64 g/L	-9.8
IgA	≤ 1.6 g/dL or ≤ 16 g/L	-1.7

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Compound	Concentration tested	Interference (%)
IgM	≤ 1.0 g/dL or ≤ 10 g/L	-3.0

Criterion: Deviation is ≤ 10 %

This assay has no biotin interference in serum concentrations up to 1200 ng/mL. Some studies have shown that serum concentrations of biotin can reach up to 355 ng/mL within the first hour after biotin ingestion for subjects consuming supplements of 20 mg biotin per day²¹ and up to 1160 ng/mL for subjects after a single dose of 300 mg biotin.²²

No false negative results due to a high-dose hook effect were found with the Elecsys Anti-SARS-CoV-2 S assay but occurrence of high-dose hook effect cannot be completely excluded.

Commonly used pharmaceuticals

In vitro tests were performed on 17 commonly used pharmaceuticals. No interference with the assay was found at 3x the daily dose, except for Itraconazole. The deviation for Itraconazole at 1.5x the daily dose is shown in the table below.

Drug	Concentration tested	Interference (%)
Acetylcysteine	150 mg/L	0.8
Acetylsalicylic acid	30 mg/L	2.7
Ampicillin	75 mg/L	3.5
Ascorbic acid	52.5 mg/L	2.8
Cefoxitin	750 mg/L	1.9
Doxycycline	18 mg/L	5.7
Heparin	3300 IU/L	3.3
Levodopa	7.5 mg/L	3.4
Methyldopa	22.5 mg/L	3.2
Metronidazole	123 mg/L	2.5
Rifampicin	48 mg/L	3.3
Acetaminophen	156 mg/L	-1.4
Cyclosporine	1.8 mg/L	-8.2
Ibuprofen	219 mg/L	-7.1
Theophylline	60 mg/L	-9.3
Phenylbutazone	321 mg/L	-6.1

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Drug	Concentration tested	Interference (%)
Itraconazole	15 mg/L	-9.1

Special pharmaceuticals

In vitro tests were performed on 17 special pharmaceuticals. The deviation for the concentration tested is shown in the table below.

Drug	Concentration tested	Interference (%)
Zanamivir	0.006 mg/mL	-0.4
Oseltamivir	0.090 mg/mL	-0.1
Ceftriaxone	2.40 mg/mL	-3.3
Levofloxacin	0.300 mg/mL	1.2
Meropenem	3.60 mg/mL	1.1
Ribavirin	0.720 mg/mL	3.8
Azithromycin	0.300 mg/mL	4.2
Lopinavir	0.720 mg/mL	-4.7
α -interferon 2b	3000 IU/mL	-0.9
Peramivir	0.360 mg/mL	-1.6
Tobramycin	0.360 mg/mL	2.1
Histamine Dihydrochl.	0.0006 mg/mL	1.1
Tocilizumab	0.384 mg/mL	0.8
α -interferon 2a	43200 IU/mL	2.2
Hydroxychloroquine sulfate C1	0.240 mg/mL	-4.0
Remdesivir	0.120 mg/mL	-1.4
Ritonavir	0.160 mg/mL	-7.6

Linearity

3 serum and 3 plasma (sodium citrate) samples containing high levels of SARS-CoV-2 antibodies were diluted with negative sample to prepare a dilution series comprised of 9 levels. Each level had 3 replicates. For serum samples, linearity was demonstrated for the interval of 0.26 U/mL to 346 U/mL with deviations from linearity within 15 %. For plasma samples, linearity was demonstrated for the interval of 0.29 U/mL to 304 U/mL with deviations from linearity within 15 %.

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Taking into consideration the estimates of Limit of Blank, Limit of Detection, Limit of Quantitation, precision, and linearity, the analytical measuring interval is 0.40 U/mL to 250 U/mL.

Clinical agreement

Negative percent agreement

A total of 5991 serum samples were tested with the Elecsys Anti-SARS-CoV-2 S assay. All samples were obtained before October 2019. 1 false positive sample was detected.

The resulting overall negative percent agreement (NPA) in the internal study was 99.98 %. The lower 95 % confidence limit was 99.91 %.

Cohort	N	Reactive	NPA %	95 % lower confidence limit, %	95 % upper confidence limit, %
Diagnostic routine (Europe)	2528	0	100	99.85	100
Blood donors (USA)	2713	1	99.96	99.79	100
Blood donors (Africa)	750	0	100	99.51	100
Overall	5991	1	99.98	99.91	100

Positive percent agreement

A total of 1485 sodium citrate plasma samples from 331 symptomatic patients (including 172 samples from 172 hospitalized patients) with a PCR confirmed SARS-CoV-2 infection were tested with the Elecsys Anti-SARS-CoV-2 S assay. 1 or more sequential samples from these patients were collected at various time points after PCR confirmation. Positive percent agreement (PPA) was correlated with days post PCR specimen collection, and the results are shown for the first bleed per time bin.

First bleed

233 of the tested samples had a sampling date of 15 days or later after diagnosis with PCR. 225 of these 233 samples were determined with ≥ 0.8 U/mL in the Elecsys Anti-SARS-CoV-2 S assay and hence considered positive, resulting in a PPA of 96.6 % (95 % CI: 93.35-98.51 %) in this sample cohort.

Days after PCR positive result	Number tested	Pos	Neg	PPA (%)	95 % CI ^{j)} (%)
0-7	32	29	3	90.6	(74.98 - 98.02)
8-14	77	67	10	87.0	(77.41 - 93.59)
≥ 15	233	225	8	96.6	(93.35 - 98.51)

j) CI = confidence interval

Titer development was investigated with the Elecsys Anti-SARS-CoV-2 S assay with sequential samples from individual patients ranging up to 126 days following reactive PCR result. None of the samples showed a decline of titers below the reactive range.

Titer development over time for patient samples ranging ≥ 100 days following a reactive PCR result is shown below. At this time, it is unknown for how long antibodies persist following infection and if the presence of antibodies confers protective immunity.

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Donor	Day* U/mL	Day U/mL	Day U/mL	Day U/mL	Day U/mL	Day U/mL	Day U/mL	Day U/mL
1	20	23	27	33	36	61	82	103
	20.4	22.2	30.5	47.4	51.7	73.5	87.7	114
2	21	24	31	34	37	62	83	104
	36.1	44.3	32.4	48.5	51.4	63.1	73.2	71.9
3	26	34	38	41	45	67	87	106
	139	223	186	153	150	198	147	155
4	21	30	33	36	41	62	83	107
	32.3	95.3	151	315	374	293	244	214
5	30	35	38	42	112	-	-	-
	33.0	29.5	31.2	41.2	59.9	-	-	-
6	20	30	38	62	71	76	86	107
	7.88	32.6	26.6	39.2	35.7	40.3	36.0	42.1
7	19	22	25	29	39	48	59	104
	20.7	40.4	101	149	115	97.7	115	175
8	15	22	30	37	40	55	79	107
	22.1	14.2	37.1	166	136	226	124	96.9
9	34	41	45	52	67	74	87	106
	181	148	148	165	152	154	125	119
10	26	29	32	35	42	52	73	103
	4.42	4.79	4.83	5.21	4.67	5.95	7.28	7.69
11	16	42	78	106	-	-	-	-
	305	296	371	408	-	-	-	-
12	28	31	40	44	47	62	86	103
	139	162	114	166	141	93.0	69.5	59.1
13	24	31	38	46	59	74	92	102
	33.9	45.6	63.7	53.4	47.4	41.8	41.9	42.8
14	25	28	33	41	47	59	76	109
	79.8	86.4	120	117	103	108	97.1	105
15	36	52	68	77	92	96	106	126
	255	165	126	94.8	122	107	141	162
16	30	44	51	58	73	85	90	104

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Donor	Day* U/mL	Day U/mL	Day U/mL	Day U/mL	Day U/mL	Day U/mL	Day U/mL	Day U/mL
	425	246	379	298	215	169	173	147
17	29	32	40	48	55	76	95	101
	220	205	177	141	136	122	116	101
18	31	39	43	53	64	68	92	102
	63.6	66.9	53.4	43.4	57.3	48.9	69.7	58.8
19	32	46	53	60	68	74	94	102
	94.5	79.5	84.3	71.8	92.1	73.6	78.9	75.8
20	38	46	68	74	82	99	106	110
	56.4	84.2	104	106	114	141	152	146
21	31	38	48	52	57	71	92	106
	9.4	10.1	8.7	9.0	8.0	8.8	10.4	10.4
22	44	49	61	70	117	-	-	-
	54.3	51.0	59.2	56.9	99.8	-	-	-
23	35.0	42.0	55.0	74.0	81.0	109	-	-
	524	451	416	386	392	345	-	-
24	44	48	51	58	63	73	90	104
	669	685	584	605	582	562	591	570
25	36	49	56	69	82	89	105	-
	64.0	83.5	78.6	83.9	100	103	121	-

* Days after initial positive PCR.

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For further information, please refer to the appropriate operator's manual for the analyzer concerned, the respective application sheets, the product information and the Method Sheets of all necessary components (if available in your country).

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see dialog.roche.com for definition of symbols used):

CONTENT	Contents of kit
SYSTEM	Analyzers/Instruments on which reagents can be used
REAGENT	Reagent

Elecsys Anti-SARS-CoV-2

CALIBRATOR

Calibrator



Volume for reconstitution

GTIN

Global Trade Item Number

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US Customer Technical Support 1-800-428-2336



CalSet Anti-SARS-CoV-2 S cobas®

REF 09289291190

→4 x 1.0 mL

For use under the Emergency Use Authorization (EUA) only**For use in the USA only****Intended use**

CalSet Anti-SARS-CoV-2 S is used for calibrating the Elecsys Anti-SARS-CoV-2 S assay on **cobas e** immunoassay analyzers.

Summary

CalSet Anti-SARS-CoV-2 S is a lyophilized human serum spiked with human serum from anti-SARS-CoV-2 S positive donors in two concentration ranges.

The CalSet can be used with all reagent lots.

Reagents - working solutions

- ACOV2S Cal1: 2 bottles, each for 1.0 mL of calibrator 1
 - ACOV2S Cal2: 2 bottles, each for 1.0 mL of calibrator 2
- Anti-SARS-CoV-2 positive serum in two concentration ranges.

cobas e 801 analyzer: The exact lot-specific calibrator values are encoded in the electronic barcode and available via the **cobas** link.

All other analyzers: The exact lot-specific calibrator values are encoded in the barcode as well as printed on the enclosed (or electronically available) calibrator barcode sheet.

Calibrator values

Traceability: The Elecsys Anti-SARS-CoV-2 S assay has been standardized against the internal Roche standard for anti-SARS-CoV-2-S. This standard consists of an equimolar mixture of 2 monoclonal antibodies that bind Spike-1 RBD at 2 different epitopes. 1 nM of these antibodies correspond to 20 U/mL of the Anti-SARS-CoV-2 S assay.

No international standard was available for anti-SARS-CoV-2-S at the time of IVD authorization.

Precautions and warnings**For Emergency Use Authorization only.**

For in vitro diagnostic use only.

This test has not been FDA-cleared or -approved; this test has been authorized by FDA under an Emergency Use Authorization (EUA) for use by authorized laboratories; by laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. 263a, that meet requirements to perform high complexity tests.

This test has been authorized only for detecting 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 emergency use of in vitro diagnostic tests for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

Exercise the normal precautions required for handling all laboratory reagents.

Disposal of all waste material should be in accordance with local guidelines.

Safety data sheet available for professional user on request.

CalSet Anti-SARS-CoV-2 S cobas®

For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:



Warning

H317 May cause an allergic skin reaction.

Prevention:

P261 Avoid breathing dust/fume/gas/mist/vapours/spray.

P272 Contaminated work clothing should not be allowed out of the workplace.

P280 Wear protective gloves.

Response:

P333 + P313 If skin irritation or rash occurs: Get medical advice/attention.

P362 + P364 Take off contaminated clothing and wash it before reuse.

Disposal:

P501 Dispose of contents/container to an approved waste disposal plant.

Product safety labeling follows EU GHS guidance.

Contact phone: 1-800-428-2336

All human material should be considered potentially infectious. All products derived from human blood are prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg and antibodies to HCV and HIV. The testing methods used assays approved by the FDA or cleared in compliance with the European Directive 98/79/EC, Annex II, List A.

The serum containing anti-SARS-CoV-2 used for calibrator material was heat-inactivated for 30 minutes at 56 °C.

However, as no inactivation or testing method can rule out the potential risk of infection with absolute certainty, the material should be handled with the same level of care as a patient specimen. In the event of exposure, the directives of the responsible health authorities should be followed.^{1,2}

Avoid foam formation in all reagents and sample types (specimens, calibrators and controls).

Handling

Carefully dissolve the contents of one bottle by adding exactly 1.0 mL of distilled or deionized water and allow to stand closed for 15 minutes to reconstitute. Mix carefully, avoiding foam formation.

Transfer aliquots of the reconstituted calibrators into empty labeled snap-cap bottles (CalSet Vials). Attach the supplied labels to the additional bottles.

cobas e 411 analyzer: The reconstituted calibrators should only be left on the analyzer during calibration at 20-25 °C. After use, close the bottles as soon as possible and store upright at 2-8 °C.

Due to possible evaporation effects, not more than 5 calibration procedures per bottle set should be performed.

cobas e 601, **cobas e 602** and **cobas e 801** analyzers: Unless the entire volume is necessary for calibration on the analyzers, transfer aliquots of the reconstituted calibrators into empty snap-cap bottles (CalSet Vials).

CalSet Anti-SARS-CoV-2 S cobas®

Attach the supplied labels to these additional bottles. Store the aliquots at 2-8 °C or at -20 °C (± 5 °C) for later use.

Perform **only one** calibration procedure per aliquot.

Please note for **cobas e 602** and **cobas e 801** analyzers: Both the vial labels, and the additional labels (if available) contain 2 different barcodes. Please turn the vial cap 180° into the correct position so that the barcode between the yellow markers can be read by the system. Place the vial on the analyzer as usual.

Storage and stability

Store at 2-8 °C.

The lyophilized calibrators are stable up to the stated expiration date.

Stability of the reconstituted calibrators:	
either at -20 °C (± 5 °C)	6 weeks
or at 2-8 °C	14 days
on cobas e 411 analyzer at 20-25 °C	up to 5 hours
on all other analyzers at 20-25 °C	use only once

Store calibrators **upright** in order to prevent the calibrator solution from adhering to the snap-cap.

Materials provided

- CalSet Anti-SARS-CoV-2 S, barcode card, 4 empty labeled snap-cap bottles, 2 x 6 bottle labels

Materials required (but not provided)

- REF 11776576322, CalSet Vials, 2 x 56 empty snap-cap bottles
- cobas e** immunoassay analyzers and Elecsys Anti-SARS-CoV-2 S assay reagents
- Distilled or deionized water

See the assay Method Sheet and the operator's manual for additionally required materials.

Assay

Place the reconstituted calibrators (in the system-compatible bottles with barcoded labels) in the sample zone.

Read in all the information necessary for calibrating the assay.

Ensure the calibrators are at 20-25 °C prior to measurement.

References

- Occupational Safety and Health Standards: Bloodborne pathogens. (29 CFR Part 1910.1030). Fed. Register.
- Directive 2000/54/EC of the European Parliament and Council of 18 September 2000 on the protection of workers from risks related to exposure to biological agents at work.

For further information, please refer to the appropriate operator's manual for the analyzer concerned, the respective application sheets, the product information and the Method Sheets of all necessary components (if available in your country).

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see dialog.roche.com for definition of symbols used):

CalSet Anti-SARS-CoV-2 S cobas®

CONTENT	Contents of kit
SYSTEM	Analyzers/Instruments on which reagents can be used
REAGENT	Reagent
CALIBRATOR	Calibrator
→	Volume after reconstitution or mixing
GTIN	Global Trade Item Number

FOR US CUSTOMERS ONLY: LIMITED WARRANTY

Roche Diagnostics warrants that this product will meet the specifications stated in the labeling when used in accordance with such labeling and will be free from defects in material and workmanship until the expiration date printed on the label. THIS LIMITED WARRANTY IS IN LIEU OF ANY OTHER WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR PARTICULAR PURPOSE. IN NO EVENT SHALL ROCHE DIAGNOSTICS BE LIABLE FOR INCIDENTAL, INDIRECT, SPECIAL OR CONSEQUENTIAL DAMAGES.

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www.roche.com

Distribution in USA by:

Roche Diagnostics, Indianapolis, IN

US Customer Technical Support 1-800-428-2336



PreciControl Anti-SARS-CoV-2 S **cobas**[®]

REF 09289313190

4 x 1.0 mL

For use under the Emergency Use Authorization (EUA) only

For use in the USA only

Intended use

PreciControl Anti-SARS-CoV-2 S is used for quality control of the Elecsys Anti-SARS-CoV-2 S immunoassay on **cobas e** immunoassay analyzers.

Summary

PreciControl Anti-SARS-CoV-2 S is a ready-for-use control serum based on human serum. The controls are used for monitoring the accuracy of the Elecsys Anti-SARS-CoV-2 S immunoassay.

Reagents - working solutions

- PC ACOV2S1: 2 bottles, each with 1.0 mL of control
based on human serum, non-reactive for anti-SARS-CoV-2 antibodies; TRIS^{a)} buffer; preservative.
- PC ACOV2S2: 2 bottles, each with 1.0 mL of control
based on human serum, reactive for anti-SARS-CoV-2 antibodies; TRIS buffer; preservative.

Note: **cobas e** 602 and **cobas e** 801 analyzers: The controls will be handled automatically by the analyzers.

All other analyzers: The controls are not barcode labeled and therefore have to be run like external controls. All values and ranges have to be entered manually. Please refer to the section "QC" in the operator's manual or to the online help of the instrument software.

Non-barcode labeled controls: Only one target value and range for each control level can be entered in the analyzer. The reagent lot-specific target values must be re-entered each time when a specific reagent lot with different control target values and ranges is used. Two reagent lots with different control target values and ranges cannot be used in parallel in the same run.

The exact lot-specific target values and ranges, given in U/mL, are printed on the enclosed (or electronically available) value sheet included in the reagent kit or PreciControl kit.

Please make sure that the correct values are used.

cobas e 602 and **cobas e** 801 analyzers: The exact lot-specific target values and ranges, given in U/mL, are available both as an electronic barcode and as a value sheet provided via the **cobas** link.

Please note: The value sheets for the **cobas e** 801 analyzer are only available electronically via the **cobas** link.

a) TRIS = Tris(hydroxymethyl)aminomethan

Target values and ranges

The target values and ranges were determined and evaluated by Roche. They were obtained using the Elecsys Anti-SARS-CoV-2 S assay reagents and analyzers available at the time of testing.

cobas e 602 and **cobas e** 801 analyzers: Updated target values and ranges are available both as an electronic barcode and as a value sheet provided via the **cobas** link.

All other analyzers: The control values and ranges must be entered manually. Please refer to the corresponding section in the operator's manual.

If the target values and control ranges are updated, this information is conveyed either via the reagent barcodes, or control barcodes (or provided electronically) and in an additional value sheet included in the reagent kit. This value sheet lists all control lots to which the new values apply. If some of the values remain unchanged, the original values conveyed via the CBC (Control Barcode), and in the value sheet included in the control kit (or provided electronically), remain valid.

PreciControl Anti-SARS-CoV-2 S cobas®

Results must be within the specified ranges. In the event that increasing or decreasing trends, or any other suddenly occurring deviations beyond the range limits are observed, all test steps must be checked.

When necessary, measurement of the patient sample tested should be repeated.

Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

Precautions and warnings

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For in vitro diagnostic use only.

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Exercise the normal precautions required for handling all laboratory reagents.

Disposal of all waste material should be in accordance with local guidelines.

Safety data sheet available for professional user on request.

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P280 Wear protective gloves.

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P362 + P364 Take off contaminated clothing and wash it before reuse.

Disposal:

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PreciControl Anti-SARS-CoV-2 S **cobas**[®]

antibodies to HCV and HIV. The testing methods used assays approved by the FDA or cleared in compliance with the European Directive 98/79/EC, Annex II, List A.

The serum containing anti-SARS-CoV-2 used for reactive control material was heat-inactivated for 30 minutes at 56 °C.

However, as no inactivation or testing method can rule out the potential risk of infection with absolute certainty, the material should be handled with the same level of care as a patient specimen. In the event of exposure, the directives of the responsible health authorities should be followed.^{1,2}

The controls may not be used after the expiration date.

Avoid foam formation in all reagents and sample types (specimens, calibrators and controls).

Handling

The controls are supplied ready-for-use in bottles compatible with the system. The controls should only be left on the analyzer during performance of quality control. After use, close the bottles as soon as possible and store upright at 2-8 °C.

When measuring non-barcoded controls, use only recommended sample tubes, "cup on tube" or "cup on rack".

Please note: Both the vial labels and the additional labels (if available) contain a barcode for the **cobas e 602** and **cobas e 801** analyzers only. Place the vial on the analyzer as usual.

Storage and stability

Store at 2-8 °C.

Stability of the control serum:	
unopened at 2-8 °C	up to the stated expiration date
after opening at 2-8 °C	7 days
after opening at -20 °C (± 5 °C)	21 days (freeze only once)
on the analyzers at 20-25 °C	up to 4 hours

Store controls **upright** in order to prevent the control solution from adhering to the snap-cap.

Materials provided

- PreciControl Anti-SARS-CoV-2 S

Materials required (but not provided)

- **cobas e** immunoassay analyzers and assay reagents

See the assay Method Sheet and the operator's manual for additionally required materials.

Assay

Treat the control serum in the system-compatible labeled bottles for analysis in the same way as patient samples.

The target values and ranges must be entered manually (except for the **cobas e 602** and **cobas e 801** analyzers). Please refer to the corresponding section in the operator's manual.

Ensure the controls are at 20-25 °C prior to measurement.

Run controls daily in parallel with patient samples, once per reagent kit, and whenever a calibration is performed. The control intervals and limits should be adapted to each laboratory's individual requirements. Follow the applicable government regulations and local guidelines for quality control.

PreciControl Anti-SARS-CoV-2 S cobas®







References

- 1 Occupational Safety and Health Standards: Bloodborne pathogens. (29 CFR Part 1910.1030). Fed. Register.
- 2 Directive 2000/54/EC of the European Parliament and Council of 18 September 2000 on the protection of workers from risks related to exposure to biological agents at work.

For further information, please refer to the appropriate operator's manual for the analyzer concerned, the respective application sheets, the product information and the Method Sheets of all necessary components (if available in your country).

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	Contents of kit
	Analyzers/Instruments on which reagents can be used
	Reagent
	Calibrator
	Volume after reconstitution or mixing
	Global Trade Item Number

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