Elecsys Anti-SARS-CoV-2

cobas®

REF		Σ	SYSTEM
09203095190	09203095501	200	**cobas e** 411 **cobas e** 601 **cobas e** 602
09203079190	09203079501	300	**cobas e** 801

Rx ONLY
For in vitro diagnostic and Laboratory Professional use. For use under the Emergency Use Authorization (EUA) only

English

For use in the USA only

System information

For **cobas e** 411 analyzer: test number 3000
For **cobas e** 601 and **cobas e** 602 analyzers: Application Code Number 737
For **cobas e** 801 analyzer: Application Code Number 10226

Warning

- Not for screening of donated blood.

Intended use

Elecsys Anti-SARS-CoV-2 is an immunoassay intended for qualitative detection of antibodies to SARS-CoV-2 in human serum and plasma (K_2-EDTA, K_3-EDTA, Li-heparin). 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. 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 assay should not be used to diagnose 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. Patients may have detectable virus present for several weeks following seroconversion.

Laboratories within the United States and its territories are required to report all positive results to the appropriate public health authorities.

The sensitivity of the Elecsys Anti-SARS-CoV-2 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 the Elecsys Anti-SARS-CoV-2 assay may occur due to cross reactivity from pre-existing antibodies or other possible causes.

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

The **e**lectro**c**hemi**l**uminescence **i**mmuno**a**ssay "ECLIA" is intended for use on **cobas e** immunoassay analyzers.

Summary

SARS-CoV-2 is an enveloped, single-stranded RNA virus of the family Coronaviridae, genus Betacoronavirus. All coronaviruses share similarities in the organization and expression of their genome, which encodes 16 nonstructural proteins and the 4 structural proteins: spike (S), envelope (E), membrane (M), and nucleocapsid (N). Viruses of this family are of zoonotic origin. They cause disease with symptoms ranging from those of a mild common cold to more severe ones such as the Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS) and Coronavirus Disease 2019 (COVID-19). Other coronaviruses known to infect people include 229E, NL63, OC43 and HKU1. The latter are ubiquitous and infection typically causes common cold or flu-like symptoms.[1,2]

The Elecsys Anti-SARS-CoV-2 assay uses a recombinant protein representing the nucleocapsid (N) antigen for the determination of antibodies against SARS-CoV-2.

Test principle

Sandwich principle. 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-specific recombinant antigen and SARS-CoV-2-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 automatically by the software by comparing the electrochemiluminescence signal obtained from the reaction product of the sample with the signal of the cutoff value previously obtained by calibration.

a) Tris(2,2'-bipyridyl)ruthenium(II)-complex ($Ru(bpy)_3^{2+}$)

Reagents - working solutions

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

The reagent rackpack (M, R1, R2) is labeled as ACOV2.

M Streptavidin-coated microparticles (transparent cap), 1 bottle, 12 mL: Streptavidin-coated microparticles 0.72 mg/mL; preservative.

R1 SARS-CoV-2-Ag~biotin, (gray cap), 1 bottle, 16 mL: Biotinylated SARS-CoV-2-specific recombinant antigen (E. coli); < 0.5 mg/L HEPES[b)] buffer 50 mmol/L, pH 7.7; preservative.

R2 SARS-CoV-2 Ag~$Ru(bpy)_3^{2+}$ (black cap), 1 bottle, 16 mL: SARS-CoV-2-specific recombinant antigen labeled with ruthenium complex; < 0.5 mg/L HEPES buffer 50 mmol/L, pH 7.7; preservative.

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

ACOV2 Cal1 Negative calibrator 1 (white cap), 1 bottle of 0.67 mL: Human serum, non-reactive for anti-SARS-CoV-2 antibodies; buffer; preservative.

ACOV2 Cal2 Positive calibrator 2 (black cap), 1 bottle of 0.67 mL: Human serum, reactive for anti-SARS-CoV-2 antibodies; buffer; preservative.

cobas e 801 analyzer:

The **cobas e** pack (M, R1, R2) is labeled as ACOV2.

M Streptavidin-coated microparticles, 1 bottle, 16 mL: Streptavidin-coated microparticles 0.72 mg/mL; preservative.

R1 SARS-CoV-2-Ag~biotin, 1 bottle, 18.8 mL: Biotinylated SARS-CoV-2-specific recombinant antigen (E. coli); < 0.5 mg/L HEPES[b)] buffer 50 mmol/L, pH 7.7; preservative.

R2 SARS-CoV-2-Ag~$Ru(bpy)_3^{2+}$, 1 bottle, 18.8 mL: SARS-CoV-2-specific recombinant antigen labeled with ruthenium complex; < 0.5 mg/L HEPES[b)] buffer 50 mmol/L, pH 7.7; preservative.

Elecsys Anti-SARS-CoV-2

cobas®

ACOV2 Cal1	Negative calibrator 1, 1 bottle of 0.67 mL: Human serum, non-reactive for anti-SARS-CoV-2 antibodies; buffer; preservative.
ACOV2 Cal2	Positive calibrator 2, 1 bottle of 0.67 mL: Human serum, reactive for anti-SARS-CoV-2 antibodies; buffer; preservative.

Precautions and warnings

For Emergency Use Authorization only.

For in vitro diagnostic use.
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.

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: 1-866-987-6243

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 (ACOV2 Cal2) 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.[3,4]

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

Reagent handling

The reagents in the kit are ready-for-use and are supplied in bottles compatible with the system.

Calibrators:

The calibrators are supplied ready-for-use in bottles compatible with the system.

cobas e 411 analyzer: The 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 4 calibration procedures per calibrator bottle set should be performed.

cobas e 801 analyzer: Store the calibrators at 2-8 °C for later use.

cobas e 601, **cobas e** 602 and **cobas e** 801 analyzers:

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

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 analyzers:

All information required for correct operation is available via the **cobas** link.

Please note for **cobas e** 602 analyzers: Both the vial labels contain 2 different barcodes. The barcode between the yellow markers is for **cobas** 8000 systems only. If using a **cobas** 8000 system, 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.

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	21 days
on the **cobas e** 411, **cobas e** 601 and **cobas e** 602 analyzers	14 days

Stability of the **cobas e** pack	
unopened at 2-8 °C	up to the stated expiration date
on the **cobas e** 801 analyzer	14 days

Stability of the calibrators	
unopened at 2-8 °C	up to the stated expiration date
after opening at 2-8 °C	72 hours
on **cobas e** 411 at 20-25 °C	up to 3 hours
on **cobas e** 601, **cobas e** 602, and **cobas e** 801 analyzers at 20-25 °C	use only once

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

Specimen collection and preparation

Only the specimens listed below were tested and found acceptable.

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

Li-heparin, K_2-EDTA and K_3-EDTA plasma.

Plasma tubes containing separating gel can be used.

Criterion: Absolute deviation of negative samples ± 0.3 COI (cutoff index) from serum value; reactive samples: recovery within 70-130 % of serum value.

Stable for 7 days at 15-25 °C, 7 days at 2-8 °C, 28 days at -20 °C (± 5 °C). The samples may be frozen once.

The sample types listed were tested with a selection of sample collection tubes or systems 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/collection system 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.

Pooled samples and other artificial material may have different effects on different assays and thus may lead to discrepant findings.

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

Do not use heat-inactivated samples.

Do not use samples and controls stabilized with azide.

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

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

The performance of the Elecsys Anti-SARS-CoV-2 assay has not been established with cadaveric samples or body fluids other than serum and plasma.

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 09216928190, PreciControl Anti-SARS-CoV-2, for 4 x 1.0 mL
- REF 03609987190, Diluent MultiAssay, 2 x 16 mL sample diluent (**cobas e** 411, 601 and 602)
- REF 07299010190, Diluent MultiAssay, 45.2 mL sample diluent (**cobas e** 801)
- 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
- 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 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 materials 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.

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

Calibrators:

Place the calibrators in the sample zone.

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

All the information necessary for calibrating the assay is automatically read into the analyzer.

cobas e 801 analyzers:

Read in all the information necessary for calibrating the assay.

After calibration has been performed, store the calibrators at 2-8 °C or discard (**cobas e** 601, **cobas e** 602 and **cobas e** 801 analyzers).

Calibration

No international standard is available for Anti-SARS-CoV-2.

Calibration frequency: Calibration must be performed once per reagent lot using ACOV2 Cal1, ACOV2 Cal2 and fresh reagent (i.e., not more than 24 hours since the reagent kit / **cobas e** pack 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 25 days when using the same reagent lot on the **cobas e** 411, **cobas e** 601 and **cobas e** 602 analyzers
- after 11 days when using the same reagent lot on the **cobas e** 801 analyzer
- after 7 days when using the same reagent pack on the **cobas e** 411, **cobas e** 601 and **cobas e** 602 analyzers
- after 14 days when using the same **cobas e** pack on the **cobas e** 801 analyzer
- as required: e.g. quality control findings outside the defined limits

Quality control

For quality control, use PreciControl Anti-SARS-CoV-2.

In addition, other suitable control material can be used.

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, 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. 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 guidelines for quality control.

Note for **cobas e** *411 and* **cobas e** *601 analyzers:*

Note: 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 have to be re-entered each time 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 are printed on the enclosed (or electronically available) value sheet in the reagent kit or PreciControl kit.

Please make sure that the correct values are used.

Alternatively, controls can be prepared as follows:

Negative control: Determine the COI of ACOV2 Cal1 by measuring it as a routine sample. Pool serum samples with a COI result of ≤ 150 % compared to the COI result of ACOV2 Cal1 (pooling of ≥ 5 non-reactive samples in this range is recommended). Mix carefully, avoiding foam formation. Prepare aliquots of at least 250 µL from this sample pool and store frozen at -20 °C (± 5 °C) or colder. Use these aliquots to perform regular quality control.

This negative control has a target value range of COI < 0.8 (qualitative assay result “non-reactive”).

Positive control: Determine the COI of ACOV2 Cal2 by measuring it as a routine sample. Pool serum samples with a COI result that is higher than the COI result of ACOV2 Cal2 (pooling of ≥ 3 reactive samples in this range is recommended). Dilute the sample pool by adding pooled negative serum (for pooling criterion see negative control) or Diluent MultiAssay to obtain a COI between 3 and 15. Mix carefully, avoiding foam formation. It is recommended to confirm calculated reactivity after dilution by a measurement. Prepare aliquots of at least 250 µL from this sample pool and store frozen at -20 °C (± 5 °C) or colder. Use these aliquots to perform regular quality control. Upon first use of this control, determine the COI of the control by measurement of the control in triplicate and using a freshly opened and calibrated reagent rack pack / **cobas e** pack.

The obtained median of these measurements serves as target value for this positive control. Subsequent measurements of all aliquots of this control material must match this target value ± 45 % (3SD = 45 %, 1SD = 15 %; qualitative assay result "reactive").

The target value of the positive control is lot specific and target value assessment as described above has to be performed for every assay lot.

After measurement, discard aliquots with a remaining volume of 250 µL or less. Aliquots with a remaining volume of more than 250 µL can be re-used if sealed tightly and stored immediately at 2-8 °C for a maximum of 3 days. In case quality control fails for any reason, thaw a new control aliquot and re-assess the performance of the assay.

Pools of plasma samples with similar reactivity can be used, however fibrin clots frequently occur with plasma after thawing. If this occurs, either discard or centrifuge the aliquot before use. Do not mix serum samples and plasma samples to prepare a sample pool.

The control intervals and limits should be adapted to each laboratory’s individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

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.

If necessary, repeat the measurement of the samples concerned.

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

Note: The controls should 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. Only one target value and range for each control level can be entered in the analyzer. The reagent lot-specific target values have to be re-entered each time 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.

Calculation

The analyzer automatically calculates the cutoff based on the measurement of ACOV2 Cal1 and ACOV2 Cal2.

The result of a sample is given either as reactive or non-reactive as well as in the form of a cutoff index (COI; signal sample/cutoff).

Interpretation of the results

Results obtained with the Elecsys Anti-SARS-CoV-2 assay can be interpreted as follows:

Numeric result	Result message	Interpretation
COI < 1.0	Non-reactive	Negative for anti-SARS-CoV-2 antibodies
COI ≥ 1.0	Reactive	Positive for anti-SARS-CoV-2 antibodies

The magnitude of the measured result above the cutoff is not indicative of the total amount of antibody present in the sample.
The individual immune response following SARS-CoV-2 infection varies considerably and might give different results with assays from different manufacturers. Results of assays from different manufacturers should not be used interchangeably.

Limitations - interference

The effect of the following endogenous substances and pharmaceutical compound on assay performance was tested. Interference was tested up to the listed concentration and no impact on results was observed.

Endogenous substances

Compound	Concentration tested
Bilirubin	≤ 1129 µmol/L or ≤ 66 mg/dL
Hemoglobin	1000 mg/dL or 10 g/L
Intralipid	2000 mg/dL
Biotin	≤ 4912 nmol/L or ≤ 1200 ng/mL
Rheumatoid factors	1200 IU/mL
IgG	7.0 g/dL or 70 g/L
IgA	1.6 g/dL or 16 g/L
IgM	1.0 g/dL or 10 g/L

- 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 day[5] and up to 1160 ng/mL for subjects after a single dose of 300 mg biotin.[6]

Limitations:

- For use under an Emergency Use Authorization Only.
- This test should not be used to diagnose or exclude acute SARS-CoV-2 infection.
- Potential interferences by pharmaceutical compounds other than biotin have not been tested and an interference cannot be excluded.
- No false negative results due to a high-dose hook effect were found with the Elecsys Anti-SARS-CoV-2 assay but occurrence of high-dose hook effect cannot be completely excluded.
- 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.
- The results should always be assessed in conjunction with the patient’s medical history, clinical examination and other findings.
- SARS-CoV-2 IgG antibodies may be below detectable levels in patients who have been exhibiting symptoms for less than 15 days.
- **A negative test result does not rule out the possibility of an infection with SARS-CoV-2. Serum or plasma samples from the early (pre-seroconversion) phase of illness can yield negative findings. Therefore, this test cannot be used to diagnose an acute infection. Also, over time, titers may decline and eventually become negative.**
- **Testing with a molecular diagnostic should be performed to evaluate for active infection in symptomatic individuals.**
- **It is not known at this time if the presence of antibodies to SARS-CoV-2 confers immunity to reinfection.**

- This test should not be used for screening of donated blood.

Conditions of Authorization for the Laboratory

The Elecsys Anti-SARS-CoV-2 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/emergency-situations-medical-devices/emergency-use-authorizations#covid19ivd. However, to assist clinical laboratories using the Elecsys Anti-SARS-CoV-2 ("your product" in the conditions below), the relevant Conditions of Authorization are listed below:

- Authorized laboratories[c)] using your product will include with result reports of your product, 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 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 reactive or false non-reactive 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".

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 (EP5-A3) of the CLSI (Clinical and Laboratory Standards Institute) with 1 run per day for 5 days with 5 determinations per sample.

The following results were obtained:

cobas e 411 analyzer					
		Repeatability[d)]		**Intermediate precision[e)]**	
Sample	Mean COI	SD COI	CV %	SD COI	CV %
HS1[f)], negative	0.063	0.002	2.4	0.003	4.4
HS2, negative	0.052	0.001	2.5	0.003	5.7
HS3, low positive for anti-SARS-CoV-2 antibodies	1.16	0.021	1.8	0.052	4.5
HS4, low positive for anti-SARS-CoV-2 antibodies	1.22	0.034	2.8	0.057	4.7
HS5, positive for anti-SARS-CoV-2 antibodies	5.02	0.137	2.7	0.209	4.2
HS6, positive for anti-SARS-CoV-2 antibodies	13.4	0.219	1.6	0.663	5.0
HS7, positive for anti-SARS-CoV-2 antibodies	22.4	0.447	2.0	0.986	4.4
HS8, high negative	0.664	0.015	2.3	0.038	5.7
HS9, high negative	0.689	0.013	1.9	0.049	7.2
PC ACOV2[g)] 1, negative for anti-SARS-CoV-2	0.059	0.002	2.6	0.003	5.0
PC ACOV2 2, positive for anti-SARS-CoV-2	2.97	0.038	1.3	0.065	2.2

d) Repeatability = within-run precision

e) Intermediate precision = between-run

f) HS = human specimen

g) PC ACOV2 = PreciControl Anti-SARS-CoV-2

cobas e 601 and **cobas e** 602 analyzers					
		Repeatability[d)]		**Intermediate precision[e)]**	
Sample	Mean COI	SD COI	CV %	SD COI	CV %
HS1[f)], negative	0.062	0.001	1.8	0.003	4.8
HS2, negative	0.051	0.001	2.5	0.003	6.5
HS3, low positive for anti-SARS-CoV-2 antibodies	1.07	0.009	0.8	0.025	2.3
HS4, low positive for anti-SARS-CoV-2 antibodies	1.15	0.013	1.1	0.031	2.7
HS5, positive for anti-SARS-CoV-2 antibodies	4.76	0.050	1.1	0.110	2.3
HS6, positive for anti-SARS-CoV-2 antibodies	12.9	0.112	0.9	0.303	2.4
HS7, positive for anti-SARS-CoV-2 antibodies	22.3	0.147	0.7	0.562	2.5
HS8, high negative	0.636	0.009	1.4	0.032	5.0
HS9, high negative	0.700	0.008	1.1	0.039	5.6
PC ACOV2 1, negative for anti-SARS-CoV-2	0.059	0.001	1.9	0.003	5.1
PC ACOV2 2, positive for anti-SARS-CoV-2	2.96	0.018	0.6	0.079	2.7

cobas e 801 analyzer					
		Repeatability[h)]		**Intermediate precision[e)]**	
Sample	Mean COI	SD COI	CV %	SD COI	CV %
HS1[f)], negative	0.067	0.002	2.9	0.003	4.4
HS2, negative	0.058	0.001	2.5	0.003	4.5
HS3, low positive for anti-SARS-CoV-2 antibodies	1.12	0.017	1.5	0.023	2.1

Elecsys Anti-SARS-CoV-2

cobas®

cobas e 801 analyzer					
		Repeatability[h)]		**Intermediate precision**[e)]	
Sample	Mean COI	SD COI	CV %	SD COI	CV %
HS4, low positive for anti-SARS-CoV-2 antibodies	1.21	0.016	1.3	0.027	2.2
HS5, positive for anti-SARS-CoV-2 antibodies	4.93	0.080	1.6	0.111	2.3
HS6, positive for anti-SARS-CoV-2 antibodies	13.3	0.221	1.7	0.312	2.3
HS7, positive for anti-SARS-CoV-2 antibodies	22.8	0.362	1.6	0.597	2.6
HS8, high negative	0.653	0.012	1.8	0.032	4.8
HS9, high negative	0.722	0.010	1.4	0.039	5.4
PC ACOV2 1, negative for anti-SARS-CoV-2	0.065	0.002	2.5	0.003	4.0
PC ACOV2 2, positive for anti-SARS-CoV-2	2.95	0.048	1.6	0.062	2.1

h) Repeatability = within-run precisions

Analytical specificity

Out of 792 potentially cross-reacting samples, 4 samples showed reactivity in the Elecsys SARS-CoV-2 assay resulting in an overall specificity in this cohort of 99.5 % (95 % CI: 98.63-99.85 %). The following are results of samples grouped by indication.

Indication	**N**	**NR**[i)]	**RX**[j)]	**Specificity, %**
Common cold panel[k)]	40	40	0	100
Coronavirus panel[l)]	40	40	0	100
CMV acute (IgM+, IgG+)	85	84	1	98.8
EBV acute (IgM+, IgG+)	105	103	2	98.1
Borrelia burgdorferi	6	6	0	100
Chlamydia pneumoniae	8	8	0	100
E. coli (anti-E. coli-reactive)	10	10	0	100
Neisseria gonorrhoeae	5	5	0	100
HAV acute (IgM+)	10	10	0	100
HAV late (IgG+)	15	15	0	100
HAV vaccinees	15	15	0	100
HBV acute (HBsAg+, HBeAg+)	12	12	0	100
HBV acute (anti-HBs+)	7	7	0	100
HBV acute (anti-HBc IgM+)	8	8	0	100
HBV chronic	12	12	0	100
HBV vaccinees	15	15	0	100
HCV acute (anti-HCV IgM+)	6	6	0	100
HCV (anti-HCV IgG+)	60	60	0	100
HEV	12	12	0	100
HIV	10	10	0	100
HSV acute (IgM+)	24	24	0	100
HTLV	6	6	0	100
Influenza vaccinees	25	25	0	100
Listeria	6	6	0	100
Measles	10	10	0	100
Mumps	14	14	0	100
Parvovirus B19	30	30	0	100
Plasmodium falciparum (Malaria)	8	8	0	100
Rubella acute (IgM+, IgG+)	12	12	0	100
Toxoplasma gondii (IgM+, IgG+)	8	8	0	100
Treponema pallidum (Syphilis)	62	62	0	100
VZV (Varicella Zoster)	30	30	0	100
AMA (anti-mitochondrial antibodies)	30	30	0	100
ANA (anti-nuclear antibodies)	26	26	0	100
SLE (systemic lupus erythematosus)	10	9	1	90.0
RA (rheumatoid arthritis)	10	10	0	100

i) NR = non-reactive

j) RX - Reactive

k) 40 potentially cross-reactive samples from individuals with common cold symptoms, collected before Dec 2019

l) 40 potentially cross-reactive samples from individuals following an infection with Coronavirus HKU1, NL63, 229E or OC43, confirmed by PCR

Specificity

A total of 10453 samples were tested with the Elecsys Anti-SARS-CoV-2 assay. All samples were obtained before December 2019. 21 false positive samples were detected.

The resulting overall specificity in the internal study was 99.80 %. The 95 % lower confidence limit was 99.69 %.

Cohort	**N**	**NR**	**RX**	**Specificity, % (95 % CI[m)])**
Diagnostic routine	6305	6293	12	99.81 (99.67 - 99.90 %)
Blood donors	4148	4139	9	99.78 (99.59 - 99.90 %)
Overall	**10453**	**10432**	**21**	**99.80 (99.69 - 99.88 %)**

m) CI = confidence interval

Sensitivity

A total of 496 samples from 102 symptomatic patients with a PCR confirmed SARS-CoV-2 infection were tested with the Elecsys Anti-SARS-CoV-2 assay. 1 or more consecutive specimens from these patients were collected after PCR confirmation at various time points.

Days post PCR confirmation	**N**	**Reactive**	**Non-reactive**	**Sensitivity, % (95 % CI)**
0-6	161	97	64	60.2 (52.3 - 67.8 %)
7-13	150	128	22	85.3 (78.6 - 90.6 %)
≥ 14	185	184	1[n)]	99.5 (97.0 - 100 %)

n) 1 patient was non-reactive at day 14 (0.696 COI) but reactive at day 16 (4.48 COI)

After recovery from infection, confirmed by a negative PCR result, 26 consecutive samples from 5 individuals were tested with the Elecsys Anti-SARS-CoV-2 assay.

Elecsys Anti-SARS-CoV-2

cobas®

Patient	Day of negative PCR*		Days after diagnosis with positive PCR						
			21-23	24-26	27-29	30-32	33-35	36-38	39-40
1	9	COI	24.7	-	27.4	31.7	38.9	56.0	-
2	12		28.8	29.8	30.6	32.7	35.7	-	-
3	17		-	46.5	53.6	-	67.1	73.7	77.0
4	21		24.1	29.8	40.7	51.2	61.5	67.5	-
5	24		-	0.990	1.12	1.55	-	1.66	1.97

* Day 0 represents initial positive PCR.

References

1 Su S, Wong G, Shi W, et al. Epidemiology, Genetic Recombination, and Pathogenesis of Coronaviruses. Trends Microbiol 2016;24(6):490-502.

2 Zhu N, Zhang D, Wang W, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med 2020;382(8):727-733.

3 Occupational Safety and Health Standards: Bloodborne pathogens. (29 CFR Part 1910.1030). Fed. Register.

4 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.

5 Grimsey P, Frey N, Bendig G, et al. Population pharmacokinetics of exogenous biotin and the relationship between biotin serum levels and in vitro immunoassay interference. Int J Pharmacokinet 2017;2:247-256, Future Science Ltd London, UK. cited 2018 Jan 1. Available from: http://www.future-science.com/doi/10.4155/ipk-2017-0013

6 Piketty ML, Prie D, Sedel F, et al. High-dose biotin therapy leading to false biochemical endocrine profiles: validation of a simple method to overcome biotin interference. Clin Chem Lab Med 2017 May 1;55(6):817-825. doi: 10.1515/cclm-2016-1183.

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
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.

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com

Distribution in USA by:
Roche Diagnostics, Indianapolis, IN
US Customer Technical Support 1-800-428-2336
US COVID-19 General Support 1-866-987-6243

Roche