Elecsys SARS-CoV-2 Antigen

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REF		Σ	SYSTEM
09345272190	09345272500	200	**cobas e** 411 **cobas e** 601 **cobas e** 602

English

System information

For **cobas e** 411 analyzer: test number 2560
For **cobas e** 601 and **cobas e** 602 analyzers: Application Code Number 72

Intended use

Elecsys SARS-CoV-2 Antigen is an immunoassay for the in vitro qualitative detection of the nucleocapsid antigen of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in nasopharyngeal, oropharyngeal and nasal swab samples from patients with signs and symptoms suggestive of COVID-19, or known or suspected exposure to SARS-CoV-2. The test is intended as an aid in the diagnosis of SARS-CoV-2 infection.

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, the causative agent of Coronavirus Disease 2019 (COVID-19), is an enveloped, single-stranded RNA Betacoronavirus.[1,2,3] 7 coronaviruses have been identified as agents of human infection, causing disease-ranging from mild common cold to severe respiratory failure.[4] Viruses of this family share similarities in their genome and organization, including the 4 structural proteins spike (S), envelope (E), membrane (M), and nucleocapsid (N).[5,6] N is the most abundant protein of SARS-CoV-2, with each virion carrying approximately 1240 copies compared to approximately 30 copies of the S protein.[7,8]

SARS-CoV-2 is transmitted primarily from person-to-person through respiratory droplets and aerosols.[9,10] The incubation period from infection to detectable viral load in the host commonly ranges from 2 to 14 days.[11,12]

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.[13,14,15] Those infected often exhibit fever and respiratory symptoms.[16,17] 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.[18,19,20]

An effective strategy for controlling the COVID-19 pandemic is to develop highly accurate methods for the rapid identification and isolation of SARS-CoV-2 infected patients.[21] Diagnostic confirmation of acute SARS-CoV-2 infection can be based on the detection of unique sequences in the viral RNA (by nucleic acid amplification testing) or detection of viral proteins (by antigen tests) in samples from infected individuals (e.g., from the human respiratory tract).[22] Viral antigens are only expressed when the virus is actively replicating, thus making antigen tests clinically useful for identification of acute or early infection.[23,24] Current research suggests active replication of SARS-CoV-2 in the throat with high viral shedding in the first 5 days of infection, and infectious virus could be isolated from respiratory samples up to the first 7-9 days post symptom onset, indicating potential feasibility of antigen detection using throat swabs.[25,26,27,28] This time period also coincides with the time when the highest viral load is generally observed in SARS-CoV-2-infected individuals.[14,29,30,31] Therefore, the best performance of antigen tests is seen around symptom onset in symptomatic individuals and the initial phase of a SARS-CoV-2 infection.[22] Testing of mildly symptomatic or asymptomatic individuals can be considered in the assessment of contacts of confirmed infected persons.[22] Antigen tests can also become part of regular testing regimens for identifying, isolating, and thus filtering out currently infected persons, including those who are asymptomatic.[32,33]

The Elecsys SARS-CoV-2 Antigen assay uses monoclonal antibodies directed against the SARS-CoV-2 nucleocapsid protein in a double-antibody sandwich assay format for the detection of SARS-CoV-2 in upper respiratory tract specimens.

Test principle

Antibody sandwich principle. Total duration of assay: 18 minutes.

- 1st incubation: 50 µL of sample, biotinylated monoclonal anti-SARS-CoV-2-Ag antibodies, and monoclonal anti-SARS-CoV-2-Ag antibodies 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. 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

The reagent rackpack (M, R1, R2) is labeled as COV2AG.

M	Streptavidin-coated microparticles (transparent cap), 1 bottle, 12 mL: Streptavidin-coated microparticles 0.72 mg/mL; preservative.
R1	Anti-SARS-CoV-2-Ag~biotin (gray cap), 1 bottle, 14 mL: Biotinylated monoclonal anti-SARS-CoV-2-Ag antibody (mouse) < 1.4 mg/L; HEPES[b)] buffer 50 mmol/L, pH 7.5; preservative.
R2	Anti-SARS-CoV-2-Ag~$Ru(bpy)_3^{2+}$ (black cap), 1 bottle, 14 mL: 2 monoclonal anti-SARS-CoV-2-Ag antibodies (rabbit) labeled with ruthenium complex < 2.3 mg/L (each); HEPES buffer 50 mmol/L, pH 7.5, preservative.

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

COV2AG Cal1	Calibrator 1 (white cap), 2 bottles (lyophilized) for 1.0 mL each: non-reactive for SARS-CoV-2 antigen; buffer; preservative.
COV2AG Cal2	Calibrator 2 (black cap), 2 bottles (lyophilized) for 1.0 mL each: reactive for SARS-CoV-2 antigen; buffer; preservative.

Precautions and warnings

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.

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.

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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: all countries: +49-621-7590

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

Reagent handling

For professional use.

The reagents in the kit have been assembled into a ready-for-use unit that cannot be separated.

All information required for correct operation is read in from the respective reagent barcodes.

Calibrators:

Carefully dissolve the contents of 1 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. Store the aliquots within 4 hours after reconstitution at -20 °C (± 5 °C) for later use.

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

Please note for **cobas e** 602 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.

Do not freeze.

Store the Elecsys reagent kit **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 analyzers	8 weeks

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

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

Specimen collection and preparation

Nasopharyngeal, oropharyngeal and nasal specimens, collected using flocked or polyester-tipped swabs, placed in 3 mL of COPAN Universal Transport Medium (UTM-RT™), BD™ Universal Viral Transport (UVT), Viral Transport Media (VTM, prepared according to CDC SOP#: DSR 052 05), or sterile saline (0.9% NaCl).

Sample stability has been assessed with the above mentioned media.

Stable for 2 days at 15-25 °C, 2 days at 2-8 °C, 14 days at -20 °C (± 5 °C).

The samples may be frozen 3 times.

Optional sample extraction: If specimens will be extracted, please refer to the appropriate SARS-CoV-2 Extraction Solution Method Sheet for instructions. For dry swabs, refer to REF 09370064190, SARS-CoV-2 Extraction Solution. For swabs in UTM/VTM, refer to REF 09370099190, SARS-CoV-2 Extraction Solution C.

Collection and handling of swab specimen shall be performed in accordance with the latest versions of the WHO's interim guidance on **"Laboratory testing for coronavirus disease (COVID-19) in suspected human cases"**[34] and the CDC's **"Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens for COVID-19".**[35]

Follow national guidelines on laboratory biosafety in all circumstances.

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, 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.

Materials provided

See "Reagents – working solutions" section for reagents.

Materials required (but not provided)

- REF 09345302190, PreciControl SARS-CoV-2 Antigen, for 6 x 2.0 mL
- REF 09370064190, SARS-CoV-2 Extraction Solution
- REF 09370099190, SARS-CoV-2 Extraction Solution C
- General laboratory equipment
- Distilled or deionized water
- **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 all analyzers:

- REF 11298500316, 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. 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. Avoid foam formation. The system automatically regulates the temperature of the reagents and the opening/closing of the bottles.

Calibrators:

Place the calibrators in the sample zone.

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

Calibration

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

Calibration frequency: Calibration must be performed once per reagent lot using COV2AG Cal1, COV2AG Cal2 and fresh reagent (i.e. not more than 24 hours since the 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 12 weeks when using the same reagent lot
- after 28 days when using the same reagent kit on the analyzer
- as required: e.g. quality control findings outside the defined limits

Quality control

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

In addition, other suitable control material can be used.

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, and following each calibration.

If necessary, repeat the measurement of the samples concerned.

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

Calculation

The analyzer automatically calculates the cutoff based on the measurement of COV2AG Cal1 and COV2AG Cal2.

Interpretation of the results

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

Numeric result	Result message	Interpretation
COI[c)] < 1.0	Non-reactive	Negative for SARS-CoV-2 antigen
COI ≥ 1.0	Reactive	Positive for SARS-CoV-2 antigen

c) COI = Cutoff Index

Limitations - interference

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
Biotin	≤ 4912 nmol/L or ≤ 1200 ng/mL
Mucin	≤ 0.50 % (w/v)
Whole blood	≤ 4.0 % (v/v)

A microbial interference study was conducted using the microorganisms and viruses listed below. Indicated concentrations of the potential interferents were spiked into a SARS-CoV-2 antigen positive sample. No false negative result was observed.

Microorganism/virus	Concentration tested
RSV type A lysate	2.50 µg/mL
Haemophilus influenzae	10^6 CFU/mL
Streptococcus salivarius	10^6 CFU/mL
Streptococcus pyopgenes	10^6 CFU/mL
Staphylococcus epidermidis	10^6 CFU/mL
Escherichia coli	10^6 CFU/mL
Candida albicans	10^6 CFU/mL
Chlamydia trachomatis lysate	2.50 µg/mL
Legionella pneumophila native extract	10^6 CFU/mL
Lactobacillus plantarum	10^6 CFU/mL
Moraxella catarrhalis	10^6 CFU/mL
Neisseria meningitidis	10^6 CFU/mL
Pseudomonas aeruginosa	10^6 CFU/mL
Neisseria subflava biovar flava	10^6 CFU/mL
Pooled human nasal wash	10%
Coronavirus lysate/strain: 229E	2.50 µg/mL
Coronavirus lysate/strain: OC43	2.50 µg/mL
Coronavirus lysate/strain: NL63	2.50 µg/mL
Adenovirus type 5 hexon protein	2.50 µg/mL
Human metapneumovirus, type B1 lysate	2.50 µg/mL
human Cytomegalovirus cell lysate	2.50 µg/mL
Parainfluenza virus type 1 lysate	2.50 µg/mL
Parainfluenza virus type 2 lysate	2.50 µg/mL
Parainfluenza virus type 3 lysate	2.50 µg/mL
Parainfluenza virus type 4A lysate	2.50 µg/mL
Parainfluenza virus type 4B lysate	2.50 µg/mL
Influenza A H1N1 pdm / virus lysate	2.50 µg/mL
Influenza B (Strain Panama/45/90) / virus lysate	2.50 µg/mL
Coxsackievirus culture fluid (heat inactivated)	10^5 pfu/mL
Streptococcus pneumoniae antigen, native extract	10^6 CFU/mL
Bordetella pertussis FHA	2.50 µg/mL
Mycobacterium tuberculosis	10^6 CFU/mL
Pneumocystis jirovecii - S. cerevisiae recombinant	10^6 CFU/mL
Mycoplasma pneumoniae antigen	2.50 µg/mL
Diphtheria toxoid (frozen)	2.50 µg/mL
Measles virus lysate	2.50 µg/mL
Mumps virus lysate	2.50 µg/mL
Staphylococcus aureus	10^6 CFU/mL
MERS-CoV Culture Fluid	10^5 pfu/mL
Rhinovirus Type 1A Lysate	2.50 µg/mL

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

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Pharmaceutical substances

In vitro tests were performed on the listed pharmaceuticals. No interference with the assay was found except for Mupirocin.

Drug	Concentration tested
Neo-Synephrine (Phenylephrine)	15 % v/v
Afrin Nasal Spray (Oxymetazoline)	15 % v/v
Saline Nasal Spray	10 % v/v
Homeopathic allergy relief medicine	5 % v/v
Homeopathic Zicam Allergy Relief Nasal Gel	5 % v/v
Sodium Cromoglycate	6.00 mg/mL
Olopatadine Hydrochloride	10.0 mg/mL
Zanamivir (influenza)	5.00 mg/mL
Oseltamivir (influenza)	5.00 mg/mL
Artemether/Lumefantrine (malaria)	50.0 µM
Doxycycline hyclate (malaria)	70.0 µM
Quinine (malaria)	150 µM
Lamivudine (retroviral medication)	1.00 mg/mL
Ribavirin (HCV)	1.00 mg/mL
Daclatasvir (HCV)	1.00 mg/mL
Acetaminophen	199 µM
Acetylsalicylic acid	3620 µM
Ibuprofen	2425 µM
Mupirocin	10.0 mg/mL
Tobramycin	4.00 µg/mL
Erythromycin	81.6 µM
Ciprofloxacin	30.2 µM
Ricola	1.50 mg/mL
Menthol	1.50 mg/mL
Dyclonine + menthol	1.50 mg/mL
Benzocain + menthol	1.50 mg/mL
Fisherman´s Friend	1.50 mg/mL
Sore Throat Phenol Spray	15 % v/v
Fluticasone Propionate	2 mg/dL

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.

cobas e 601 and **cobas e** 602 analyzers:
Make sure that in the Special Wash List (Screen → Utility → Special Wash → Immune) the Elecsys Anti-SARS-CoV-2 assay is combined with all assays performed on the analyzer - including the Elecsys Anti-SARS-CoV-2 assay itself:

From test	Step	To test	Step 0	Step 1	Step 2
Anti-SARS-CoV-2	1	Anti-SARS-CoV-2	x	x	x
Anti-SARS-CoV-2	1	each other assay	x	x	x

If new tests are installed, make sure that the Special Wash List is updated accordingly.

The described additions to the Special Wash List have to be entered manually. Please refer to the operator's manual.

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

A negative test result does not rule out the possibility of an infection with SARS-CoV-2. For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, the presence of clinical signs and symptoms suggestive for COVID-19 or a suspected exposure to SARS-CoV-2.
Inadequate sample collection, storage or handling may result in a negative result.

Specific performance data

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

Detection limit

The detection limit in different transport media was determined by limiting dilution studies using an inactivated viral lysate (USA-WA1/2020). The detection limit is defined as the lowest detectable concentration of SARS-CoV-2 at which a minimum of 19 from 20 replicates per concentration generate a reactive test result (≥ 1.0 COI), and expressed as TCID50[d)]/mL.

Transport medium	TCID50/mL
COPAN universal transport medium (UTM-RT)	22.5
CDC viral transport medium	22.5
Sterile saline (0.9 % NaCl)	37.5
SARS-CoV-2 Extraction Solution	22.5

d) Median Tissue Culture Infectious Dose

Precision

Precision was determined using Elecsys reagents, samples and controls in a protocol (EP05-A3) of the CLSI (Clinical and Laboratory Standards Institute): 2 runs per day in duplicate each for 21 days (n = 84). The following results were obtained:

cobas e 411 analyzer					
		Repeatability		**Intermediate precision**	
Sample	Mean COI	SD COI	CV %	SD COI	CV %
UTM-Sample-1	0.802	0.022	2.8	0.053	6.6
UTM-Sample-2	0.891	0.032	3.6	0.053	6.0
UTM-Sample-3	1.26	0.067	5.3	0.074	5.8
UTM-Sample-4	6.64	0.118	1.8	0.168	2.5
UTM-Sample-5	41.8	0.983	2.4	1.30	3.1
PC[e)] COV2AG1	0.780	0.028	3.6	0.055	7.0
PC COV2AG2	3.38	0.035	1.0	0.074	2.2

e) PC = PreciControl

cobas e 601 and **cobas e** 602 analyzer					
		Repeatability		**Intermediate precision**	
Sample	Mean COI	SD COI	CV %	SD COI	CV %
UTM-Sample-1	0.603	0.013	2.2	0.017	2.8
UTM-Sample-2	0.806	0.017	2.1	0.019	2.3
UTM-Sample-3	1.54	0.051	3.3	0.054	3.5
UTM-Sample-4	11.6	0.271	2.3	0.338	2.9
UTM-Sample-5	79.0	1.11	1.4	1.87	2.4
PC COV2AG1	0.585	0.015	2.5	0.015	2.6

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		Repeatability		**Intermediate precision**	
Sample	Mean COI	SD COI	CV %	SD COI	CV %
PC COV2AG2	4.82	0.058	1.2	0.090	1.9

Analytical specificity

No cross-reactivity to the following respiratory microorganisms and viruses using the indicated concentrations of the potential cross-reactant has been observed. The Elecsys SARS-CoV-2 Antigen assay does not differentiate between SARS-CoV and SARS-CoV-2.

Microorganism/Virus	**Concentration tested**
RSV type A lysate	2.50 µg/mL
Haemophilus influenzae	10^6 CFU/mL
Streptococcus salivarius	10^6 CFU/mL
Streptococcus pyogenes	10^6 CFU/mL
Staphylococcus epidermidis	10^6 CFU/mL
Escherichia coli	10^6 CFU/mL
Candida albicans	10^6 CFU/mL
Chlamydia trachomatis lysate	2.50 µg/mL
Legionella pneumophila native extract	10^6 CFU/mL
Lactobacillus plantarum	10^6 CFU/mL
Moraxella catarrhalis	10^6 CFU/mL
Neisseria meningitidis	10^6 CFU/mL
Pseudomonas aeruginosa	10^6 CFU/mL
Neisseria subflava biovar flava	10^6 CFU/mL
Pooled human nasal wash	10 %
Coronavirus lysate / strain: 229E	2.50 µg/mL
Coronavirus lysate / strain: OC43	2.50 µg/mL
Coronavirus lysate / strain: NL63	2.50 µg/mL
Adenovirus type 5 hexon protein	2.50 µg/mL
Human metapneumovirus, type B1 lysate	2.50 µg/mL
human Cytomegalovirus cell lysate	2.50 µg/mL
Parainfluenza virus type 1 lysate	2.50 µg/mL
Parainfluenza virus type 2 lysate	2.50 µg/mL
Parainfluenza virus type 3 lysate	2.50 µg/mL
Parainfluenza virus type 4A lysate	2.50 µg/mL
Parainfluenza virus type 4B lysate	2.50 µg/mL
Influenza A H1N1 pdm / virus lysate	2.50 µg/mL
Influenza B (strain panama/45/90) / virus lysate	2.50 µg/mL
Coxsackievirus culture fluid (heat inactivated)	10^5 pfu/mL
Streptococcus pneumoniae antigen, native extract	10^6 CFU/mL
Bordetella pertussis FHA	2.50 µg/mL
Mycobacterium tuberculosis	10^6 CFU/mL
Pneumocystis jirovecii - S. cerevisiae recombinant	10^6 CFU/mL
Mycoplasma pneumoniae antigen	2.50 µg/mL
Diphtheria toxoid (frozen)	2.50 µg/mL
Measles virus lysate	2.50 µg/mL
Mumps virus lysate	2.50 µg/mL
Staphylococcus aureus	10^6 CFU/mL
MERS-CoV Culture Fluid	10^5 pfu/mL
Rhinovirus Type 1A Lysate	2.50 µg/mL

Human coronavirus HKU1 was not available for testing. With a protein sequence homology of < 37 %, cross-reactivity of assay antibodies to HKU1-hCoV nucleocapsid protein is unlikely.

Clinical data

Performance was evaluated using a total of 3191 nasopharyngeal and oropharyngeal swab specimens, collected from individuals with signs and symptoms suggestive of COVID-19 (cohort 1), with known or suspected exposure to SARS-CoV-2 (cohort 2), and from individuals undergoing pre-admission screening before hospitalization for surgical intervention unrelated to an infectious disease (cohort 3).

Nasal swab specimens were collected from 200 individuals with or without symptoms suggestive of COVID-19. Performance with nasal swabs was evaluated using 116 of these nasal swab specimens, collected from those individuals with signs and symptoms suggestive of COVID-19.

All subjects included in the analysis were characterized using the **cobas** SARS-CoV-2 RT-PCR assay.[36] RT-PCR positive samples were further stratified using Target 2 (structural protein envelope E-gene/pan-Sarbecovirus detection) cycle threshold (Ct) values.

Relative sensitivity

The following table correlates the performance of the Elecsys SARS-CoV-2 Antigen assay in all RT-PCR positive naso- and oropharyngeal swab samples from symptomatic and asymptomatic individuals to the **cobas** SARS-CoV-2 Ct values.

cobas SARS-CoV-2 Ct value	**N* (cumulative)**	**Elecsys SARS-CoV-2 Antigen reactive, N (cumulative)**	**Relative sensitivity, % (95 % CI, two-sided)**
Ct < 26	177	176	99.4 (96.9-100)
Ct < 27	194	192	99.0 (96.3-99.9)
Ct < 28	207	202	97.6 (94.5-99.2)
Ct < 29	226	219	96.9 (93.7-98.7)
Ct < 30	248	230	92.7 (88.8-95.6)
Ct < 31	265	242	91.3 (87.3-94.4)
Ct < 32	285	245	86.0 (81.4-89.8)
Ct < 33	299	250	83.6 (78.9-87.6)
Ct < 34	320	255	79.7 (74.9-84.0)
Ct < 35	344	256	74.4 (69.5-78.9)
Overall (up to Ct ≤ 40)	442	257	58.1 (53.4-62.8)

* 2 samples without reported Ct values for cobas SARS-CoV-2 Target 2 were excluded from the analysis.

The relative sensitivity of the Elecsys SARS-CoV-2 Antigen assay was assessed in **cobas** SARS-CoV-2 RT-PCR positive samples.

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The resulting overall relative sensitivity in symptomatic individuals with a **cobas** SARS-CoV-2 Target 2 Ct value < 30 was **94.5 %** (95 % CI, two-sided: 90.4 - 97.2 % [189/200]).

The tables below show additional analyses based on days post-symptom onset (DPSO) and stratification by a Ct value of 30 with the **cobas** SARS-CoV-2 RT-PCR, below which samples are considered to have a relatively high viral load.[37]

Cohort and cohort description		N Ct < 30*	Elecsys SARS-CoV-2 Antigen non-reactive, N	Elecsys SARS-CoV-2 Antigen reactive, N	Relative sensitivity, % (95 % CI, two-sided)
1	Symptomatic ≤ 5 DPSO	119	3	116	97.5 (92.8-99.5)
	Symptomatic ≤ 10 DPSO	158	8	150	94.9 (90.3-97.8)
	Symptomatic > 10 DPSO	4	1	3	75.0 (19.4-99.4)
	Symptomatic with unknown DPSO	38	2	36	94.7 (82.3-99.4)
2	Known or suspected exposure	27	3	24	88.9 (70.8-97.6)
3	Screening	21	4	17	81.0 (58.1-94.6)

* 2 samples without reported Ct values for target 2 were excluded from the analysis

Cohort and cohort description		N Ct ≥ 30*	Elecsys SARS-CoV-2 Antigen non-reactive, N	Elecsys SARS-CoV-2 Antigen reactive, N	Relative sensitivity, % (95 % CI, two-sided)
1	Symptomatic ≤ 5 DPSO	30	22	8	26.7 (12.3-45.9)
	Symptomatic ≤ 10 DPSO	78	60	18	23.1 (14.3-34.0)
	Symptomatic > 10 DPSO	18	15	3	16.7 (3.6-41.4)
	Symptomatic with unknown DPSO	17	13	4	23.5 (6.8-49.9)
2	Known or suspected exposure	51	50	1	1.96 (0.0496-10.4)
3	Screening	30	29	1	3.33 (0.0844-17.2)

* 2 samples without reported of Ct values for target 2 were excluded from the analysis

The following table summarizes the performance in RT-PCR positive naso- and oropharyngeal swab samples from symptomatic patients, stratified by DPSO and a **cobas** SARS-CoV-2 Target 2 Ct value of 30.

DPSO, Days	Relative sensitivity (cumulative), % (95 % CI, two-sided)	
	Ct value < 30 [N Elecsys SARS-CoV-2 Antigen reactive / N total]	Ct value ≥ 30 [N Elecsys SARS-CoV-2 Antigen reactive / N total]
0	100 (15.8-100) [2/2]	--- (---) [0/0]
≤ 1	97.6 (87.1-99.9) [40/41]	0.0 (---) [0/7]
≤ 2	97.2 (90.2-99.7) [69/71]	7.7 (0.2-36.0) [1/13]
≤ 3	96.6 (90.3-99.3) [84/87]	27.3 (10.7-50.2) [6/22]
≤ 4	97.2 (92.0-99.4) [103/106]	28.0 (12.1-49.4) [7/25]
≤ 5	97.5 (92.8-99.5) [116/119]	26.7 (12.3-45.9) [8/30]
≤ 6	96.9 (92.1-99.1) [123/127]	22.2 (10.1-39.2) [8/36]
≤ 7	96.5 (92.1-98.9) [139/144]	28.3 (16.0-43.5) [13/46]
≤ 8	96.6 (92.3-98.9) [144/149]	25.9 (15.3-39.0) [15/58]
≤ 9	94.9 (90.2-97.8) [149/157]	23.2 (13.9-34.9) [16/69]
≤ 10	94.9 (90.3-97.8) [150/158]	23.1 (14.3-34.0) [18/78]
> 10	75.0 (19.4-99.4) [3/4]	16.7 (3.6-41.4) [3/18]
Unknown	94.7 (82.3-99.4) [36/38]	23.5 (6.8-49.9) [4/17]

The following table correlates the performance of the Elecsys SARS-CoV-2 Antigen assay in all RT-PCR positive nasal swab samples from symptomatic individuals to the **cobas** SARS-CoV-2 Ct values.

cobas SARS-CoV-2 Ct value	N* (cumulative)	Elecsys SARS-CoV-2 Antigen reactive, N (cumulative)	Relative sensitivity, % (95 % CI, two-sided)
< 26	39	39	100 (91.0-100)
< 27	46	46	100 (92.3-100)
< 28	49	49	100 (92.7-100)
< 29	53	52	98.1 (89.9-100)
< 30	62	60	96.8 (88.8-99.6)
< 31	64	60	93.8 (84.8-98.3)
< 32	73	65	89.0 (79.5-95.1)
< 33	79	65	82.3 (72.1-90.0)
< 34	84	67	79.8 (69.6-87.7)
< 35	88	67	76.1 (65.9-84.6)
Overall (up to Ct ≤ 40)	116	67	57.8 (48.2-66.9)

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The following table summarizes the performance in RT-PCR positive nasal swab samples from symptomatic patients, stratified by DPSO and a **cobas** SARS-CoV-2 Target 2 Ct value of 30.

DPSO, Days	Relative sensitivity (cumulative), % (95 % CI, two-sided)	
	Ct value < 30 [N Elecsys SARS-CoV-2 Antigen reactive / N total]	Ct value ≥ 30 [N Elecsys SARS-CoV-2 Antigen reactive / N total]
≤ 1	100 (15.8-100) [2/2]	0.0 (---) [0/1]
≤ 2	100 (66.4-100) [9/9]	12.5 (0.316-52.7) [1/8]
≤ 3	100 (87.2-100) [27/27]	22.2 (6.41-47.6) [4/18]
≤ 4	96.7 (88.7-99.6) [59/61]	14.3 (5.94-27.2) [7/49]
≤ 5	96.8 (88.8-99.6) [60/62]	13.0 (5.37-24.9) [7/54]

Relative specificity

The relative specificity was assessed in all **cobas** SARS-CoV-2 RT-PCR negative samples for both symptomatic and asymptomatic individuals, as indicated in the table below.

The resulting overall relative specificity was 99.9 % (95 % CI, two-sided: 99.6-100 % [2743/2747]).

Cohort	N	Elecsys SARS-CoV-2 Antigen, non-reactive	Elecsys SARS-CoV-2 Antigen, reactive	Relative specificity, % (95 % CI, two-sided)
Cohort 1: Symptomatic	548*	548	0	100 (99.3-100)
Cohort 2 & 3: Known / suspected exposure and screening	2199**	2195	4	99.8 (99.5-100)

*3 / **12 samples invalid with cobas SARS-CoV-2 RT-PCR, but negative with another SARS-CoV-2 RT-PCR test

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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).

A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

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 for reconstitution
GTIN	Global Trade Item Number

CE

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