510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT

I Background Information:

A 510(k) Number

K252280

B Applicant

Roche Diagnostics

C Proprietary and Established Names

Elecsys Anti-SARS-CoV-2 S

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
QVP	Class II	21 CFR 866.3983 - SARS-Cov-2 Serology Test	MI - Microbiology
JJX	Class I	21 CFR 862.1660 - Quality control material (assayed and unassayed)	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

To obtain clearance for a new device.

B Measurand:

Total antibodies against SARS-CoV-2.

C Type of Test:

Electrochemiluminescence immunoassay (ECLIA).

III Intended Use/Indications for Use:

A Intended Use(s):

Elecsys Anti-SARS-CoV-2 S is an electrochemiluminescence immunoassay intended for quantitative detection of total antibodies to SARS-CoV-2 in human serum and plasma (lithium heparin, K2-EDTA, K3-EDTA, and sodium citrate) samples collected on or after 15 days post-symptom onset. 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.

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

B Indication(s) for Use:

NA

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

For use on **cobas e** 801 analyzer.

IV Device/System Characteristics:

A Device Description:

The Elecsys Anti-SARS-CoV-2 S is an automated two-step double-antigen sandwich immunoassay using streptavidin microparticles, a biotinylated recombinant SARS-CoV-2-specific antigen and a separate SARS-CoV-2-specific recombinant antigen labeled with a ruthenium complex for electrochemiluminescence detection. The results are determined automatically by the software comparing the electrochemiluminescence signal obtained from the reaction product of the sample with the signal of the cutoff value previously obtained by calibration to establish reactivity, and then separately converting that signal intensity from the sample into a final concentration using a 2-point calibration and a master curve from the reagent barcode.

The assay is performed using the Elecsys Anti-SARS-CoV-2 S Reagent Pack in combination with the CalSet Anti-SARS-CoV-2 S calibrator and the PreciControl Anti-SARS-CoV-2 S controls.

The Elecsys Anti-SARS-CoV-2 S Reagent Pack contains:

- M: Streptavidin-coated microparticles.
- R1: Biotin-labeled SARS-CoV-2-S recombinant Ag.
- R2: Ruthenium complex-labeled SARS-CoV-2-S recombinant Ag.

The following additional materials are required, and provided separately:

- CalSet Anti-SARS-CoV-2 S: Two-level positive calibrators (ACOV2S Cal1 and ACOV2S Cal2:) containing anti-SARS-CoV-2 antibody in human serum spiked with serum from anti-SARS-CoV-2-S positive donors in 2 concentration ranges.
- PreciControl Anti-SARS-CoV-2 S - Two-level quality controls, PC ACOV2S1 (non-reactive), and PC ACOV2S2 (reactive)
- Diluent Universal for sample dilution
- Instrument reagents - System solutions for processing/measurement and cleaning solutions for maintenance.

The following additional materials are optional, not provided with the assay:

- CalCheck Anti-SARS-CoV-2 S five-level calibration verification material:
    - CalCheck 1 non-reactive in analyte free human serum and
    - CalCheck 2 to 5, containing serum spiked with human serum from anti-SARS-CoV-2 S positive donors in varying concentrations.

B Principle of Operation:

This assay is based on the sandwich principle. Total duration of assay is 18 minutes.

- 1st incubation: 12 µL of sample, 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 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 e-barcode.

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

Interpretation of Results: The **cobas e** system automatically calculates the analyte concentration of each sample in the international standard units BAU/mL (binding antibody units).

Table 1. Elecsys Anti-SARS-CoV-2 S Results Interpretation

Result	Interpretation	Description
< 0.40 BAU/mL	Negative. Result below the lower limit of quantitation (LLOQ) of the method. Numerical result is reported outside the laboratory indicating that the result is below 0.40 BAU/mL.	Antibodies for SARS-CoV-2 are not detected
≥ 0.40 – < 0.80 BAU/mL	Negative. Result above the LLOQ but below the assay cutoff. Numerical result is reported outside the laboratory, with numeric value within the analytical measuring interval (AMI).	Antibodies to SARS-CoV-2 are detected at levels above the LLoQ and below the assay cutoff. At this level of antibodies, samples are negative.
≥ 0.80 BAU/mL – ≤ 250 BAU/mL	Positive. Numerical result is reported outside the laboratory, with numeric value within the analytical measuring interval (AMI)	Antibodies for SARS-CoV-2 are detected
> 250 BAU/mL – ≤ 100000 BAU/mL	Positive. Numerical result is reported outside the laboratory, with numeric value within the extended measuring interval (EMI, specimen requires dilution per IFU)	Antibodies for SARS-CoV-2 are detected
> 100000 BAU/mL	Positive. Report outside the laboratory indicates that the result is above 100000 BAU/mL	Antibodies for SARS-CoV-2 are detected

C Instrument Description Information:

1. Instrument Name:

   Cobas e 801 analyzer

2. Specimen Identification:

   The Elecsys Anti-SARS-CoV-2-S is intended for use with Serum, lithium-heparin, dipotassium EDTA (K2-EDTA), tripotassium EDTA (K3-EDTA), and sodium citrate plasma specimens.

3. Specimen Sampling and Handling:

   - Samples may be stored for up to 14 days at room temperature (15-25 °C) or at 2 - 8 °C.
   - Samples may be stored frozen at ≤ -20 °C for 3 months.
   - Samples may be subjected to up to three freeze-thaw cycles.

4. Calibration:

CalSet Anti-SARS-CoV-2 S is used for calibrating the Elecsys Anti-SARS-CoV-2 S assay on **cobas e** immunoassay analyzers. The CalSet contains anti-SARS-CoV-2 antibody in human serum spiked with serum from anti-SARS-CoV-2-S positive donors in 2 concentration ranges (Cal1 and Cal2).

The calibrator is supplied lyophilized and requires reconstitution with 1.0 mL of distilled or deionized water. Results are calculated in BAU/mL based on standardization against the International Standard for anti-SARS-CoV-2 immunoglobulin (human), NIBSC code: 20/136.

The assay results are determined using an instrument-specific calibration curve that combines a master curve (provided through the reagent kit's electronic barcode) with a 2-point on-site calibration.

5. Quality Control:

The PreciControl Anti-SARS-CoV-2 S controls are provided separately and contain Control 1 (PC ACOV2S1): Anti-SARS-CoV-2 non-reactive human serum control and Control 2 (PC ACOV2S2): Anti-SARS-CoV-2 reactive human serum control. Target values and ranges were determined by Roche and available electronically or via barcodes.

V Substantial Equivalence Information:

A Predicate Device Name(s):

VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Reagent Pack, VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Calibrators

B Predicate 510(k) Number(s):

DEN210040

C Comparison with Predicate(s):

Device & Predicate Device(s):	Predicate Device DEN210040	Candidate Device K252280
Device Trade Name	VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Reagent Pack, VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Calibrators	Elecsys Anti-SARS-CoV-2 S
Intended Use/Indications For Use	The VITROS lmmunodiagnostic Products Anti-SARS-CoV-2 TotaJ Reagent Pack when used in combination with the VITROS lmmunodiagnostic Products Anti-SARS-CoV-2 Total	Elecsys Anti-SARS-CoV-2 S is an electrochemiluminescence immunoassay intended for quantitative detection of total antibodies to SARS-CoV-2 in human serum and plasma (lithium heparin, K_2-EDTA,

	Calibrator is a chemiluminescent immunoassay intended for the qualitative detection of total antibodies to SARS-CoV-2 in human serum and plasma (K2-EDTA, K3-EDTA and lithium heparin) samples collected on or after 15 days post-symptom onset using the VTTROS ECi/ECiQ/3600 Immunodiagnostic Systems and the VITROS 5600/XT 7600 Integrated Systems. The VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total 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.	K_3-EDTA, and sodium citrate) samples collected on or after 15 days post-symptom onset. 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. The **e**lectro**c**hemi**l**uminescence **i**mmuno**a**ssay "ECLIA" is intended for use on **cobas e** immunoassay analyzers.
Regulation Number	21 CFR 866.3983	Same
Regulatory Class	II	Same
Product Code	QVP	Same
Analyte	Total anti-SARS-CoV-2 antibodies	Total anti-SARS-CoV-2 antibodies
Technology	CLIA	ECLIA, similar chemiluminescence detection as CLIA with difference in light signal generation.
Streptavidin/ Biotin Technology	Yes	Same
Sample Type/ Matrix	Serum, Li-Heparin, K2-EDTA, K3-EDTA	Serum, Li-Heparin, K2-EDTA, K3-EDTA Sodium Citrate
Controls(s)	1 non-reactive, 1 reactive	1 non-reactive, 1 reactive
Analyte Detection	Qualitative detection of total antibodies to SARS-CoV-2	Quantitative detection of total antibodies to SARS-CoV-2
Test principle	Two-stage immunometric technique with HRP-labeled antigen	Double-antigen sandwich with ruthenium complex
Assay Duration	37 min incubation, 48 min to first result	18 minutes total
Sample Volume	80 µL	12 µL

Interpretation of Results	S/C < 1.0: Non-reactive S/C ≥ 1.0: Reactive	< 0.40 BAU/mL: Negative. Result below the lower limit of quantitation (LLOQ) of the method. Numerical result is reported outside the laboratory indicating that the result is below 0.40 BAU/mL. ≥ 0.40 – < 0.80 BAU/mL: Negative. Result above the LLOQ but below the assay cutoff. Numerical result is reported outside the laboratory, with numeric value within the analytical measuring interval (AMI). ≥ 0.80 BAU/mL – ≤ 250 BAU/mL BAU/mL: Positive. Numerical result is reported outside the laboratory, with numeric value within the analytical measuring interval (AMI) > 250 BAU/mL – ≤ 100000 BAU/mL: Positive. Numerical result is reported outside the laboratory, with numeric value within the extended measuring interval (EMI, specimen requires dilution per IFU) > 100000 BAU/mL: Positive. Report outside the laboratory indicates that the result is above 100000 BAU/mL
Platform	VITROS ECi/ECiQ/3600/5600/XT 7600 Systems	**cobas e** 801 analyzer
Calibrators	2 calibrators (positive and negative)	2 positive calibrators: CalSet with 2 concentration ranges (Cal1, Cal2)
Reagent Components	- Coated wells with SARS-CoV-2 antigen - HRP-labeled conjugate - Assay reagent buffer	- Streptavidin-coated microparticles - Biotinylated RBD antigen - Ruthenium-labeled RBD antigen

VI Standards/Guidance Documents Referenced:

- CLSI EP05-A3 Evaluation of Precision of Quantitative Measurement Procedures; Approved
- Guideline - Third Edition
- CLSI EP06 Evaluation of the Linearity of Quantitative Measurement Procedures- Second Edition
- CLSI EP07 Interference testing in Clinical Chemistry- Third Edition
- CLSI EP12-A2 User Protocol for Evaluation of Qualitative Test Performance; Approved Guideline - Second Edition
- ISO 17511 Second edition 2020-04 In vitro diagnostic medical devices – Requirements for establishing metrological traceability of values assigned to calibrators trueness control materials and human samples.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Within-Laboratory Precision: A within-laboratory precision study was performed using 2 lots of the Elecsys Anti-SARS-CoV-2 S reagent packs, 2 lots of the CalSet Anti-SARS-CoV-2 S calibrators, and one **cobas e** 801 analyzer. One PreciControl PC ACOV2S2 (Positive Control, PC) and 6 human serum pools were tested in 3 replicates 2 separate times per day on 5 days using 4 reagent pack lot/calibrator lot combinations. The within-laboratory precision data are summarized below in Table 2.

Table 2. Elecsys Anti-SARS-CoV-2 S assay Within-Laboratory Precision

Sample	Mean (BAU/mL)	N	Repeatability (Within-Run)		Between-Run		Between-Day		Between-Calibrator Lot		Between-Reagent Lot		Overall, Within-Laboratory	
			SD	%CV	SD	%CV	SD	%CV	SD	% CV	SD	%CV	SD	%CV
1	0.708	120	0.0141	1.99	0.00752	1.06	0.0018	0.255	0.00274	0.387	0.0214	3.02	0.0269	3.8
2	0.904	120	0.012	1.33	0.0147	1.62	0	0	0.00207	0.229	0.00421	0.466	0.0195	2.16
3	13.2	120	0.106	0.805	0.0832	0.63	0.0877	0.663	0	0	0.199	1.51	0.256	1.94
4	122	120	1.17	0.958	0	0	0.765	0.628	0	0	0.357	0.293	1.44	1.18
5	206	120	1.50	0.731	0.558	0.272	1.31	0.64	0	0	0	0	2.07	1.01
6	231	120	2.29	0.988	1.41	0.611	0.372	0.161	0	0	2.60	1.13	3.76	1.63
PC	9.16	120	0.078	0.852	0.0959	1.05	0.0463	0.506	0	0	0.0347	0.347	0.136	1.48

Reproducibility Study (multi-site precision): A 5-day reproducibility study was conducted at 3 sites (two external and one internal site), using 7 human serum pool samples (1 negative and 6 positive) and 2 control samples (1 negative and 1 positive) in **cobas e** 801 analyzers. Three aliquots per sample were evaluated in 2 runs per day over 5 days using one lot of reagent packs, calibrators, and controls per site.

Table 3. Elecsys Anti-SARS-CoV-2 S assay Reproducibility

Sample	Mean (BAU/mL)	N	Repeatability		Between-Run		Between-Day		Between-Site		Reproducibility	
			SD	% CV	SD	% CV	SD	% CV	SD	% CV	SD	% CV
1	0.727	90	0.0441	6.06	0	0	0	0	0	0	0.0441	6.06
2	0.913	90	0.0152	1.67	0.00333	0.364	0.00844	0.924	0.0102	1.12	0.0205	2.24
3	13.1	90	0.14	1.06	0.0578	0.441	0.0696	0.531	0.101	0.769	0.194	1.48
4	123	90	1.43	1.16	0.741	0.6	0.678	0.549	1.01	0.82	2.02	1.63
5	207	90	2.06	0.992	1.13	0.544	1.23	0.591	1.9	0.918	3.26	1.57
6	235	90	2.43	1.03	1.35	0.574	1.2	0.511	1.75	0.743	3.5	1.49
PC	9.23	90	0.11	1.19	0.0643	0.696	0.072	0.78	0.0165	0.179	0.147	1.59

*Reproducibility metrics (SD, CV) were not calculated for the negative samples, as their concentrations fell below the assay's quantifiable range.

2. Linearity:

A linearity study was conducted to establish the analytical measuring interval (AMI) of the Elecsys Anti-SARS-CoV-2 assay. Six high concentration native samples (3 sodium citrate plasma, 3 serum) were serially diluted with their respective negative matrix to create 15 dilutions spanning the concentration range from ~0.2 BAU/mL to ~280-300 BAU/mL (Serum samples were diluted with negative serum, and plasma samples were diluted with negative plasma). Each sample dilution was measured in one run with four replicates using one reagent/calibrator lot combination. Linearity was assessed by calculating deviations from the best-fitted straight line for each dilution level. The study employed weighted least squares regression to generate the best fitted straight line, with deviations calculated as the difference between measured mean values and predicted values from this regression line.

The linearity for the Elecsys Anti-SARS-CoV-2 S assay was demonstrated across the analytical measuring range of 0.4 BAU/mL to 250 BAU/mL using both serum and plasma samples.

3. Analytical Specificity/Interference:

a. Potential Cross-Reactivity:

The Elecsys Anti-SARS-CoV-2 S assay was evaluated for potential cross-reactivity by testing 1582 human serum and plasma samples collected before October 2019 from individuals with antibodies to other microorganisms or autoimmune disorders. Testing was performed on **cobas e** 801 analyzers in single determination. The summary of the data is shown in the following table.

Table 4. Elecsys Anti-SARS-CoV-2 S assay Cross-Reactivity study

Disease/Infectious agent Positive Sera	Number of Samples Tested (n)	Elecsys Anti-SARS-CoV-2 S Results	
		Non-reactive	Reactive
SARS-CoV-2 related:			
MERS CoV (anti-S1 IgG+)	51	51	0
Common Corona virus panels[a]	151	151	0
SARS-CoV-1 IgG	10	10	0
Infectious respiratory diseases:			
Bordetella pertussis	39	39	0
Chlamydia pneumonia	36	36	0
Common cold panel	21	21	0
Enterovirus (IgG+ IgM+)	35	35	0
Haemophilus influenzae B	75	75	0
Influenza A (IgM+ IgG+ IgA+)	40	40	0
Influenza B (IgG+ IgM+ IgA+)	45	45	0
Influenza vaccines	25	25	0
Metapneumovirus (MPV)	15	14	1**
Mycobacterium tuberculosis (IgG)	15	15	0
Mycoplasma pneumoniae (IgG+ IgM+)	46	46	0
Parainfluenza	82	82	0
Pneumocystis jirovecii IgG	14	14	0
Pseudomonas aeruginosa	15	15	0
Respiratory syncytial virus	51	51	0
Streptococcus pneumoniae	15	15	0
Other infectious diseases:			
Adenovirus	25	25	0
Borrellia	6	6	0
Candida albicans	13	13	0
Chlamydia trachomatis	12	12	0
CMV acute (IgM+ IgG+)	86	86	0
E. coli (anti-E. coli reactive)	10	10	0
EBV acute (IgM+ VCA IgG+)	106	106	0

Disease/Infectious agent Positive Sera	Number of Samples Tested (n)	Elecsys Anti-SARS-CoV-2 S Results	
		Non-reactive	Reactive
Gonorrhea (Tripper)	5	5	0
HAV acute (IgM+)	10	10	0
HAV late (IgG+)	15	15	0
HAV vaccinees	15	15	0
HBV acute	12	12	0
HBV chronic	12	12	0
HBV vaccinees	15	15	0
HCV	50	50	0
HEV	12	12	0
HIV infection	10	10	0
HSV acute (IgM+)	24	24	0
HTLV	6	6	0
Legionella (IgGAM+)	7	7	0
Listeria	6	6	0
Measles	10	10	0
Mumps	14	14	0
Parvovirus B19	30	30	0
Plasmodium falciparum (Malaria)	8	8	0
Rubella acute (IgM+, IgG+)	12	12	0
Staphylococcus epidermis	15	15	0
Streptococcus pyogenes	15	15	0
Toxoplasma gondii (IgM+, IgG+)	8	8	0
Treponema pallidum (Syphilis)	62	62	0
VZV (Varicella zoster)	30	30	0
Auto-immune diseases:			
AMA (anti-mitochondrial antibodies)	30	30	0
ANA (anti-nuclear antibodies)	17	17	0
Hemophiliacs	15	15	0
RA (rheumatoid arthritis)	10	10	0
SLE (systemic lupus erythematosus)	10	10	0

Disease/Infectious agent Positive Sera	Number of Samples Tested (n)	Elecsys Anti-SARS-CoV-2 S Results	
		Non-reactive	Reactive
Hepatic diseases:			
Alcohol induced hepatitis/cirrhosis	13	13	0
Drug induced hepatitis/cirrhosis	10	10	0
Fatty liver	10	10	0
Liver cancer	10	10	0
Non-viral liver disease	15	15	0
Total	**1582**	**1581**	**1**

*One out of 15 samples with human metapneumovirus showed a false positive result

[a]Common Coronavirus panel includes pre-pandemic samples, which showed serologic reactivity to at least 1 of the endemic Coronavirus HKU1, NL63, 229E, or OC43.

Cross-reactivity with antibodies to Rhinovirus has not been evaluated, and the potential for false positive results in this population is unknown.

b. Potentially Endogenous Interfering Substances:

The Elecsys Anti-SARS-CoV-2 S assay was evaluated for potential interference caused by endogenous substances using serum and K2-EDTA plasma samples with the following SARS-CoV-2 antibodies concentrations: one positive sample (>50.0 BAU/mL), one low positive sample (between 0.8 and 5.0 BAU/mL), and one negative sample (<0.8 BAU/mL).

No interference was observed for the following potential endogenous substances at the following concentrations.

Table 5. Endogenous Interfering Substances Evaluated

Substance	**Concentrations Tested**
Biotin	1200 ng/mL
Intralipid	2000 mg/dL
Bilirubin	66.0 mg/dL
Hemoglobin	1000 mg/dL
Rheumatoid Factors	1200 IU/mL
Human IgG	70.0 mg/mL
Human IgM	10.0 mg/mL
Human IgA	16.0 mg/mL
Human Serum Albumin	70.0 mg/mL
Cholesterol	400.0 mg/dL

Triglycerides	2000 mg/dL
Anti-Nuclear Antibody (ANA)	1:1280 titer

c. Potentially Exogenous Interfereing Substances:

The Elecsys Anti-SARS-CoV-2 S assay was evaluated for potential interference caused by exogenous substances using one negative sample and one low positive sample. The acceptance criterion was recovery within 100 ±10% of reference. No significant interference was observed for the substances at the concentrations listed in the table below, except for Itraconazole and Ritonavir which showed interference above indicated concentrations.

Table 6. Exogenous Interfering Substances and Concentrations with NO Interference in assay performance

Substance	**Concentrations Tested**
Acetylcysteine	150 mg/L
Acetylsalicylic acid	30 mg/L
Ampicillin	75 mg/L
Ascorbic acid	52.5 mg/L
Cefoxitin	750 mg/L
Doxycycline	18 mg/L
Heparin	3300 IU/L
Levodopa	7.5 mg/L
Methyldopa	22.5 mg/L
Metronidazole	123 mg/L
Rifampicin	48 mg/L
Acetaminophen	156 mg/L
Cyclosporine	1.8 mg/L
Ibuprofen	219 mg/L
Theophylline	60 mg/L
Phenylbutazone	321 mg/L
Itraconazole	15 mg/L
Special Drugs Tested:	
Zanamivir	0.006 mg/mL
Oseltamivir	0.090 mg/mL
Ceftriaxone	2.40 mg/mL
Levofloxacin	0.300 mg/mL
Meropenem	3.60 mg/mL
Ribavirin	0.720 mg/mL
Azithromycin	0.300 mg/mL
Lopinavir	0.720 mg/mL
α-interferon 2b	3000 IU/mL

Peramivir	0.360 mg/mL
Tobramycin	0.360 mg/mL
Histamine Dihydrochloride	0.0006 mg/mL
Tocilizumab	0.384 mg/mL
α-interferon 2a	43200 IU/mL
Hydroxychloroquinsulfate	0.240 mg/mL
Remdesivir	0.120 mg/mL
Ritonavir	0.160 mg/mL

4. Assay Reportable Range:

The Elecsys Anti-SARS-CoV-2 S assay has the following ranges:

- AMI (Analytical Measuring Interval): 0.40 to 250 BAU/mL
- EMI (Extended Measuring Interval): 250 to 100,000 BAU/mL
- Reportable Interval: 0.40 to 100,000 BAU/mL

The analytical measuring interval was validated through comprehensive studies including establishing the limit of quantitation, and demonstrating precision, linearity using clinical samples, and accuracy studies using certified reference material traceable to the First International Standard for anti-SARS-CoV-2 immunoglobulin (NIBSC code: 20/136).

The assay's EMI (Extended measuring interval) is 250-100,000 BAU/mL based on automated dilutions (1:30 initial, 1:400 for high samples).

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

Calibrator Traceability:

The Elecsys Anti-SARS-CoV-2 S assay was standardized against the First International Standard Material for anti-SARS-CoV-2 immunoglobulin (NIBSC 20/136) with results reported in BAU/mL units.

Specimen Stability:

Specimen stability was evaluated in serum and plasma matrices (K2-EDTA, lithium heparin and sodium citrate) using the Elecsys Anti-SARS-CoV-2 S assay on the **cobas e** 801 analyzer. Storage conditions tested included room temperature (15-25°C), refrigerated (2-8°C), frozen (≤-20°C), and freeze-thaw cycles.

Native negative samples and low positive samples prepared by spiking with specimens containing high-concentrations of anti-SARS-CoV-2 antibodies were used to achieve target concentrations across the analytical range. Percent difference to baseline was calculated for each storage condition.

Results support specimen stability for
- 14 days at 15-25°C and 2-8°C,
- 3 months at -20°C (±5°C),
- 3 freeze-thaw cycles

6. Detection Limit:

The limit of blank (LoB), limit of detection (LoD), and Lower Limit of Quantitation (LLoQ) for the
Elecsys Anti-SARS-CoV-2 S assay were evaluated using 3 lots of Elecsys Anti-SARS-CoV-2 S reagent packs on one **cobas e** 801 analyzer over three days.

Table 7. Elecsys Anti-SARS-CoV-2 S assay Detection Limits

Parameter	BAU/mL
LoB[a]	0.30
LoD[b]	0.35
LLoQ[c]	0.40

[a]The LoB represents the 95th percentile value from n ≥ 60 measurements of analyte-free samples over several independent series, defined as the concentration at which there is a 95% probability that a sample is analyte-free.

[b]The LoD represents the concentration at which there is a 95% probability that a sample contains analyte, determined based on the LoB and the standard deviation of low concentration samples using the formula: LoD = LoB + 1.645 × SD total.

[c]The LLoQ is defined as the lowest amount of analyte in a sample that can be accurately quantified with a maximum allowable total error of 20%, considering the CV of result precision and systematic bias to the First International Standard for anti-SARS-CoV-2 immunoglobulin (NIBSC code: 20/136). The The LLoQ has been determined using low concentration of anti-SARS-CoV-2 samples.

7. Assay Cut-Off:

The Elecsys Anti-SARS-CoV-2 S assay cutoff was established using 899 clinical samples: 727 pre-pandemic negative samples (collected before October 2019) and 172 positive samples collected from hospitalized patients with prior PCR-confirmed SARS-CoV-2 infection (collected 0-29 days post-PCR confirmation). Receiver Operating Characteristic (ROC) analysis was performed to determine the optimal assay cutoff value that maximized both sensitivity and specificity. The resulting ROC curve demonstrated high sensitivity and specificity for the Elecsys Anti-SARS-CoV-2 S assay at the established cutoff of 0.8 BAU/mL.

8. Hook Effect:

A study was performed to demonstrate that the Elecsys Anti-SARS-CoV-2 S assay is not susceptible to high dose hook effect, a phenomenon in which excessively high antibody levels form immune complexes that saturate the assay and produce false non-reactive results. Four plasma samples with high titer for the analyte (analyte concentrations between 1200 and 1500 BAU/mL) were each serially diluted with an anti-SARS-CoV-2 antibody negative plasma sample to generate a 12-member dilution series. Each dilution was tested in duplicate with one kit lot of the Elecsys Anti-SARS-CoV-2 S assay on the **cobas e** 801 analyzer. The results demonstrate the absence of high-dose hook effect for the Elecsys Anti-SARS-CoV-2 S assay across the tested concentration range.

9. Accuracy:

An analytical accuracy study was conducted to evaluate the recovery and linearity of the Elecsys Anti-SARS-CoV-2 S assay using the closest calibrator material to the certified reference material (CCRM) in Roche's metrological traceability calibration hierarchy.

The CCRM was serially diluted in anti-SARS-CoV-2 negative serum to create 10 dilution levels spanning 0.286 to 278 BAU/mL (covering the entire AMI from 5-20% below the lower limit of quantitation, the LLoQ, to 5-20% above the upper limit of quantitation, the ULoQ). The study was conducted using one reagent pack lot with two calibrator lots across two **cobas e** 801 analyzers, generating four reagent/calibrator/analyzer combinations. Each dilution level was tested with 6 replicates.

Table 8. Elecsys Anti-SARS-CoV-2 S Accuracy Study Summary

Combination	Recovery Range	Linearity Deviation Range	Slope	Pearson's r	R^2
1	96 – 100%	-4.9% to 6.2%	1.041	1.00	0.999
2	96 – 100%	-5.0% to 9.9%	1.049	1.00	1.00
3	96 – 100%	-5.0% to 6.1%	1.059	1.00	0.999
4	96 – 100%	-3.8% to 8.2%	1.061	1.00	0.999

The accuracy study confirms that the Elecsys Anti-SARS-CoV-2 S assay provides accurate quantitative results traceable to the First International Standard for anti-SARS-CoV-2 immunoglobulin (NIBSC code: 20/136) across the entire analytical measuring interval.

10. Carry-Over:

N/A

B Comparison Studies:

1. Method Comparison:

The clinical performance of the Elecsys Anti-SARS-CoV-2 S assay was evaluated at three testing sites using 614 unique specimens retrospectively collected from two populations. Population 1 consisted of 124 specimens collected from individuals with prior confirmed SARS-CoV-2 infection based on positive RT-PCR results using highly sensitive FDA-cleared or authorized assays. These specimens were collected in the United States between April 17, 2020, to August 27, 2020. Population 2 consisted of 490 specimens collected prior to January 18, 2020 (before the widespread outbreak of COVID-19 in the US).

Of the 124 specimens in Population 1, 1 specimen was collected 0–7 days from symptom onset, 5 specimens were collected 8–14 days from symptom onset, and 118 specimens were collected ≥15 days from symptom onset.

Both populations demonstrated diverse representation across age groups (21-79 years), sex distribution (population 1: 38.7% male, 61.3% female; population 2: 42.2% male, 57.8% female), and varied racial/ethnic backgrounds.

Table 9. Demographic Characteristics by Days Post Symptom Onset: Population 1 (n=124)

Characteristic	0-7 days (n=1)	8-14 days (n=5)	≥15 days (n=118)	Total (n=124)
Race, n (%)				
White	1 (100.0)	4 (80.0)	30 (25.42)	35 (28.23)
Black or African American	0 (0.0)	0 (0.0)	20 (16.95)	20 (16.13)
Asian	0 (0.0)	0 (0.0)	1 (0.85)	1 (0.81)
Other	0 (0.0)	0 (0.0)	2 (1.69)	2 (1.61)
Unknown	0 (0.0)	1 (20.0)	65 (55.08)	66 (53.23)
Ethnicity, n (%)				
Not Hispanic or Latino	0 (0.0)	0 (0.0)	13 (11.02)	13 (10.48)
Hispanic or Latino	1 (100.0)	5 (100.0)	82 (69.49)	88 (70.97)
Unknown	0 (0.0)	0 (0.0)	23 (19.49)	22 (18.55)
Sex, n (%)				
Male	1 (100.00)	2 (40.00)	45 (38.14)	48 (38.71)
Female	0 (0.00)	3 (60.00)	73 (61.86)	76 (61.29)
Age				
Mean (SD)	N/A	30.20 (12.52)	43.04 (11.74)	42.44 (11.97)
Median	N/A	27	43	42
Range	N/A	21-52	22-77	21-77
25th - 75th Percentile	N/A	23-28	35-50	32-50

Note: All samples were plasma matrix. SD = Standard Deviation; N/A = Not applicable for single observation.

Clinical performance was evaluated by comparing the Elecsys Anti-SARS-CoV-2 S assay results to a composite comparator method comprising three SARS-CoV-2 serology assays. SARS-CoV-2 seropositivity was determined using majority rule (≥2 out of 3 positive results) from the composite comparator. Positive percent agreement (PPA) and negative percent agreement (NPA) with respective 95% confidence intervals were calculated.

The following tables present the PPA and NPA of the Elecsys Anti-SARS-CoV-2 S assay compared to the composite comparator method.

Table 10. Performance of Elecsys Anti-SARS-CoV-2 S - Population 1

Days Post Symptom Onset	Elecsys Anti-SARS-CoV-2 S	Composite Comparator		PPA [%] (95% CI)	NPA [%] (95% CI)
		Reactive	Non-Reactive		
0-7 days	Reactive	0	0	-	**100.00%** (1/1) (20.65% - 100.00%)
	Non-Reactive	0	1		
	Total	0	1		
8-14 days	Reactive	3	1	**100.00%** (3/3) (43.85% - 100.00%)	**50.00%** (1/2) (9.45% - 90.55%)
	Non-Reactive	0	1		
	Total	3	2		
≥15 days	Reactive	116	0	**100.00%** (116/116) (96.79% - 100.00%)	**100.00%** (2/2) (34.24% - 100.00%)
	Non-Reactive	0	2		
	Total	116	2		

Table 11. Performance of Elecsys Anti-SARS-CoV-2 S - Population 2

	Elecsys Anti-SARS-CoV-2 S	Composite Comparator		PPA [%] (95% CI)	NPA [%] (95% CI)
		Reactive	Non-Reactive		
	Reactive	0	0	NA	**100.00%** (489/489) (99.25%–100.00%)
	Non-Reactive	1	489		
	Total	1	489		

Additional Clinical Performance Evaluation:
In addition to the studies above, the Negative Percent Agreement (NPA) was also evaluated in a separate study using 3,612 samples (Population 3) collected before October 2019 (and presumed negative for SARS-CoV-2 antibodies). One false positive sample was detected, resulting in an NPA of 99.97% (95% CI lower limit of 99.84%).

Table 12. Performance of Elecsys Anti-SARS-CoV-2 S - Population 3

Cohort	N	Non-Reactive	Reactive	NPA, % (95% CI)
Diagnostic Routine (Europe)	2528	2528	0	100.00% (99.85%–100.00%)
Blood donors (US)	1084	1083	1	99.91% (99.48%–99.98%)
Overall	**3612**	**3611**	**1**	99.97% (99.84%–100.00%)

2. Matrix Comparison:

Matrix comparison study was performed to verify the types of blood collection tubes that can be used with the Elecsys Anti-SARS-CoV-2 assay. Specimens were obtained in matched serum and plasma collection tubes. The number of donors varied slightly for each comparison: 70 donors for the K3-EDTA plasma comparison, 67 donors for the Sodium Citrate plasma comparison, and 66 donors for both the Lithium Heparin and K2-EDTA plasma comparisons. Serum was used as the control (reference) tube type. Data was analyzed using comparing concentrations of all matrices to serum. All blood collection tube types tested are acceptable for use with the Elecsys Anti-SARS-CoV-2 assay. Statistical evaluation data are summarized below.

Table 13. Elecsys Anti-SARS-CoV-2 S Matrix Equivalency Statistical Results Summary

Collection Tube	Slope (Passing-Bablok)	Correlation (Pearson r)	Bias at assay cutoff of 0.8 BAU/mL, Based on Passing-Bablok
Li-Heparin	0.988	0.999	-1.2
K2-EDTA	1.008	0.999	0.8
K3-EDTA	1.009	1.000	0.9
Na-Citrate	0.997	0.998	-0.3

Intercept (Constrained to Zero)

C Clinical Studies:

1. Clinical Sensitivity:

Not applicable.

2. Clinical Specificity:

Not applicable.

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Not applicable.

D Clinical Cut-Off:

Not applicable

E Expected Values/Reference Range:

Not applicable

F Other Supportive Instrument Performance Characteristics Data:

Not applicable

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.