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

I Background Information:

A 510(k) Number

K250768

B Applicant

Roche Diagnostics

C Proprietary and Established Names

Elecsys Anti-SARS-CoV-2

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
QVP	Class II	21 CFR 866.3983 - SARS-Cov-2 Serology Test	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:
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):
See Indications for Use below.

B Indication(s) for Use:

Elecsys Anti SARS CoV 2 is an immunoassay intended for the in vitro qualitative detection of total antibodies to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in human serum and Li-heparin, K2-EDTA and K3-EDTA plasma collected on or after 15 days post-

symptom onset. The test is intended as an aid in identifying individuals with an adaptive immune response to SARS-CoV-2, indicating recent or prior infection.

The electrochemiluminescence immunoassay "ECLIA" is intended for use on cobas e 601 immunoassay analyzer.

C Special Conditions for Use Statement(s):
Rx - For Prescription Use Only

D Special Instrument Requirements:
For use on **cobas e** 601 analyzer.

IV Device/System Characteristics:

A Device Description:

The Elecsys Anti-SARS-CoV-2 is an automated two-step sandwich immunoassay with streptavidin microparticles, biotinylated recombinant SARS-CoV-2-specific antigen labeled with a ruthenium complex and 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. The test system contains the human serum-based calibrators intended for use with the system.

Reagents and calibrators are packaged together in the Elecsys Anti-SARS-Cov-2 assay kit, while the associated PreciControl is packaged separately.

The following reagents are provided in the Elecsys Anti-SARS-CoV-2 reagent rackpack (ACOV2):

- M: Streptavidin-coated microparticles.
- R1: SARS-CoV-2-Ag~biotin: Biotinylated SARS-CoV-2-specific antigen.
- R2: SARS-CoV-2 Ag~Ru(bpy): SARS-CoV-2-specific recombinant antigen labeled with ruthenium complex.
- ACOV2 Cal1: Negative calibrator (Human serum, non-reactive for anti-SARS-CoV-2 antibodies).
- ACOV2 Cal2: Positive calibrator (Human serum, reactive for anti-SARS-CoV-2 antibodies).

The following required materials are provided separately:

- PC ACOV2 1: PreciControl 1 Anti-SARS-CoV-2 - Negative control. (Human serum, non-reactive for anti-SARS-CoV-2 antibodies)
- PC ACOV2 2: PreciControl 2 Anti-SARS-CoV-2 – reactive control. (Human serum, reactive for anti-SARS-CoV-2 antibodies)

B Principle of Operation:

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

- 1st incubation: 20 µL of sample, 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 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 ($Ru(bpy)_3^{2+}$)

Results are 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

C Instrument Description Information:

1. Instrument Name:
   cobas e 601 analyzer.

2. Specimen Identification:

   The Elecsys Anti-SARS-CoV-2 is intended to be used with following specimen types: Serum and Li-heparin, K_2-EDTA and K_3-EDTA plasma.

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):	Candidate Device K250768	Predicate Device DEN210040
Device Trade Name	Elecsys Anti-SARS-CoV-2	VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Reagent Pack, VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Calibrator
General Device Characteristic Similarities		
Intended Use/ Indications For Use	Elecsys Anti SARS CoV 2 is an immunoassay intended for	The VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total

	the in vitro qualitative detection of total antibodies to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in human serum and Li heparin, K2 EDTA and K3 EDTA plasma collected on or after 15 days post-symptom onset. The test is intended as an aid in identifying individuals with an adaptive immune response to SARS CoV 2, indicating recent or prior infection. The electrochemiluminescence immunoassay "ECLIA" is intended for use on **cobas e** 601 immunoassay analyzer.	Reagent Pack when used in combination with the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total 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 VITROS 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. For use in the calibration of the VITROS ECi/ECiQ/3600 Immunodiagnostic Systems and the VITROS 5600/XT 7600 Integrated Systems for the in vitro qualitative detection of total antibodies to SARS-CoV-2 in human serum and plasma.
Analyte	Same	Total anti-SARS-CoV-2 antibodies
Regulation	Same	21 CFR 866.3983
Classification	Same	Class II Special Controls
Product Code	Same	QVP
Technology	ECLIA	CLIA
Instrument	Same	Fully automated analyzer
Test Type	Same	Qualitative
Sample Type/Matrix	Same	Serum, Li-Heparin, K2-EDTA, K3-EDTA
Calibrators	Same	Yes. Two levels
External Controls	Same	Yes. Two levels
Streptavidin/Biotin Technology	Same	Yes
General Device Characteristic Differences		
Antigen	Nucleocapsid	Spike S1
Interpretation of results	COI < 1.0: Non-reactive COI ≥ 1.0: Reactive	S/C < 1.0: Non-reactive S/C ≥ 1.0: Reactive

VI Standards/Guidance Documents Referenced:

- Class II special controls for SARS-CoV-2 serology tests.

- CLSI EP05-A3 *Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition.*
- CLSI EP12-A2 *User Protocol for Evaluation of Qualitative Test Performance; Approved Guideline- Second Edition.*
- CLSI EP07 *Interference Testing in Clinical Chemistry.*

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

1) Within Laboratory Precision

Within laboratory precision was determined on **cobas e** 601 analyzer using one Elecsys Anti-SARS-CoV-2 kit lot with two runs per day for 21 non-consecutive days and two aliquots per sample in single determination with calibration performed per the IFU. Eight samples and two PreciControls were tested.

Table 1. Results of precision study on **cobas e** 601 analyzer.

Sample	Mean COI	N	Repeatability		Between-Run		Between-Day		Within-Laboratory	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
Sample1	4.90	84	0.084	1.7	0.045	0.9	0.216	4.4	0.236	4.8
Sample2	0.063	84	0.002	2.5	0.0008	1.3	0.002	3.8	0.003	4.7
Sample3	0.869	84	0.014	1.6	0.017	2.0	0.035	4.0	0.042	4.8
Sample4	20.8	84	0.388	1.9	0.153	0.7	1.09	5.3	1.17	5.6
Sample5	1.14	84	0.020	1.7	0.021	1.9	0.049	4.3	0.057	5.0
Sample6	0.910	84	0.020	2.2	0.010	1.0	0.052	5.7	0.057	6.2
Sample7	0.063	84	0.002	2.7	0.0007	1.2	0.003	4.2	0.003	5.1
Sample8	0.977	84	0.015	1.5	0.015	1.6	0.053	5.5	0.058	5.9
Control 1	0.076	84	0.002	2.4	0.0000	0.0	0.003	4.1	0.004	4.8
Control 2	2.53	84	0.028	1.1	0.041	1.6	0.140	5.5	0.149	5.9

2) Reproducibility

Reproducibility was assessed on the **cobas e** 601 analyzer. Three lots of Elecsys Anti-SARS-CoV-2 and PreciControl Anti-SARS-CoV-2 were tested at three test sites, with all three lots tested at each site (two external U.S. sites and one internal ex-U.S. site). Samples and controls were tested in triplicate in two runs per day for five days. Results are shown in **Table 2**.

Table 2. Results of reproducibility study.

			Repeatability		Between-Run		Between-Day		Between-Lot		Between-Site		Reproducibility	
Sample	**Mean COI**	**N**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
PC ACOV2 1	0.10	270	0.00	3.52	0.00	0.68	0.00	1.90	0.00	1.76	0.01	5.02	0.01	6.69
PC ACOV2 2	2.79	270	0.04	1.38	0.02	0.64	0.03	1.06	0.04	1.32	0.01	0.33	0.06	2.30
HSP 03	0.09	270	0.00	3.67	0.00	1.83	0.00	1.92	0.00	2.19	0.00	5.66	0.01	7.57
HSP 04	0.52	270	0.01	1.27	0.00	0.49	0.01	1.34	0.02	3.09	0.00	0.55	0.02	3.67
HSP 05	2.53	270	0.04	1.44	0.01	0.54	0.03	1.29	0.05	1.99	0.04	1.38	0.08	3.14
HSP 06	7.39	270	0.11	1.44	0.03	0.37	0.09	1.17	0.29	3.88	0.12	1.63	0.34	4.61

2. Linearity:

   Not applicable since this is not a quantitative assay.

3. Analytical Specificity/Interference:

   1) Cross-Reactivity

   A study was conducted to evaluate the Elecsys Anti-SARS-CoV-2 assay for potential cross-reactivity. The study was performed by testing 1836 samples collected before December 2019 from individuals with antibodies to other microorganisms or autoimmune disorders.

   The comparison data to the comparator assay are presented in **Table 3**.

Table 3. Potential cross-reactivity – summary of the results.

Potential cross-reactants	**N of Samples Tested**	**Elecsys Anti SARS CoV 2 Results**	
		NR[a)]	**RX[b)]**
Common cold panel[c)]	40	40	0
Coronavirus panel[d)]	40	40	0
CMV (Cytomegalovirus) Antibodies	116	115	1
EBV (Epstein-Barr virus) Antibodies	105	103	2
Borrelia burgdorferi Antibodies	6	6	0
Chlamydia pneumoniae Antibodies	8	8	0
E. coli (anti-E. coli-reactive)	10	10	0
Neisseria gonorrhoeae infection	5	5	0
HAV (Hepatitis A virus) Antibodies	40	40	0
HBV (Hepatitis B virus) Antibodies	71	71	0
HCV (Hepatitis C virus) Antibodies	66	66	0

HEV (Hepatitis E virus) Antibodies	12	12	0
HIV (Human immunodeficiency virus) Antibodies	10	10	0
HSV-1 and HSV-2 (Herpes Simplex virus) Antibodies	24	24	0
HTLV (Human T-lymphotropic virus) Antibodies	6	6	0
Influenza vaccinees	25	25	0
Listeria Antibodies	6	6	0
Measles Antibodies	10	10	0
Mumps Antibodies	14	14	0
Parvovirus B19 Antibodies	30	30	0
Plasmodium falciparum (Malaria) Antibodies	8	8	0
Rubella Antibodies	12	12	0
Toxoplasma gondii Antibodies	8	8	0
Treponema pallidum (Syphilis) Antibodies	62	62	0
VZV (Varicella Zoster) Antibodies	30	30	0
AMA (anti-mitochondrial antibodies)	30	30	0
ANA (anti-nuclear antibodies)	26	26	0
SLE (systemic lupus erythematosus)	10	9	1
RA (rheumatoid arthritis)	10	10	0
Parainfluenza 1-3 IgG	31	31	0
Haemophilus influenzae B IgG	40	40	0
Candida albicans IgG	13	13	0
MERS-CoV Glycoprotein (S1) IgG	7	5	2
Enterovirus Antibodies	38	38	0
RSV (Respiratory syncytial virus) IgG	66	66	0
Bordetella pertussis IgG	34	34	0
Coronavirus HKU1 Antibodies	44	44	0
Coronavirus OC43 Antibodies	54	54	0
Coronavirus 229E Antibodies	57	57	0
Coronavirus NL63 Antibodies	44	44	0
EBV Nuclear Antigen (EBNA)	38	38	0
Mycoplasma pneumoniae IgG	54	54	0
C. pneumoniae IgG	47	47	0
C. trachomatis IgG	6	6	0
Influenza B Virus Antibodies	70	70	0

Influenza A Virus Antibodies	59	59	0
Dengue IgG	14	14	0
Parainfluenza 1-4 IgG	51	51	0
Adenovirus IgG	25	25	0
M. pneumoniae IgM	12	12	0
Legionella Antibodies	7	7	0
B. pertussis IgM	15	15	0
C. pneumoniae IgM	7	7	0
H. influenzae IgG	49	49	0
Metapneumovirus (MPV) IgG	15	15	0
M. tuberculosis IgG	15	15	0
Pneumocystis jirovecii IgG	15	15	0
Pseudomonas aeruginosa IgG	14	14	0
Staphylococcus epidermidis IgG	15	15	0
Streptococcus pneumoniae IgG	15	14	1
Streptococcus pyogenes IgG	15	14	1
SARS-CoV-1 IgG	10	10	0
Total	1836		

a) NR = non-reactive

b) RX = reactive

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

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

2) Interference

The Elecsys Anti-SARS-CoV-2 assay was evaluated for potential interference of biotin, endogenous and exogenous (drugs) substances using anti-SARS-CoV-2 nonreactive and low and moderate reactive samples. The testing was performed on the **cobas e** 601 immunoassay analyzer, and the recovery for each sample was calculated by comparison to the reference (unspiked), with an acceptance criteria of sample recovery of ± 0.2 COI for samples <1.0 COI, and 80-120% recovery of samples ≥1.0 COI.

a. Biotin

The Elecsys Anti-SARS-CoV-2 assay shows biotin tolerance of ≤1,200 ng/mL.

b. Potential Endogenous Interfering Agents

The potential interferent effect of elevated levels of endogenous substances was evaluated on the Elecsys Anti-SARS-CoV-2 assay using dilution series with 10

dilution steps for all substances with the exception of ANA, where a high ANA concentration was tested without titration. No interference was observed for the following potential endogenous substances at the following concentrations:

- Bilirubin: ≤66.0 mg/dL
- Hemoglobin: ≤1000 mg/dL
- Intralipid: ≤2000 mg/dL
- Rheumatoid Factors: ≤1200 IU/mL
- Human IgA: ≤1.6 g/dL
- Human IgG: ≤7 g/dL
- Human IgM: ≤1g/dL
- Cholesterol: ≤400 mg/dL
- Triglycerides: ≤2000 mg/dL
- ANA: ≤1:1280

c. Exogenous Interference

The potential interferent effect of exogenous substances (17 common drugs and 18 special drugs) was evaluated on Elecsys Anti-SARS-CoV-2 assay. No interference was observed with the following exogenous substances at the indicated concentrations:

Table 4. Exogenous substances and concentrations.

Substance	Test Concentration	Substance	Test Concentration
Acetaminophen	156 mg/L	Itraconazole	30 mg/L
Acetylcysteine	150 mg/L	Levodopa	7.5 mg/L
Acetylsalicylic acid	30 mg/L	Levofloxacin	0.300 mg/mL
Actemra (Tocilizumab)	0.384 mg/mL	Lopinavir	0.480 mg/mL
Ampicillin -Na	75 mg/L	Meropenem	3.60 mg/mL
Arbidol	0.120 mg/mL	Methyldopa	22.5 mg/L
Ascorbic acid	52.5 mg/L	Metronidazole	123 mg/L
Azithromycin	0.300 mg/mL	Oseltamivir	0.090 mg/mL
Cefoxitin	750 mg/L	Peramivir	0.360 mg/mL
Ceftriaxone	2.40 mg/mL	Phenylbutazone	321 mg/L
Cyclosporine	1.8 mg/L	Remdesivir	0.120 mg/mL
Doxycycline	18.0 mg/L	Ribavirin	0.750 mg/mL
Fexofenadine	0.108 mg/mL	Rifampicin	48 mg/L
Heparin	3300 IU/L	Ritonavir	0.240 mg/mL
Hydroxychloroquine	0.480 mg/mL	Theophylline	60 mg/L
Ibuprofen	219 mg/L	Tobramycin	0.360 mg/mL
Interferon alpha-2a	21600 IU/mL	Zanamivir	0.006 mg/mL
Interferon alpha-2b	3000 IU/mL		

4. Stability:

Kit Real-Time Stability Studies

Several studies were conducted to support the storage conditions recommended for the different components of the Elecsys Anti-SARS-CoV-2 assay. The data support the following storage conditions for the Elecsys Anti-SARS-CoV-2 assay:

Stability Study	Claims
Reagent unopened shelf-life	Up to the stated expiration date at 2-8°C
Open reagent on-board	Up to 28 days
Reagent after opening (stored off-board)	30 days at 2-8°C
Calibrator unopened shelf-life	Up to the stated expiration date at 2-8°C
Calibrator after opening (stored off-board)	30 days at 2-8°C
Controls unopened shelf-life	Up to the stated expiration date at 2-8°C
Open controls on-board	Up to 10 hours
Open controls stored off-board	28 days at 2-8°C
Calibration frequency (same reagent lot)	Every 25 days
Calibration frequency (same reagent pack)	Every 7 days

Specimen Stability

The stability of specimens stored under different conditions was evaluated by testing a panel of natural and contrived samples (including serum, K2-EDTA and Lithium Heparin plasma on the Elecsys Anti-SARS-CoV-2 assay. The data support the following specimen storage conditions: 28 days frozen (-20°C), 14 days refrigerated (2 to 8°C), 7 days at room temperature (15 to 25°C) and up to 3 freeze/thaw cycles.

5. Analytical Sensitivity at the Cutoff:

The analytical sensitivity of the Elecsys Anti-SARS-CoV-2 at the cutoff was determined using serial dilutions of the First International Standard (IS) for Anti-SARS-CoV-2 Immunoglobulin (Human), code 20/136 (certified reference material, or CRM) to generate a total of 13 dilution steps using human negative serum. Samples included in the study were prepared covering a 0.125 BAU/mL to 10 BAU/mL range (**Table 5**). The study was conducted on the **cobas e** 601 analyzer. Each dilution was tested in duplicates using one lot of kit reagents.

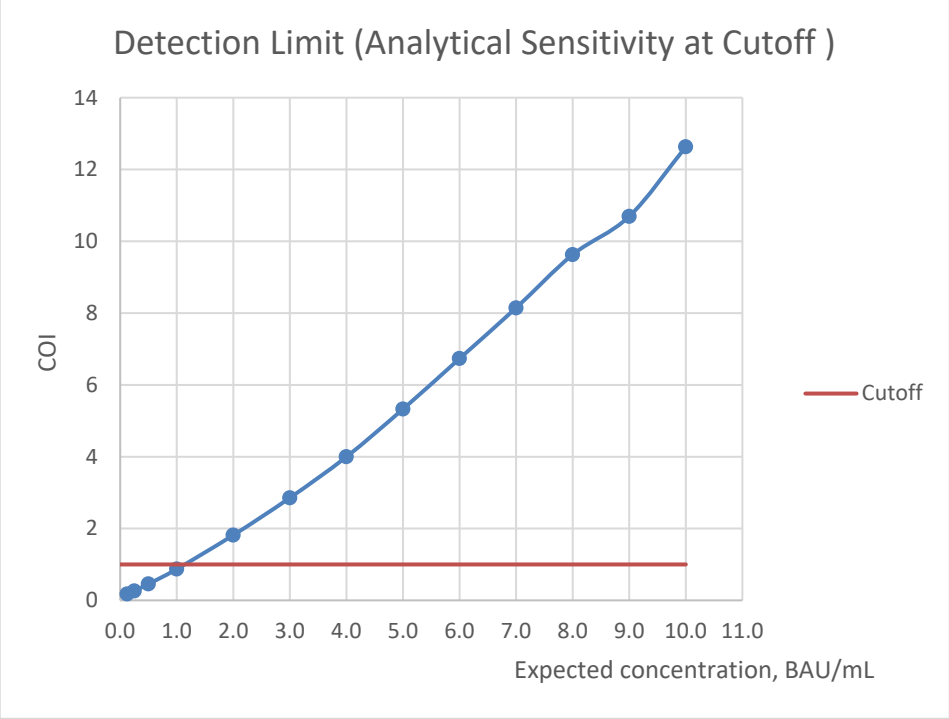
The COI values were collected for each dilution step and compared to the expected BAU/mL values. The data was analyzed using the least-squares regression analysis. The graph with the X-axis representing the corresponding BAU/mL values and the Y-axis the COI values for each sample is shown in **Figure 1**. The BAU/mL value at the assay cutoff (COI = 1.00) was calculated using the regression equation. The data analysis shows that a COI of 1.00 corresponds to 1.137 BAU/mL using the Elecsys Anti-SARS-CoV-2 assay.

Table 5. CRM serial dilutions COI results and calculation of BAU/mL at the cutoff.

Dilution Step	Expected CRM Concentration [BAU/mL]	Replicate 1 [COI]	Replicate 2 [COI]	Mean [COI]
1	0.125	0.175	0.175	0.175
2	0.25	0.263	0.264	0.263
3	0.50	0.462	0.451	0.457
4	1.00	0.865	0.876	0.870
5	2.00	1.81	1.83	1.82
6	3.00	2.84	2.87	2.86

7	4.00	4.04	3.95	4.00
8	5.00	5.36	5.29	5.33
9	6.00	6.73	6.74	6.73
10	7.00	8.21	8.08	8.15
11	8.00	9.61	9.65	9.63
12	9.00	10.7	10.7	10.7
13	10.0	12.7	12.6	12.6

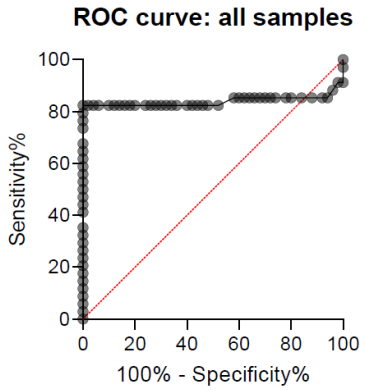
Figure 1. Analytical sensitivity regression analysis.



6. Assay Cut-Off:

A study was performed to determine the Elecsys Anti-SARS-CoV-2 assay cutoff. The study included testing clinical human anti-SARS-CoV-2 negative samples collected prior to the COVID-19 pandemic and positive samples collected from individuals with a prior SARS-COV-2 RT-PCR positive result. All samples were tested in singlicate using one Elecsys Anti-SARS-CoV-2 kit lot. A Receiver Operating Characteristic (ROC) curve analysis was performed to optimize for those cutoff values that maximize both sensitivity and specificity. At the cutoff COI = 1 .00 the resultant ROC curve was confirming high sensitivity and specificity of the established COI cutoff value (**Figure 2**).

Figure 2. ROC analysis for all negative and positive samples tested.



7. Carry-Over:

No sample carryover was observed.

8. High-Dose Hook Effect

A study was performed to demonstrate that Elecsys Anti-SARS-CoV-2 assay is not sensitive to high dose hook effect, i.e. that high levels of antibodies do not form immune complexes leading to saturation and an increased risk of false non-reactive results.

Three high titer samples positive for anti-SARS-CoV-2 antibodies were serially diluted in an anti-SARS-CoV-2 antibody negative sample in a minimum of 20 dilution steps to generate a dilution series that covered the range from high positive to negative. All dilution preparations were tested in single determination on the **cobas e** 601 immunoassay analyzer. The acceptance criterion was no false negative results for the tested samples. Results are summarized in the **Table 6** below:

Table 6. Results of Hook Effect study for Elecsys Anti-SARS-CoV-2.

Sample 1			**Sample 2**			**Sample 3**		
Dilution Factor	Counts	COI	Dilution Factor	Counts	COI	Dilution Factor	Counts	COI
1.00	507448	101	1.00	555788	111	1.00	340886	68.1
1.11	487458	97.4	1.11	559951	112	1.11	319147	63.7
1.18	474133	94.7	1.18	563371	113	1.25	293311	58.6
1.25	450392	90.0	1.25	553930	111	1.43	264014	52.7
1.33	432743	86.4	1.33	555684	111	1.67	233048	46.5
1.43	406705	81.2	1.43	558584	112	2.00	195967	39.1
1.54	389352	77.8	1.54	557886	111	2.50	152976	30.5
1.67	363506	72.6	1.67	553872	111	3.33	109668	21.9
1.82	337039	67.3	1.82	547028	109	4.00	88403	17.6

	2.00	312396	62.4	2.00	546050	109	5.00	67048	13.3
	2.22	282193	56.3	2.22	535011	107	6.67	44398	8.82
	2.50	252781	50.5	2.50	519659	104	10.0	24376	4.82
	2.86	217805	43.5	2.86	503993	101	12.5	17764	3.50
	3.33	185335	37.0	3.33	475165	94.9	16.7	11550	2.26
	4.00	149314	29.8	4.00	435392	87.0	25.0	6618	1.27
	5.00	115406	23.0	5.00	382692	76.4	50.0	2778	0.507
	6.67	78116	15.6	6.67	304276	60.8	n.a	613	< 1.0
	10.0	45274	9.00	10.0	203876	40.7			
	20.0	28727	5.69	20.0	92521	18.4			
	n.a	602	< 1.0	n.a	618	< 1.0			

The data demonstrate the absence of high-dose hook effect in the dilution range presented in the study for the Elecsys Anti-SARS-CoV-2 assay.

B Comparison Studies:

1. Method Comparison with Predicate Device

   See Section C. Clinical Studies.

2. Matrix Comparison

   Studies were conducted to verify the types of blood collection tubes that can be used with the Elecsys Anti-SARS-CoV-2 assay. Samples were collected into matched serum and plasma collection tubes from 60 donors and assayed in singlicate on the **cobas e** 601 immunoassay analyzer. Sixty matched pairs were collected in the evaluation of each of the following blood collection tubes:

   - dipotassium EDTA
   - tripotassium EDTA
   - lithium heparin

   Statistical evaluations were performed to analyze the COI data for overall bias using orthogonal linear regression, which will reveal any relevant overall proportional bias (see **Table 7**).

   Table 7. Results of matrix comparison study.

Specimen type	Slope (95% CI)	Intercept (95% CI)	Correlation Coefficient (R)
Dipotassium EDTA plasma	1.002 (0.989 ; 1.015)	-0.056 (-0.126 ; 0.014)	1.000
Tripotassium EDTA plasma	0.988 (0.961 ; 1.016)	-0.088 (-0.235 ; 0.060)	1.000
Lithium heparin plasma	0.995 (0.982 ; 1.008)	0.017 (-0.055 ; 0.090)	0.999

C Clinical Studies:

The clinical performance of the Elecsys Anti-SARS-CoV-2 assay was established using data from a traditional clinical study and real-world data.

Traditional clinical study

The purpose of this study was to evaluate the clinical performance of the Elecsys Anti-SARS-CoV-2 assay on the **cobas e** 601 analyzer. The clinical performance of the Elecsys Anti-SARS-CoV-2 was evaluated testing clinicals samples from the following populations, as indicated below:

(a) Nine thousand and seven (9,007) presumed anti-SARS-CoV-2 negative samples collected prior to the COVID-19 pandemic (6,305 from Germany and 2,702 samples were from blood donors in the US.

(b) Three hundred and three archived clinical samples collected from individuals confirmed to have a prior SARS-CoV-2 positive result by RT-PCR were tested. These individuals were non-immunocompromised, non-vaccinated, US-enrolled, with COVID-19 symptoms onset information, and prior RT PCR positive test result.

Demographic information from the 303 individuals with prior confirmed COVID-19 is provided in **Table 8**:

Table 8. Demographic information for subjects enrolled with prior COVID-19.

Days post symptom onset (DPSO)	White N (%)	Black or African American N (%)	Asian N (%)	American Indian or Alaska Native N (%)	Other N (%)	Unknown N (%)	Total N (%)
8-14	14 (93.33)	1 (6.67)	0 (0)	0 (0)	0 (0)	0 (0)	15 (4.95)
>15	199 (69.10)	29 (10.07)	9 (3.13)	2 (0.69)	17 (5.90)	32 (11.11)	288 (95.05)
Total	213 (70.3)	30 (9.90)	9 (2.97)	2 (0.66)	17 (5.61)	32 (10.56)	303 (100.0)

Negative percent agreement (NPA)

To establish the NPA of the assay, a total of 9007 pre-pandemic specimens were tested with the Elecsys Anti-SARS-CoV-2 assay. All specimens were presumed negative because they were obtained before December 2019; 2702 specimens were collected in the United States and 6305 specimens were collected in Germany. Out of 9007 specimens, 17 false positive results were observed, resulting in an NPA of 99.81% (**Table 9**). The lower limit of the 95% confidence interval was 99.70 %.

Table 9. NPA of Elecsys Anti-SARS-CoV-2.

Number of Specimens Tested (obtained prior to the COVID-19 pandemic)	Negative	NPA	95 % Confidence Interval (%) (Wilson Score)
9007	8990	99.81	(99.70 - 99.88 %)

Positive percent agreement (PPA)

The clinical performance of Elecsys Anti-SARS-CoV-2 was evaluated in a clinical study in which results were obtained under routine laboratory conditions and compared to the results of a composite comparator method comprised of three SARS-CoV-2 serology assays. SARS-CoV-2 seropositivity of the specimens evaluated was determined by the composite comparator method by majority rule (≥ 2 out of 3) of the three Anti-SARS-CoV-2 serology assays (the predicate and two Emergency Use Authorized (EUA) Anti-SARS-CoV-2 serology assays). Performance of Elecsys Anti-SARS-CoV-2 relative to the composite comparator was established using specimens collected from individuals with a history of SARS-CoV-2 infection confirmed by a prior SARS CoV-2 positive FDA authorized RT PCR test and calculated and reported as PPA.

Serum and plasma samples were tested at two clinical laboratories on the **cobas e** 601 analyzer. Due to clinical relevance, the performance of the Elecsys Anti-SARS-CoV-2 immunoassay was determined by the results from samples collected ≥ 15 days post symptom onset (DPSO) and excluded immunocompromised subjects.

A total of unique 303 specimens (157 serum and 146 plasma) were tested on the Elecsys Anti-SARS-CoV-2 assay and the composite comparator method. Blood samples were collected within the United States between April and December of 2020. Of these, 15 were collected between 8 and 14 DPSO and 288 were collected at or after 15 DPSO; no specimens were collected between 0 and 8 DPSO). PPA and NPA with corresponding Wilson score 95% confidence intervals were calculated and are summarized in **Table 10** below.

Table 10. PPA of Elecsys Anti-SARS-CoV-2.

			Composite Comparator Results		PPA (n/N) (95% CI)	NPA (n/N) (95% CI)
DPSO*			**Positive**	**Negative**		
8 – 14	**Elecsys Anti-SARS-CoV-2**	**Positive**	7	0	**53.85%** (7/13) (29.14% - 76.79%)	**100.00%** (2/2) (34.24% - 100.00%)
		Negative	6	2		
		Total	**13**	**2**		
≥15	**Elecsys Anti-SARS-CoV-2**	**Positive**	251	1	**98.82%** (251/254) (96.59% - 99.60%)	**97.06%** (33/34) (85.08% - 99.48%)
		Negative	3	33		
		Total	**254**	**34**		

*DPSO: Days post symtoms onset

PPA Estimation Using Real-World Data (RWD)

In addition, the clinical performance of the Elecsys Anti-SARS-CoV-2 was assessed using real-world data with SARS-CoV-2 RT-PCR result information as the comparator. The samples from the RWD set were collected during routine clinical practice at a collaborating institution in the United States from March 2020 to March 2021, when the original B.1 lineage of the Wuhan-Hu-1 strain was the prevalent strain.

Testing data (results from the Elecsys Anti-SARS-CoV-2 and SARS-CoV-2 PCR tests) were collected directly from the laboratory information system (LIS), whereas patient demographics and clinical variables were manually extracted through medical chart review. The PPA was calculated as the percentage of positive serology test results among evaluable samples.

An initial cohort of 1178 subjects who tested positive on an FDA authorized SARS-CoV-2 RT-PCR test and were also tested with the Elecsys Anti-SARS-CoV-2 assay during the specified period were identified. Out of 1178 subjects, 611 were excluded based on pre-specified criteria (e.g., with incomplete information such as having no reported date of symptom onset, having no serology test result on or after symptom onset, or potentially having received a COVID-19 vaccination), and remaining 567 eligible subjects were included in the final cohort.

Out of these 567 subjects, 376 samples were collected from non-immunocompromised, non-vaccinated subjects with a positive SARS-CoV-2 RT-PCR test (within 7 days before or 14 days after symptom onset) and having serology samples collected at least 15 days after symptom onset (N = 285 samples). As presented in **Table 11**, the PPA in this population was 96.49 % (95 % CI:93.66, 98.08 %).

Table 11: PPA based on RWD.

Days Post Symptom Onset	Number of Samples Tested (with positive RT-PCR result) (N)	Elecsys Anti-SARS-CoV-2 Results		
		Reactive (n)	Positive Percent Agreement (%) (n/N)	95 % Confidence Interval Wilson Score (%)
0-7 days	64	34	53.13 (34/64)	41.07-64.82
8-14 days	27	18	66.67 (18/27)	47.82-81.36
≥ 15 days	285	275	96.49 (275/285)	93.66-98.08
Total	376			

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.