Elecsys IL-6

cobas®

REF		Σ	SYSTEM
05109442190	05109442501	100	**cobas e** 411 **cobas e** 601 **cobas e** 602
07027532190	07027532501	100	**cobas e** 801

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

For use in the USA only

System information

For **cobas e** 411 analyzer: test number 590
For **cobas e** 601 and **cobas e** 602 analyzers: Application Code Number 203
For **cobas e** 801 analyzer: Application Code Number 10085

Warning

- This test has not been FDA cleared or approved;
- This test has been authorized by FDA under an EUA for use by authorized laboratories;
- This test has been authorized only to assist in identifying severe inflammatory response, when used as an aid in determining the risk of intubation with mechanical ventilation in confirmed COVID-19 patients; and
- This test is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of medical devices under Section 564(b)(1) of the Act, 21 U.S.C § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

Intended use

Elecsys IL-6 immunoassay is an in vitro diagnostic test for the quantitative determination of IL-6 (interleukin-6) in human serum and plasma. This assay is used to assist in identifying severe inflammatory response in patients with confirmed COVID-19 illness to aid in determining the risk of intubation with mechanical ventilation, in conjunction with clinical findings and the results of other laboratory testing.
The Elecsys IL-6 immunoassay is an **e**lectro**c**hemi**l**uminescence **i**mmuno**a**ssay “ECLIA” and is intended for use on **cobas e** immunoassay analyzers.
The Elecsys IL-6 immunoassay is only for use under the Food and Drug Administration’s Emergency Use Authorization. For use by health care providers. For prescription use only. For in vitro diagnostic use only. Testing is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform moderate complexity tests.

Test principle

Sandwich principle. Total duration of assay: 18 minutes.

- 1st incubation: 30 µL of sample (**cobas e** 411, **cobas e** 601, and **cobas e** 602 analyzers) or 18 µL of sample (**cobas e** 801 analyzer) are incubated with a biotinylated monoclonal IL-6-specific antibody.

- 2nd incubation: After addition of a monoclonal IL-6-specific antibody labeled with a ruthenium complex[a)] and streptavidin-coated microparticles, the antibodies form a sandwich complex with the antigen of the sample.
- The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with ProCell/ProCell M/ProCell II M. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier.
- Results are determined via a calibration curve which is instrument-specifically generated by 2-point calibration and a master curve provided via the reagent barcode or e-barcode.

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

Reagents - working solutions

cobas e 411, **cobas e** 601, and **cobas e** 602 analyzers:
The reagent rackpack is labeled as IL6.

M Streptavidin-coated microparticles (transparent cap), 1 bottle, 6.5 mL:
Streptavidin-coated microparticles 0.72 mg/mL; preservative.

R1 Anti-IL-6-Ab~biotin (gray cap), 1 bottle, 9 mL:
Biotinylated monoclonal anti-IL-6 antibody (mouse) 0.9 µg/mL; phosphate buffer 95 mmol/L, pH 7.3; preservative.

R2 Anti-IL-6-Ab~$Ru(bpy)_3^{2+}$ (black cap), 1 bottle, 9 mL:
Monoclonal anti-IL-6 antibody (mouse) labeled with ruthenium complex 1.5 µg/mL; phosphate buffer 95 mmol/L, pH 7.3; preservative.

cobas e 801 analyzer:
The **cobas e** pack is labeled as IL6.

M Streptavidin-coated microparticles, 1 bottle, 5.8 mL:
Streptavidin-coated microparticles 0.72 mg/mL; preservative.

R1 Anti-IL-6-Ab~biotin, 1 bottle, 9.9 mL:
Biotinylated monoclonal anti-IL-6 antibody (mouse) 0.9 µg/mL; phosphate buffer 95 mmol/L, pH 7.3; preservative.

R2 Anti-IL-6-Ab~$Ru(bpy)_3^{2+}$, 1 bottle, 7.6 mL:
Monoclonal anti-IL-6 antibody (mouse) labeled with ruthenium complex 1.5 µg/mL; phosphate buffer 95 mmol/L, pH 7.3; preservative.

Precautions and warnings

For Emergency Use Authorization only.
For in vitro diagnostic use. Exercise the normal precautions required for handling all laboratory reagents.
Disposal of all waste material should be in accordance with local guidelines. Safety data sheet available for professional user on request.
For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.
This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:
2-methyl-2H-isothiazol-3-one hydrochloride

EUH 208 May produce an allergic reaction.

Product safety labeling follows EU GHS guidance.
Avoid foam formation in all reagents and sample types (specimens, calibrators and controls).

Do not test samples from patients who have indicated or whose clinical status or history would indicate they are currently taking high doses of biotin (> 10 mg per day). If biotin interference is suspected, follow your established internal procedures to investigate the interference per CLIA and GLP recommendations.

Reagent handling

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

Storage and stability

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

Stability:	
Reagent stability:	
unopened at 2-8 °C	up to the stated expiration date
For **cobas e** 411, **cobas e** 601, and **cobas e** 602 analyzers: after opening at 2-8 °C	12 weeks
on the **cobas e** 411, **cobas e** 601, and **cobas e** 602 analyzers:	4 weeks
on the **cobas e** 801 analyzer:	16 weeks
Sample stability:	
serum or plasma	6 hours at 20-25 °C 2 days at 2-8 °C 24 months at -20 °C (± 5 °C) Freeze only once

Specimen collection and preparation

Only the specimens listed below were tested and found acceptable.
Serum collected using standard sampling tubes or tubes containing separating gel.
Li-heparin, K_2-EDTA and K_3-EDTA plasma.
Plasma tubes containing separating gel can be used.
The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube manufacturer.
Centrifuge samples containing precipitates before performing the assay.
Do not use heat-inactivated samples.
Do not use samples and controls stabilized with azide.

Elecsys IL-6

Ensure the samples, calibrators, and controls (**cobas e** 411, **cobas e** 601, and **cobas e** 602 analyzers) are at 20-25 °C prior to measurement.
Due to possible evaporation effects, samples, calibrators, and controls (**cobas e** 411, **cobas e** 601, **cobas e** 602, and **cobas e** 801 analyzers) 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 05109469190, IL-6 CalSet, for 4 x 2.0 mL
- REF 05341787160, PreciControl Multimarker, for 6 x 2.0 mL
- REF 03609987190, Diluent MultiAssay, 2 x 16 mL sample diluent
- REF 07299010190, Diluent MultiAssay, 45.2 mL sample diluent
- General laboratory equipment
- **cobas e** analyzer

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

- REF 11662988122, ProCell, 6 x 380 mL system buffer
- REF 11662970122, CleanCell, 6 x 380 mL measuring cell cleaning solution
- REF 11930346122, Elecsys SysWash, 1 x 500 mL washwater additive
- REF 11933159001, Adapter for SysClean
- REF 11706802001, AssayCup, 60 x 60 reaction cups
- REF 11706799001, AssayTip, 30 x 120 pipette tips
- REF 11800507001, Clean-Liner

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

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

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

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

Additional materials for all analyzers:

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

Assay

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator's manual for analyzer-specific assay instructions.
Resuspension of the microparticles takes place automatically prior to use.
cobas e 411, **cobas e** 601, and **cobas e** 602 analyzers:
Read in the test-specific parameters via the reagent barcode. If in exceptional cases the barcode cannot be read, enter the 15-digit sequence of numbers. Bring the cooled reagents to approximately 20 °C and place on the reagent disk (20 °C) of the analyzer
cobas e 801 analyzer:
Place the cooled (stored at 2-8 °C) **cobas e** pack on the reagent manager.
Avoid foam formation. The system automatically regulates the temperature of the reagents and the opening/closing of the bottles and **cobas e** pack.

Calibration

Traceability: This method has been standardized against the NIBSC (National Institute for Biological Standards and Control) 1st IS 89/548 Standard.

cobas e 411, **cobas e** 601, and **cobas e** 602 analyzers: Every Elecsys reagent set has a barcoded label containing specific information for calibration of the particular reagent lot.
The predefined master curve is adapted to the analyzer using the relevant CalSet.
Calibration frequency: Calibration must be performed once per reagent lot using fresh reagent (i.e. not more than 24 hours since the reagent kit/**cobas e** pack was registered on the analyzer).
Calibration interval may be extended based on acceptable verification of calibration by the laboratory.
Renewed calibration is recommended as follows for **cobas e** 411, **cobas e** 601, and **cobas e** 602 analyzers:

- after 1 month (28 days) when using the same reagent lot
- after 7 days (when using the same reagent kit on the analyzer)
- as required: e.g. quality control findings outside the defined limits

Renewed calibration is recommended as follows for **cobas e** 801 analyzer:

- after 12 weeks when using the same reagent lot
- after 28 days (when using the same **cobas e** pack on the analyzer)
- as required: e.g. quality control findings outside the defined limits

Quality control

For quality control, use PreciControl Multimarker.
In addition, other suitable control material can be used.
Controls for the various concentration ranges should be run individually at least once every 24 hours when the test is in use, once per reagent kit / **cobas e** pack, and following each calibration.
The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.
If necessary, repeat the measurement of the samples concerned.
Follow the applicable government regulations and local guidelines for quality control.

Calculation

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

Elecsys IL-6

cobas®

Limitations - interference

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

Endogenous substances

Compound	Concentration tested
Bilirubin	≤ 684 µmol/L or ≤ 40 mg/dL
Hemoglobin	≤ 0.621 mmol/L or ≤ 1000 mg/dL
Intralipid	≤ 1500 mg/dL
Biotin[b)]	≤ 123 nmol/L or ≤ 30 ng/mL
Rheumatoid factors	≤ 1200 IU/mL

b) Biotin concentrations above 30 ng/mL were not tested. Patients undergoing treatment for COVID-19 may not be expected to have elevated biotin levels.

Specifications: For concentrations of IL-6 equal to 1.5-25 pg/mL recovery is within ± 4 pg/mL of the initial value. For IL-6 concentrations > 25 pg/mL, the recovery is within ± 15 % of the initial value.

Pharmacokinetic studies have shown that serum concentrations of biotin can reach up to 355 ng/mL within the first hour after biotin ingestion for subjects consuming supplements of 20 mg biotin per day[1] and up to 1160 ng/mL for subjects after a single dose of 300 mg biotin.[2]

There is no high-dose hook effect at IL-6 concentrations up to 200000 pg/mL.

Pharmaceutical substances

In vitro tests were performed on 16 commonly used pharmaceuticals. No interference with the assay was found.

In addition, the following special therapeutic drugs were tested. No interference with the assay was found.

Special therapeutic drugs

Drug	Concentration tested mg/mL
Imipenem	≤ 1.18
Cefotaxime	≤ 0.9
Vancomycin	≤ 3.5
Dopamine	≤ 0.13
Noradrenaline	≤ 0.002
Dobutamine	≤ 0.0112
Furosemide	≤ 0.02
Fentanyl	≤ 0.01

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.

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

Elecsys IL-6

Conditions of Authorization for the Laboratory

The Elecsys IL-6 assay Letter of Authorization, along with the authorized Fact Sheet for Healthcare Providers, the authorized Fact Sheet for Patients, and authorized labeling are available on the FDA website: https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations#covid19ivd. However, to assist clinical laboratories using the Elecsys IL-6 assay ("your product" in the conditions below), the relevant Conditions of Authorization are listed below:

- Authorized laboratories[c)] using your product will include with result reports of your product, all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.
- Authorized laboratories using your product will use your product as outlined in the Instructions for Use. Deviations from the authorized procedures, including the authorized instruments, authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and authorized materials required to use your product are not permitted.
- Authorized laboratories using your product will have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
- Authorized laboratories will collect information on the performance of your product and report to DIHD/OHT7-OIR/OPEQ/ CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov) and Roche (1-866-987-6243) any suspected occurrence of false reactive or false non-reactive results and significant deviations from the established performance characteristics of your product of which they become aware.
- All laboratory personnel using your product must be appropriately trained in automated immunoassay techniques and use appropriate laboratory and personal protective equipment when handling this kit, and use your product in accordance with the authorized labeling. All laboratory personnel using the assay must also be trained in and be familiar with the interpretation of results of the product.
- Roche, authorized distributors, and authorized laboratories using your product will ensure that any records associated with this EUA are maintained until otherwise notified by FDA. Such records will be made available to FDA for inspection upon request.

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

Analytical measuring interval

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

Measuring interval

1.5-5000 pg/mL (defined by the lower detection limit and the maximum of the master curve). Please note: When reporting values < 2.5 pg/mL, the client report should be annotated with the following information: "Values < 2.5 pg/mL are not reliable as the intermediate precision CV is > 20 %." Values above the measuring range are reported as > 5000 pg/mL (or up to 50000 pg/mL for 10-fold diluted samples).

Lower limits of measurement

Lower detection limit of the test

Lower detection limit: approximately 1.5 pg/mL

The lower detection limit is determined based on the Limit of Blank and the standard deviation of low concentration samples. The Limit of Detection corresponds to the lowest analyte concentration which can be detected (value above the Limit of Blank with a probability of 95 %).

cobas e 801 analyzer:

Measuring interval

1.5-5000 pg/mL (defined by the Limit of Detection and the maximum of the master curve). Values below the Limit of Detection are reported as < 1.5 pg/mL. Please note: When reporting values < 2.5 pg/mL, the client report should be annotated with the following information: "Values < 2.5 pg/mL are not reliable as the intermediate precision CV is > 20 %." Values above the measuring range are reported as > 5000 pg/mL (or up to 50000 pg/mL for 10-fold diluted samples).

Lower limits of measurement

Limit of Blank, Limit of Detection and Limit of Quantitation

Limit of Blank = 1.0 pg/mL

Limit of Detection = 1.5 pg/mL

Limit of Quantitation = 2.5 pg/mL

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

The Limit of Blank is the 95th percentile value from n ≥ 60 measurements of analyte-free samples over several independent series. The Limit of Blank corresponds to the concentration below which analyte-free samples are found with a probability of 95 %.

The Limit of Detection is determined based on the Limit of Blank and the standard deviation of low concentration samples. The Limit of Detection corresponds to the lowest analyte concentration which can be detected (value above the Limit of Blank with a probability of 95 %).

The Limit of Quantitation is the lowest analyte concentration that can be reproducibly measured with an intermediate precision[d)] CV of ≤ 20 %.

d) intermediate precision = within-laboratory

Linearity

Linearity was assessed according to CLSI EP06-A by diluting human samples with Diluent MultiAssay. Samples ranged in concentration from 1.5 to 5000 pg/mL. The following table shows the assessment of the serum samples:

Sample	Range (pg/mL)	Slope (95 % CI[e)])	Y-intercept (95 % CI)	R2[f)]	Recovery (%)
HS[g)]1	0.77-5182	0.949 (0.928, 0.97)	-0.107 (-0.149, -0.064)	0.995	94.6 - 103.4
HS 2	0.77-5222	0.930 (0.907, 0.953)	-0.135 (-0.181, -0.089)	0.993	91.8 - 105.2
HS 3	0.81-5481	1.004 (0.984, 1.024)	-0.131 (-0.174, -0.087)	0.995	96.4 - 103.3

e) CI = confidence interval

f) R2 = correlation coefficient

g) HS = human serum

Dilution

Samples with IL-6 concentrations above the measuring range can be diluted with Diluent MultiAssay if the neat value exceeds the measuring interval of 5000 pg/mL. The recommended dilution is 1:10 (either automatically by the analyzers, or manually). To avoid potential matrix effect, the concentration of the diluted sample must be: **cobas e** 411, **cobas e** 601, and **cobas e** 602 analyzers: > 50 pg/mL. **cobas e** 801 analyzer: ≥ 450 pg/mL.

After manual dilution, multiply the result by the dilution factor.

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

Expected values

In an external study using the Elecsys IL-6 assay on samples from 817 apparently healthy individuals, a reference range up to 7 pg/mL IL-6 (95th percentile) was determined.

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

Matrix comparison: serum vs plasma

In addition to serum specimen, Li-heparin, K_2-EDTA and K_3-EDTA plasma were tested and found acceptable based on the following criterion:
Criterion: Slope 0.9-1.1 + intercept within ≤ ± 3 pg/mL + coefficient of correlation ≥ 0.95.

Sample	Range (pg/mL)	Slope (95 % CI)	y-intercept (95 % CI)	Correlation coefficient r2
Li-heparin	1.98 - 4712	1.058 (1.043 - 1.090)	-0.360 (-0.574 - -0.224)	0.999
K_2-EDTA	1.98 - 4372	1.068 (1.018 - 1.087)	-0.522 (-0.925 - 0.0348)	0.999
K_3-EDTA	1.98 - 4372	1.065 (1.022 - 1.090)	-0.397 (-0.843 - 0.0068)	0.999

Clinical performance

The following clinical data are from Munich, Germany from polymerase chain reaction (PCR) confirmed symptomatic COVID-19 patients presenting in the Emergency Department (ED). In this validation data set of 49 hospitalized patients, 19 patients required intubation for respiratory support subsequent to ED presentation. The Elecsys IL-6 assay, using a cutoff of 35 pg/mL, correctly identified 16 of the 19 patients that required intubation (Positive predictive value: 59 % (95 % CI = 47 % to 71 %); Negative predictive value: 86 % (95 % CI = 68 % to 95 %); prevalence of mechanical ventilation in COVID-19 confirmed, hospitalized patients: 39 % (95 % CI = 25 % to 54 %).[3] The cutoff was established on retrospectively collected samples (n = 37) and validated with prospectively collected samples (n = 49) based on the need for mechanical ventilation during the hospitalization. The receiver operator curve was calculated for the first assessment value of Elecsys IL-6 at presentation to the ED. Sensitivity and specificity is shown for patients who subsequently underwent or did not undergo intubation with mechanical ventilation.

Elecsys IL-6 sensitivity and specificity		
	Mechanical ventilation patients	No mechanical ventilation required
IL-6 >35 pg/mL	16	11
IL-6 ≤ 35 pg/mL	3	19
Sensitivity	84 % (95 % CI: 60 % to 97 %)	
Specificity		63 % (95 % CI: 44 % to 80 %)

Cutoff determination

Cutoff was established for Elecsys IL-6 assay using 37 confirmed COVID-19 patients and validated in 49 confirmed COVID-19 patients using receiver operating curves (ROC) and calculated area under the curve (AUC) to compare predictive value for the need for mechanical ventilation. The cutoff was optimized by maximizing the Youden's index.[4]

Results and interpretation

Based on the available clinical data, PCR-confirmed COVID-19 patients with IL-6 concentrations > 35 pg/mL at presentation are at risk for mechanical ventilation during their hospitalization. IL-6 values should be used

in conjunction with clinical findings and the results of other laboratory parameters. IL-6 values alone are not indicative of the need for endotracheal intubation or mechanical ventilation.

Specific performance data

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

Precision

Precision was determined using Elecsys reagents, samples and controls according to the recommended protocol (EP05-A2) of the CLSI (Clinical and Laboratory Standards Institute): 2 runs per day in duplicate each for 21 days (n = 84). The samples were sourced from uncharacterized blood donors that were spiked with recombinant IL-6. The following results were obtained:

cobas e 411 analyzer					
		Repeatability		**Intermediate precision**[h)]	
Sample	Mean pg/mL	SD pg/mL	CV %	SD pg/mL	CV %
Human serum 1	17.3	1.03	6.0	1.46	8.5
Human serum 2	117	2.90	2.5	3.71	3.2
Human serum 3	891	22.8	2.6	25.5	2.9
PC MM[i)] 1	38.3	0.540	1.4	1.04	2.7
PC MM 2	229	3.29	1.4	6.71	2.9

h) Intermediate precision = within-laboratory precision

i) PC MM = PreciControl Multimarker

cobas e 601 and **cobas e** 602 analyzers					
		Repeatability		**Intermediate precision**	
Sample	Mean pg/mL	SD pg/mL	CV %	SD pg/mL	CV %
Human serum 1	12.1	0.346	2.9	0.371	3.1
Human serum 2	49.0	0.657	1.3	0.782	1.6
Human serum 3	1966	17.2	0.9	22.2	1.1
PC MM 1	37.7	1.27	3.4	1.60	4.2
PC MM 2	229	5.20	2.3	7.63	3.3

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 samples were sourced from uncharacterized blood donors that were spiked with recombinant IL-6. The following results were obtained:

cobas e 801 analyzer					
		Repeatability		**Intermediate precision**	
Sample	Mean pg/mL	SD pg/mL	CV %	SD pg/mL	CV %
Human serum 1	1.82	0.262	14.4	0.316	17.4
Human serum 2	6.44	0.317	4.9	0.329	5.1
Human serum 3	189	2.66	1.4	3.41	1.8
Human serum 4	2234	24.9	1.1	41.0	1.8
Human serum 5	4461	53.8	1.2	87.4	2.0
PC MM 1	37.6	0.448	1.2	0.644	1.7
PC MM 2	240	2.83	1.2	3.95	1.6

Analytical specificity

The Elecsys IL-6 assay does not show any significant cross-reactivity with the following substances, tested with IL-6 concentrations of approximately 3 pg/mL and 4000 pg/mL (maximum tested concentration):

Substances	**Non-interfering concentrations (pg/mL)**
Interleukin-1α	50000
Interleukin-1β	50000
Interleukin-2	50000
Interleukin-3	50000
Interleukin-4	50000
Interleukin-8	50000
Interferon-γ	50000
TNF-α	50000

References

1 Grimsey P, Frey N, Bendig G, et al. Population pharmacokinetics of exogenous biotin and the relationship between biotin serum levels and in vitro immunoassay interference. International Journal of Pharmacokinetics 2017 Sept 14;2(4):247-256.

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

3 Herold T, Jurinovic V, Arnreich C, et al. Elevated levels of interleukin-6 and CRP predict the need for

mechanical ventilation in COVID-19, Journal of Allergy and Clinical Immunology (2020), doi: https://doi.org/10.1016/j.jaci.2020.05.008

4 Youden WJ. Index for rating diagnostic tests. Cancer 1950; 3:32-5.

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

Symbols

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

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

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

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim

www.roche.com

Distribution in USA by:

Roche Diagnostics, Indianapolis, IN

US Customer Technical Support 1-800-428-2336

Roche