Elecsys IgE II

cobas®

REF		Σ	SYSTEM
04827031190* 04827031214*	04827031500	100	**cobas e** 411 **cobas e** 601 **cobas e** 602

* Some kits shown may not be available in all countries.

English

System information

For **cobas e** 411 analyzer: test number 630
For **cobas e** 601 and **cobas e** 602 analyzers: Application Code Number 116

Intended use

Immunoassay for the in vitro quantitative determination of immunoglobulin E in human serum and plasma.

Determination of total IgE is useful as an aid in the diagnosis of allergic diseases.

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

Summary

Immunoglobulin E (IgE) plays an important role in immunological protection against parasitic infections and in allergy (type 1 hypersensitivity). Type 1 hypersensitivity is characterized by the occurrence of allergic reactions immediately following re-exposure to an allergy-initiating antigen (allergen) such as encountered in atopic disorders (e.g., allergic asthma), insect venom or latex and in some food allergies. The binding of the allergen to sensitized tissue mast cells or blood basophilic cells leads to cross-linking of the IgE on the cell membrane. This in turn causes cell degranulation and the release of inflammation mediators (e.g. histamine, serotonin, lipid mediators, proteases and cytokines), which produce the typical symptoms of type 1 hypersensitivity, an exaggerated immune response to foreign antigens, such as pollen, dust mites, and certain foods.[1,2,3,4,5]

The IgE concentration in serum is normally very low as IgE is the least abundant antibody in serum (0.05 % of the IgG concentration). The IgE concentration is age-dependent, with the lowest values being measured at birth. Its concentration gradually increases and becomes stabilized between the age of 5-7, although the IgE values vary greatly within particular age groups.[1,6]

Elevated IgE concentrations can be found in patients with allergic diseases such as hay fever, atopic bronchitis and dermatitis.[4] Normal IgE values do not, however, mean that an allergic disease can be ruled out. For this reason the quantitative determination of serum IgE concentrations is useful for clinical differentiation between atopic (i.e., predisposition to excessive IgE reaction) and non-atopic (non-IgE mediated) allergic diseases only in combination with other clinical findings.[1,6,7]

Elevated serum IgE concentrations can also occur in non-allergic diseases, e.g. congenital immunodeficiency syndromes, HIV infection, graft-versus-host disease, severe burns and parasitic diseases.[4]

Test principle

Sandwich principle. Total duration of assay: 18 minutes.

- 1st incubation: IgE in the sample (10 µL), a biotinylated monoclonal IgE-specific antibody, and a monoclonal IgE-specific antibody 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 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

The reagent rackpack is labeled as IGE II.

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

R1 Anti-IgE-Ab~biotin (gray cap), 1 bottle, 10 mL:
Biotinylated monoclonal anti-IgE antibody (mouse) 2.5 mg/L; phosphate buffer 85 mmol/L, pH 6.5; preservative.

R2 Anti-IgE-Ab~$Ru(bpy)_3^{2+}$ (black cap), 1 bottle, 10 mL:
Monoclonal anti-IgE antibody (mouse) labeled with ruthenium complex 5.5 mg/L; phosphate buffer 85 mmol/L, pH 6.5; preservative.

Precautions and warnings

For in vitro diagnostic use for health care professionals. Exercise the normal precautions required for handling all laboratory reagents.

Infectious or microbial waste:
Warning: handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Environmental hazards:
Apply all relevant local disposal regulations to determine the safe disposal.

Safety data sheet available for professional user on request.

For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

Warning

H317	May cause an allergic skin reaction.
Prevention:	
P261	Avoid breathing mist or vapours.
P272	Contaminated work clothing should not be allowed out of the workplace.
P280	Wear protective gloves.
Response:	
P333 + P313	If skin irritation or rash occurs: Get medical advice/attention.
P362 + P364	Take off contaminated clothing and wash it before reuse.
Disposal:	
P501	Dispose of contents/container to an approved waste disposal plant.

Product safety labeling follows EU GHS guidance.

Contact phone: all countries: +49-621-7590, USA: 1-800-428-2336

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

Reagent handling

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.

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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:	
unopened at 2-8 °C	up to the stated expiration date
after opening at 2-8 °C	12 weeks
on the analyzers	8 weeks

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, Na-heparin, K_3-EDTA and sodium citrate plasma. When sodium citrate is used, the results must be corrected by + 10 %.

Criterion: Recovery within 90-110 % of serum value or slope 0.9-1.1 + intercept within < ± 2x analytical sensitivity (LDL) + coefficient of correlation > 0.95.

The results obtained with sodium fluoride/potassium oxalate plasma are approximately 18 % lower than those obtained with serum.

Stable for 7 days at 2-8 °C, 6 months at -20 °C (± 5 °C).[8] Samples may be frozen 5 times.

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.

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.

Sample stability claims were established by experimental data by the manufacturer or based on reference literature and only for the temperatures/time frames as stated in the method sheet. It is the responsibility of the individual laboratory to use all available references and/or its own studies to determine specific stability criteria for its laboratory.

Materials provided

See "Reagents – working solutions" section for reagents.

Materials required (but not provided)

- REF 11930427122, IgE CalSet, 4 x 1.0 mL
- REF 11731416190, PreciControl Universal, for 4 x 3.0 mL
- REF 11731416160, PreciControl Universal, for 4 x 3.0 mL (for USA)
- REF 11732277122, Diluent Universal, 2 x 16 mL sample diluent or
  REF 03183971122, Diluent Universal, 2 x 36 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 all analyzers:

- REF 11298500316, ISE Cleaning Solution/Elecsys SysClean, 5 x 100 mL system cleaning solution
- REF 11298500160, ISE Cleaning Solution/Elecsys SysClean, 5 x 100 mL system cleaning solution (for USA)

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.

Calibration

Traceability: This method has been standardized against the 2nd IRP WHO Reference Standard 75/502.

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 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 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

Quality control

For quality control, use PreciControl Universal.

In addition, other suitable control material can be used.

Controls for the various concentration ranges should be run individually at least once every 24 hours when the test is in use, once per reagent kit, and following each calibration.

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

If necessary, repeat the measurement of the samples concerned.

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

Calculation

The analyzer automatically calculates the analyte concentration of each sample (either in IU/mL or ng/mL).

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Conversion factors: IU/mL x 2.40 = ng/mL

ng/mL x 0.42 = IU/mL

Limitations - interference

The assay is unaffected by icterus (bilirubin < 633 µmol/L or < 37 mg/dL), hemolysis (Hb < 0.062 mmol/L or < 0.1 g/dL; do not analyze samples that show visible signs of hemolysis), lipemia (triglycerides < 30.8 mmol/L or < 2200 mg/dL) and biotin (< 409 nmol/L or < 100 ng/mL).

Criterion: Recovery within ± 10 % of initial value.

Samples should not be taken from patients receiving therapy with high biotin doses (i.e. > 5 mg/day) until at least 8 hours following the last biotin administration.

No interference was observed from rheumatoid factors up to a concentration of 6000 IU/mL (method comparison: Elecsys IgE assay and a commercially available IgE test on 50 samples).

There is no high-dose hook effect at IgE concentrations up to 50000 IU/mL (120000 ng/mL).

In vitro tests were performed on 37 commonly used pharmaceuticals. An interference was found for samples from patients treated with Xolair (omalizumab). Do not use samples from patients under treatment with Xolair (omalizumab) or similar drugs containing anti-IgE antibodies.

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.

Limits and ranges

Measuring range

0.100-2500 IU/mL or 0.240-6000 ng/mL (defined by the lower detection limit and the maximum of the master curve). Values below the lower detection limit are reported as < 0.100 IU/mL or < 0.240 ng/mL. Values above the measuring range are reported as > 2500 IU/mL or > 6000 ng/mL (or up to 50000 IU/mL or 120000 ng/mL for 20-fold diluted samples).

Lower limits of measurement

Lower detection limit of the test

Lower detection limit: 0.100 IU/mL (0.240 ng/mL)

The lower detection limit represents the lowest measurable analyte level that can be distinguished from zero. It is calculated as the value lying two standard deviations above that of the lowest standard (master calibrator, standard 1 + 2 SD, repeatability study, n = 21).

Dilution

Samples with IgE concentrations above the measuring range can be diluted with Diluent Universal. The recommended dilution is 1:20 (either automatically by the analyzers or manually). The concentration of the diluted sample must be > 125 IU/mL (> 300 ng/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

The IgE concentrations in healthy, non-atopic subjects are greatly dependent on age. The lowest values are found in neonates. Normal values raise in childhood and decrease again in adults.[9,10,11]
Recommended threshold values:[11]

Age group	IU/mL	ng/mL
Neonates	1.5	3.6
Infants in 1st year of life	15	36
Children aged 1-5 years	60	144
Children aged 6-9 years	90	216
Children aged 10-15 years	200	480
Adults	100	240

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

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, pooled human sera and controls in a modified protocol (EP5-A) of the CLSI (Clinical and Laboratory Standards Institute): 6 times daily for 10 days (n = 60); repeatability on MODULAR ANALYTICS E170 analyzer, n = 21. The following results were obtained:

cobas e 411 analyzer					
			Repeatability		
Sample	Mean		SD		CV
	IU/mL	ng/mL	IU/mL	ng/mL	%
Human serum 1	32.7	78.5	1.3	3.12	4.1
Human serum 2	265	636	6.3	15.1	2.4
Human serum 3	1295	3108	34	81.6	2.6
PreciControl U[b)]1	82.3	198	1.6	3.84	2.0
PreciControl U2	340	815	7.7	18.5	2.3

b) U = Universal

cobas e 411 analyzer					
			Intermediate precision		
Sample	Mean		SD		CV
	IU/mL	ng/mL	IU/mL	ng/mL	%
Human serum 1	32.7	78.5	1.7	4.1	5.1
Human serum 2	265	636	10	24	3.8
Human serum 3	1295	3108	50.4	121	3.9
PreciControl U1	82.3	198	3.1	7.4	3.7
PreciControl U2	340	815	13.4	32.2	4.0

cobas e 601 and **cobas e** 602 analyzers					
	Repeatability				
Sample	Mean		SD		CV
	IU/mL	ng/mL	IU/mL	ng/mL	%
Human serum 1	4.4	10.6	0.06	0.14	1.4
Human serum 2	261	628	1.92	4.61	0.7
Human serum 3	1018	2444	9.71	23.3	1.0
PreciControl U1	78.1	188	0.49	1.18	0.6
PreciControl U2	340	817	2.4	5.76	0.7

cobas e 601 and **cobas e** 602 analyzers					
	Intermediate precision				
Sample	Mean		SD		CV
	IU/mL	ng/mL	IU/mL	ng/mL	%
Human serum 1	30.2	72.5	0.83	1.99	2.7
Human serum 2	245	588	6.88	16.5	2.8
Human serum 3	1207	2899	41.3	99.1	3.4
PreciControl U1	78.1	187	2.8	6.7	3.6
PreciControl U2	328	787	11.5	27.6	3.6

Method comparison

A comparison of the Elecsys IgE II assay (y) with the Elecsys IgE assay (x) using clinical samples gave the following correlations (IU/mL):

Number of samples measured: 72

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Passing/Bablok[12]	Linear regression
y = 0.93x + 0.14	y = 0.95x - 2.35
τ = 0.985	r = 0.998

The sample concentrations were between approximately 3 and 1755 IU/mL (approximately 7.2 and 4212 ng/mL).

Analytical specificity

The monoclonal antibodies used are highly specific for immunoglobulin E.

No cross-reactivities with the immunoglobulins G, A and M were detectable.

Functional sensitivity

0.500 IU/mL (1.20 ng/mL)

The functional sensitivity is the lowest analyte concentration that can be reproducibly measured with an intermediate precision CV of < 20 %.

References

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For further information, please refer to the appropriate operator's manual for the analyzer concerned, the respective application sheets 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.

Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.

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

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.

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