Elecsys Progesterone III

cobas®

REF		Σ	SYSTEM
			cobas e 411
07092539190	07092539500	100	**cobas e** 601
			cobas e 602

English

System information

For **cobas e** 411 analyzer: test number 1380
For **cobas e** 601 and **cobas e** 602 analyzers: Application Code Number 235

Intended use

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

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

Summary

Progesterone measurements, performed with this device, in human serum and plasma are used as an aid in diagnosis of female fertility.

The gestagen progesterone is a steroid hormone which is mainly formed in the cells of the corpus luteum in the ovaries and during pregnancy in the placenta. Minor sources of progesterone are the adrenal cortex in both sexes and the testes in men.

The progesterone concentration correlates with the development and regression of the corpus luteum. Whereas progesterone is barely detectable in the follicular phase of the female cycle, a rise in the progesterone level is observed one day prior to ovulation. Increased progesterone synthesis occurs during the luteal phase. In the second half of the cycle pregnanediol is excreted in urine as the main degradation product of progesterone.[1]

Progesterone brings about the conversion of the uterine mucosa into a tissue rich in glands (luteal phase), in order to prepare for the intrauterine implantation of the fertilized ovum.[1] During pregnancy, progesterone maternal serum concentrations increase, inhibiting the contraction of the myometrium and maintaining pregnancy. In the mammary gland, progesterone (together with estrogens) promotes the proliferation, secretion and disposition of the alveoli. [1,2,3,4]

Progesterone determination is used in fertility diagnosis to detect ovulation and assess the luteal phase.[5]

Test principle

Competition principle. Total duration of assay: 18 minutes.

- 1st incubation: By incubating the sample (20 µL) with a progesterone-specific biotinylated antibody, immunocomplexes are formed, the amount of which is dependent upon the analyte concentration in the sample.
- 2nd incubation: After addition of streptavidin-coated microparticles and an progesterone derivative labeled with a ruthenium complex[a)], the still-vacant sites of the biotinylated antibodies become occupied, with formation of an antibody-hapten complex. The entire 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 PROG III.

M Streptavidin-coated microparticles (transparent cap), 1 bottle, 6.5 mL:

Streptavidin-coated microparticles 0.72 mg/mL; preservative.

R1 Anti-progesterone-Ab~biotin (gray cap), 1 bottle, 10 mL:

Biotinylated monoclonal anti-progesterone antibody (recombinant, sheep) 30 ng/mL, phosphate buffer 25 mmol/L, pH 7.0; preservative.

R2 Progesterone-peptide~$Ru(bpy)_3^{2+}$ (black cap), 1 bottle, 9 mL:

Progesterone (of vegetable origin) coupled to a synthetic peptide labeled with ruthenium complex, 2 ng/mL; phosphate buffer 25 mmol/L, pH 7.0; 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.

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

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.

Storage and stability

Store at 2-8 °C.

Do not freeze.

Elecsys Progesterone III

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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, K_2-EDTA and K_3-EDTA plasma. Li-heparin plasma tubes containing separating gel can be used.

Criterion: slope 0.9-1.1 + intercept within < ± 0.1 ng/mL + coefficient of correlation (Pearson) ≥ 0.95.

Stable for 1 day at 20-25 °C, 5 days at 2-8 °C, 6 months at -20 °C (± 5 °C). Freeze only once.

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.

Materials provided

See "Reagents – working solutions" section for reagents.

Materials required (but not provided)

- REF 07092547190, Progesterone III CalSet, for 4 x 1.0 mL
- REF 11731416190, PreciControl Universal, for 4 x 3.0 mL
- REF 03028542122, Diluent Estradiol/Progesterone, 2 x 22 mL sample diluent
- REF 09762582190, Elecsys Progesterone Diluent, 2 x 22 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 03004899190, PreClean M, 5 x 600 mL detection cleaning solution
- REF 12102137001, AssayTip/AssayCup, 48 magazines x 84 reaction cups or pipette tips, waste bags
- REF 03023150001, WasteLiner, waste bags
- REF 03027651001, SysClean Adapter M

Additional materials for all analyzers:

- REF 11298500316, ISE Cleaning Solution/Elecsys SysClean, 5 x 100 mL system cleaning solution

Assay

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator's manual for analyzer-specific assay instructions.

Resuspension of the microparticles takes place automatically prior to use. Read in the test-specific parameters via the reagent barcode. If in exceptional cases the barcode cannot be read, enter the 15-digit sequence of numbers.

cobas e 601 and **cobas e** 602 analyzers: PreClean M solution is necessary.

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: The Elecsys Progesterone III assay is traceable via ID-GC/MS (isotope dilution gas chromatography/mass spectrometry) to highly purified progesterone by weight analogously to BCR-348R and ERM-DA347.[6]

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 nmol/L, ng/mL or in µg/L).

Conversion factors: nmol/L x 0.314 = ng/mL (µg/L)

ng/mL x 3.18 = nmol/L

Limitations - interference

The assay is unaffected by icterus (bilirubin ditaurate ≤ 923 µmol/L or ≤ 54 mg/dL), hemolysis (Hb ≤ 0.621 mmol/L or ≤ 1.0 g/dL), lipemia (Intralipid ≤ 200 mg/dL) and biotin (≤ 123 nmol/L or ≤ 30 ng/mL).

Criterion: Recovery within ± 10 % of initial value with samples > 2 ng/mL, ± 15 % with samples > 0.5 to 2 ng/mL and ≤ ± 0.2 ng/mL with samples ≤ 0.5 ng/mL.

Visibly turbid samples give a false low result.

Elecsys Progesterone III

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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 1200 IU/mL.

In vitro tests were performed on 16 commonly used pharmaceuticals. Of these, only phenylbutazone at therapeutic dosage levels showed interference with the assay (progesterone values depressed). No interference was observed with clomiphene citrate.

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

0.159-191 nmol/L or 0.05-60 ng/mL (defined by the Limit of Detection and the maximum of the master curve). Values below the Limit of Detection are reported as < 0.159 nmol/L or < 0.05 ng/mL. Values above the measuring range are reported as > 191 nmol/L or > 60 ng/mL.

Lower limits of measurement

Limit of Blank, Limit of Detection and Limit of Quantitation

Limit of Blank = 0.080 nmol/L (0.025 ng/mL)

Limit of Detection = 0.159 nmol/L (0.05 ng/mL)

Limit of Quantitation = 0.636 nmol/L (0.2 ng/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-A 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 defined as the lowest amount of analyte in a sample that can be accurately quantitated with a total allowable error of ≤ 20 %.

Dilution

Samples with progesterone concentrations above the measuring range can be diluted with Elecsys Progesterone Diluent or a suitable human serum with a low analyte concentration. The recommended dilution is 1:10. The concentration of the diluted sample must be ≥ 3.18 nmol/L (≥ 1 ng/mL).

After dilution, multiply the result by the dilution factor.

Depending on the biological variance of the diluted patient sample and the human serum matrix used for production of Elecsys Progesterone Diluent, lower recovery of diluted samples may be observed.

Expected values

The expected ranges were determined by testing specimens drawn from 147 apparently healthy males, 142 apparently healthy, post-menopausal women over the age of 50, and from 416 apparently healthy pregnant women between the ages of 18 and 50 (137 in the first trimester, 140 in the second trimester, and 139 in the third trimester). The expected range for healthy women was determined by collecting blood at multiple time points of one menstrual cycle from 85 apparently healthy subjects with a natural menstrual cycle that were not taking any hormonal contraceptives. A menstrual cycle was defined as the phase between two subsequent menstrual bleedings. Cycle length (29 days) and day of ovulation (day 15) were standardized to account for variation in cycle length within the study population and to enable determination of expected values for further sub-phases. Only ovulatory menstrual cycles were used for value analysis. Based on a central 90 % interval, the following ranges were obtained:

Test subjects	N	5th percentile nmol/L (90 % CI*)	Median nmol/L (90 % CI)	95th percentile nmol/L (90 % CI)
Healthy men	147	< 0.159 (< 0.159-< 0.159)	< 0.159 (< 0.159-< 0.159)	0.474 (0.442-0.614)
Healthy postmenopausal women				
• Postmenopause	142	< 0.159 (< 0.159-< 0.159)	< 0.159 (< 0.159-< 0.159)	0.401 (0.343-0.480)
Healthy pregnant women				
• 1st trimester	137	35.0 (24.8-40.4)	76.3 (73.1-82.3)	141 (126-156)
• 2nd trimester	140	80.8 (71.3-86.2)	151 (144-159)	265 (251-315)
• 3rd trimester	139	187 (167-218)	342 (328-372)	679 (607-826)

* CI = confidence interval

Healthy women Cycle Phase	N **	5th percentile nmol/L (90 % CI)	Median nmol/L (90 % CI)	95th percentile nmol/L (90 % CI)
Follicular	85	< 0.159 (< 0.159-< 0.159)	0. 212 (0.186- 0.244)	0.616 (0.584-0.897)
Ovulation	81	0.175 (< 0.159- 0.301)	1.81 (1.57-2.26)	13.2 (6.19-19.4)
Luteal	85	13.1 (8.34-15.6)	28.8 (26.4-31.4)	46.3 (43.2-64.8)

** N = number of patients contributing to the data in this menstrual cycle phase (not number of samples); differences in N per phase are due to cycle standardization procedure

Healthy women Cycle Sub-Phase	N	5th percentile nmol/L (90 % CI)	Median nmol/L (90 % CI)	95th percentile nmol/L (90 % CI)
Early follicular	78	< 0.159 (< 0.159-< 0.159)	0.38 (0.32-0.47)	1.03 (0.802-2.58)
Intermediate follicular	83	< 0.159 (< 0.159-< 0.159)	0.21 (0.168-0.252)	0.7 (0.619-3.44)
Late follicular	84	< 0.159 (< 0.159-< 0.159)	0.188 (< 0.159-0.234)	0.688 (0.579-12.3)
Ovulation	79	< 0.159 (< 0.159-0.171)	1.59 (1.09-1.85)	7.49 (5.91-19.4)
Early luteal	85	7.53 (4.66-9.53)	22.6 (20.3-24.9)	48 (39.9-54.1)
Intermediate luteal	81	15.2 (5.39-22.9)	39.2 (36.4-44.4)	66.5 (63.4-78.5)
Late luteal	84	1.71 (< 0.159-3.46)	18.2 (16.6-20.5)	43.1 (38.5-72.3)

Test subjects	N	5th percentile ng/mL (90 % CI)	Median ng/mL (90 % CI)	95th percentile ng/mL (90 % CI)
Healthy men	147	< 0.050 (< 0.050-< 0.050)	< 0.050 (< 0.050-< 0.050)	0.149 (0.139-0.193)
Healthy postmenopausal women				

Elecsys Progesterone III

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Test subjects	N	5th percentile ng/mL (90 % CI)	Median ng/mL (90 % CI)	95th percentile ng/mL (90 % CI)
• Postmenopause	142	< 0.050 (< 0.050-< 0.050)	< 0.050 (< 0.050-< 0.050)	0.126 (0.108-0.151)
Healthy pregnant women				
• 1st trimester	137	11.0 (7.81-12.7)	24.0 (23.0-25.9)	44.3 (39.6-48.9)
• 2nd trimester	140	25.4 (22.4-27.1)	47.5 (45.2-50.0)	83.4 (78.9-99.1)
• 3rd trimester	139	58.7 (52.7-68.5)	107 (103-117)	214 (191-260)

Healthy women Cycle Phase	N	5th percentile ng/mL (90 % CI)	Median ng/mL (90 % CI)	95th percentile ng/mL (90 % CI)
Follicular	85	< 0.050 (< 0.050-< 0.050)	0.067 (0.058-0.077)	0.193 (0.183-0.282)
Ovulation	81	0.055 (< 0.050-0.095)	0.568 (0.493-0.709)	4.14 (1.94-6.09)
Luteal	85	4.11 (2.62-4.9)	9.04 (8.29-9.84)	14.5 (13.5-20.3)

Healthy women Cycle Sub Phase	N	5th percentile ng/mL (90 % CI)	Median ng/mL (90 % CI)	95th percentile ng/mL (90 % CI)
Early follicular	78	< 0.050 (< 0.050-< 0.050)	0.119 (0.1-0.147)	0.323 (0.252-0.809)
Intermediate follicular	83	< 0.050 (< 0.050-< 0.050)	0.066 (0.053-0.079)	0.22 (0.194-1.08)
Late follicular	84	< 0.050 (< 0.050-< 0.050)	0.059 (< 0.050-0.074)	0.216 (0.182-3.87)
Ovulation	79	< 0.050 (< 0.050-0.0547)	0.499 (0.342-0.581)	2.35 (1.86-6.09)
Early luteal	85	2.36 (1.46-2.99)	7.11 (6.37-7.8)	15.1 (12.5-17)
Intermediate luteal	81	4.76 (1.69-7.19)	12.3 (11.4-13.9)	20.9 (19.9-24.6)
Late luteal	84	0.537 (< 0.050-1.09)	5.72 (5.2-6.43)	13.5 (12.1-22.7)

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 protocol (EP05-A3) of the CLSI (Clinical and Laboratory Standards Institute): 2 runs per day in duplicate each for 21 days (n = 84). The following results were obtained:

cobas e 411 analyzer					
			Repeatability		
Sample	Mean		SD		CV
	nmol/L	ng/mL	nmol/L	ng/mL	%
Human serum 1	0.700	0.220	0.083	0.026	11.8
Human serum 2	2.34	0.737	0.080	0.025	3.3
Human serum 3	9.48	2.98	0.232	0.073	2.5
Human serum 4	65.7	20.7	1.39	0.437	2.1
Human serum 5	164	51.6	2.04	0.642	1.2
PreciControl U[b)]1	24.7	7.78	0.477	0.150	1.9
PreciControl U2	51.4	16.2	1.37	0.432	2.7

b) U = Universal

cobas e 411 analyzer					
			Intermediate precision		
Sample	Mean		SD		CV
	nmol/L	ng/mL	nmol/L	ng/mL	%
Human serum 1	0.700	0.220	0.162	0.051	23.1
Human serum 2	2.34	0.737	0.245	0.077	10.4
Human serum 3	9.48	2.98	0.490	0.154	5.2
Human serum 4	65.7	20.7	2.33	0.734	3.6
Human serum 5	164	51.6	5.93	1.87	3.6
PreciControl U1	24.7	7.78	0.910	0.286	3.7
PreciControl U2	51.4	16.2	2.16	0.680	4.2

cobas e 601 and **cobas e** 602 analyzers					
			Repeatability		
Sample	Mean		SD		CV
	nmol/L	ng/mL	nmol/L	ng/mL	%
Human serum 1	0.502	0.158	0.060	0.019	11.9
Human serum 2	2.35	0.739	0.124	0.039	5.3
Human serum 3	4.68	1.47	0.175	0.055	3.7
Human serum 4	28.5	8.96	0.836	0.263	2.9
Human serum 5	174	54.6	4.15	1.30	2.4
PreciControl U1	24.9	7.84	0.566	0.178	2.3
PreciControl U2	50.8	16.0	1.27	0.399	2.5

cobas e 601 and **cobas e** 602 analyzers					
			Intermediate precision		
Sample	Mean		SD		CV
	nmol/L	ng/mL	nmol/L	ng/mL	%
Human serum 1	0.502	0.158	0.113	0.036	22.5
Human serum 2	2.35	0.739	0.193	0.061	8.2
Human serum 3	4.68	1.47	0.306	0.096	6.5
Human serum 4	28.5	8.96	1.11	0.349	3.9
Human serum 5	174	54.6	5.72	1.80	3.3
PreciControl U1	24.9	7.84	0.785	0.247	3.2
PreciControl U2	50.8	16.0	1.69	0.531	3.3

Method comparison

A comparison of the Elecsys Progesterone III assay (y) with ID-GC/MS (x) gave the following correlations (ng/mL):

Number of samples measured: 40

Elecsys Progesterone III

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Passing/Bablok[7]	Linear regression
y = 0.993x + 0.011	y = 0.912x + 0.610
τ = 0.943	r = 0.993

The sample concentrations were between 0.541 and 179 nmol/L (0.17 and 56.3 ng/mL).

Analytical specificity

For the Elecsys Progesterone III assay, the following cross-reactivities (CR; in %) were found at the respective additive concentration (AC; in ng/mL), tested with progesterone concentrations of approximately 0.4 ng/mL and 5.5 ng/mL:

	CR (%)	AC (ng/mL)
Androstendiol	n. d.[c)]	4000
Androstendione	n. d.	80
Aldosterone	n. d.	1000
Allopregnanolone	0.362	2000
Corticosterone	0.682	200
Cortisol	0.004	20000
Danazol	0.001	100000
DHEA-S	n. d.	16000
Norgestrel	n. d.	1000
Estradiol	n. d.	400
Ethisterone	0.002	1000
Ethynodiol diacetate	n. d.	1000
Medroxyprogesterone	n. d.	5000
Norethindrone	n. d.	1000
Norethindrone acetate	n. d.	1000
Testosterone	0.075	2000
21-Deoxycortisol	0.079	2000
11-Deoxycorticosterone	3.93	600
11-Deoxycortisol	0.014	6000
5-α-Dihydrotestosterone	0.24	20
5-β-Dihydroprogesterone	0.247	240
Pregnenolone	0.423	16000
Pregnanolone	0.119	2000
Medroxyprogesterone acetate	0.012	1000
6α-Methylprednisolone	n. d.	1000
17α-Hydroxypregnenolone	0.007	2000
17α-Hydroxyprogesterone	n. d.	2000
20α-Hydroxy-4-pregnen-3-one	0.670	250

c) n. d. = not detectable

References

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7 Bablok W, Passing H, Bender R, et al. A general regression procedure for method transformation. Application of linear regression procedures for method comparison studies in clinical chemistry, Part III. J Clin Chem Clin Biochem 1988 Nov;26(11):783-790.

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

CE 0123

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