ms_05608546190V3.0

PTH (1-84)

cobas®

Parathyroid hormone (parathormone, parathyrin) - PTH, biointact = whole PTH

REF	Σ	SYSTEM
05608546 190	100	Elecsys 2010 MODULAR ANALYTICS E170 **cobas e** 411 **cobas e** 601 **cobas e** 602

English

Please note

The measured PTH (1-84) value of a patient's sample can vary depending on the testing procedure used. The laboratory finding must therefore always contain a statement on the PTH (1-84) assay method used. PTH (1-84) values determined on patient samples by different testing procedures cannot be directly compared with one another and could be the cause of erroneous medical interpretations. Therefore, the results reported by the laboratory to the physician should include: "The following results were obtained with the Elecsys PTH (1-84) assay. Results from assays of other manufacturers cannot be used interchangeably."

The performance characteristics for this assay have not been established for pediatric specimens.

Intended use

Immunoassay for the in vitro quantitative determination of biointact parathyroid hormone, PTH (1-84) in human serum and plasma for the differential diagnosis of hypercalcemia and hypocalcemia. This assay can be used intraoperatively.

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

Summary

Parathyroid hormone (PTH) is formed in the parathyroid glands and secreted into the blood stream. PTH (1-84), also called PTH biointact, consists of a single polypeptide chain containing 84 amino acids and has a molecular weight of approximately 9500 daltons.[1]

PTH has a half-life of only a few minutes and is cleaved into various fragments and cleared very rapidly from the circulation.[2] Measurement of the biologically intact PTH (1-84) permits direct ascertainment of the secretory activity of the parathyroid glands.[3,4]

The main role of PTH is to increase serum calcium, which is achieved by stimulating the release of calcium from bone and its renal reabsorption in the distal tubule. The constancy of the blood calcium level is ensured by the interaction of PTH and calcitonin. The secretion of PTH is inhibited by high calcium concentrations and promoted by low calcium concentrations. PTH also stimulates the activity of the 1-alpha hydroxylase enzyme in the renal proximal tubule, enhancing the synthesis of 1,25 dihydroxy-vitamin D, the active metabolite of vitamin D, which in turn increases intestinal absorption of calcium and exerts an endocrine feed-back on the secretion of PTH at the parathyroid level. PTH also decreases the renal reabsorption of phosphate in the proximal tubule, thereby decreasing serum phosphate.[5]

Furthermore, PTH stimulates bone formation by binding to osteoblastic PTH receptors, therefore enhancing synthesis of collagen type I.[6] This osteoanabolic effect is now used in clinical practice for the treatment of osteoporosis.[7]

Parathyroid gland disorders lead to elevated or depressed blood calcium levels (hypercalcemia or hypocalcemia) caused by a change in the secretion of PTH. Detection of subfunctioning parathyroid glands (hypoparathyroidism) requires the use of a highly sensitive test in order to be able to measure PTH levels well below normal.[8,9]

Hyperfunctioning of the parathyroid glands results in an increased secretion of PTH (hyperparathyroidism). Primary causes are adenomas of the parathyroid glands. In secondary hyperparathyroidism the blood calcium level is low as a result of other pathological states (e.g. vitamin D deficiency). Today, great significance is attached to the determination of the PTH and calcium concentrations when assessing hyperparathyroidism.

Clinical investigations in intraoperative use

The determination of PTH intraoperatively during adenoma resection in the parathyroid glands has also been reported for primary hyperparathyroidism,[10,11,12] secondary hyperparathyroidism relating to renal failure,[13,14] and tertiary hyperparathyroidism post renal transplant surgery.[15]

Because PTH has a reported half life of 3-5 minutes,[16] a significant drop in PTH levels after resection of the abnormal gland enables the surgeon to assess the completeness of resection and whether all hyperfunctioning parathyroid tissue has been removed from the patient.[17]

In 2006, the National Academy of Clinical Biochemistry published their Laboratory Medicine Practice Guidelines for point of care testing, entitled Evidence Based Practice for Point of Care Testing.[18]

The guidelines recommend the use of intraoperative parathyroid hormone testing

1. for patients undergoing surgery for hyperparathyroidism, especially in minimally invasive or directed procedures
2. for patients undergoing reoperation and
3. as a replacement for traditional laboratory measurements of PTH during venous localization in order to help the angiography team guide sampling

The guidelines further recommend for patients undergoing parathyroidectomy for hyperparathyroidism that baseline samples be obtained preoperation exploration and pre-excision of the gland, and that post-excision sampling be drawn at 5 and 10 minutes post resection with a 50 % reduction in PTH concentrations from the highest baseline level which can be used as criteria for surgical success. Additional samples may be necessary as it has been shown that sensitivity can increase with time.[19]

Failure of PTH to drop below recommended levels indicates that

1. either residual hyperfunctioning tissue is still present and further exploration may be necessary, as was in the case of two patients, both with a fifth ectopic parathyroid gland requiring further surgery,[12]
2. or a spike in PTH levels during adenoma mobilization occurred[20]

Intraoperative PTH measurements offer fast, reliable assessment when all hyperfunctioning parathyroid tissue has been removed during the surgical process.

Measurement of PTH (1-84) in patients with chronic kidney disease (CKD)

PTH levels serve as surrogates for bone histology in patients with end-stage renal disease (ESRD), and they are an essential guide to ongoing clinical management, particularly during the treatment of secondary hyperparathyroidism with vitamin D sterols.[21]

The Kidney Disease Outcomes Quality Initiative (KDOQI) and Kidney Disease Improving Global Outcomes (KDIGO) guidelines recommend that serum PTH concentration should be measured regularly in patients with CKD and maintained within the target ranges that are defined according to the stage of CKD.[22,23]

The Elecsys PTH (1-84) assay is a third generation PTH assay[1] as it specifically measures the biologically intact molecule of PTH, PTH (1-84). This can be of advantage in chronic renal failure patients as it was shown that fragments of PTH (i.e. PTH 7-84) accumulate in patients on dialysis presumably due to reduced excretion.[24] However, the proportion of these

PTH (1-84)

cobas®

Parathyroid hormone (parathormone, parathyrin) - PTH, biointact = whole PTH

fragments increases as glomerular filtration rate (GFR) falls, suggesting that this relationship might vary with the severity of renal failure.[25]

Since then, several studies have demonstrated that, in animal or cellular models, PTH (7-84) exerts effects that are opposite to those of PTH (1-84) (decrease in serum calcium and urine phosphate, inhibition of bone resorption), and is produced by the parathyroid glands in response to an increase in serum calcium levels.[26]

Also the ratio between PTH (1-84) and PTH (7-84) was proposed as a predictor for the severity of secondary hyperparathyroidism in dialysis patients.[27,28]

The Elecsys PTH (1-84) assay employs a sandwich test principle in which a biotinylated monoclonal antibody reacts with the N-terminal fragment PTH and a monoclonal antibody labeled with a ruthenium complex[a)] reacts with the C-terminal fragment PTH.

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

Test principle

Sandwich principle. Total duration of assay: 18 minutes.

- 1st incubation: 50 µL of sample, a biotinylated monoclonal PTH-specific antibody, and monoclonal PTH-specific antibody labeled with a ruthenium complex 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.

Reagents - working solutions

The reagent rackpack is labeled as PTH (1-84).

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

R1 Anti-PTH-Ab~biotin (gray cap), 1 bottle, 7 mL: Biotinylated monoclonal anti-PTH antibody (mouse) 2.0 mg/L; phosphate buffer 100 mmol/L, pH 7.0; preservative.

R2 Anti-PTH-Ab~$Ru(bpy)_3^{2+}$ (black cap), 1 bottle, 7 mL: Monoclonal anti-PTH antibody (mouse) labeled with ruthenium complex 1.0 mg/L; phosphate buffer 100 mmol/L, pH 7.0; preservative.

Precautions and warnings

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.

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.

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	84 days
on the analyzers	56 days

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.

K_2-EDTA, K_3-EDTA and Li-heparin plasma as well as Li-heparin plasma tubes containing separating gel.

Because of the short half-life of PTH, it is recommended that, when serum is needed, the blood must be centrifuged immediately.

Preference should be given to K_2-EDTA or K_3-EDTA plasma, as it is stable longer than serum.

Criterion: Method comparison serum versus plasma, slope 0.9-1.1 + intercept within < ± 2 x Limit of Blank (LoB) + coefficient of correlation > 0.95.

Serum: Stable for 7 hours at 15-25 °C, 24 hours at 2-8 °C, 12 weeks at -20 °C.

Plasma (K_2-EDTA, K_3-EDTA): Stable for 24 hours at 15-25 °C, 48 hours at 2-8 °C, 24 weeks at -20 °C.

Plasma (Li-heparin): Stable for 24 hours at 15-25 °C, 48 hours at 2-8 °C, 12 weeks at -20 °C.

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 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 05608554190, PTH (1-84) CalSet, for 4 x 1 mL
- REF 11972227122, PreciControl Bone, for 2 x 2 mL each of PreciControl Bone 1, 2, and 3 or
  REF 05618860190, PreciControl Varia, for 2 x 3 mL each of PreciControl Varia 1 and 2
- REF 11732277122, Diluent Universal, 2 x 16 mL sample diluent or
  REF 03183971122, Diluent Universal, 2 x 36 mL sample diluent
- General laboratory equipment
- Elecsys 2010, MODULAR ANALYTICS E170 or **cobas e** analyzer

Accessories for Elecsys 2010 and **cobas e** 411 analyzers:

- 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, Elecsys 2010 AssayCup, 60 x 60 reaction vessels
- REF 11706799001, Elecsys 2010 AssayTip, 30 x 120 pipette tips

Accessories for MODULAR ANALYTICS E170, **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 Combimagazine M, 48 magazines x 84 reaction vessels or pipette tips, waste bags
- REF 03023150001, WasteLiner, waste bags
- REF 03027651001, SysClean Adapter M

Accessories for all analyzers:

- REF 11298500316, 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.

MODULAR ANALYTICS E170, **cobas e** 601 and **cobas e** 602 analyzers: PreClean M solution is necessary.

Bring the cooled reagents to approx. 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 WHO international standard 95/646.

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). Renewed calibration is recommended as follows:

- after 12 weeks 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 Bone or PreciControl Varia.

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.

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

Calculation

The analyzer automatically calculates the analyte concentration of each sample (either in pg/mL or pmol/L).

Conversion factors:	pg/mL x 0.106 = pmol/L
	pmol/L x 9.43 = pg/mL

Limitations - interference

The assay is unaffected by icterus (bilirubin < 1112 µmol/L or < 65 mg/dL), lipemia (Intralipid < 1500 mg/dL), IgG < 28 g/L, IgM < 8 g/L, IgA < 16 g/L, albumin < 120 g/L and biotin (< 205 nmol/L or < 50 ng/mL).

The assay is affected by hemolysis ≥ 0.1 g/dL. Do not analyze samples that show visible signs of hemolysis.

Criterion: Recovery within ± 12 % of initial value for samples ≥ 25 pg/mL or ± 3 pg/mL for samples < 25 pg/mL.

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 1500 IU/mL.

There is no high-dose hook effect at PTH (1-84) concentrations up to 30000 pg/mL (3180 pmol/L).

In vitro tests were performed on 18 commonly used and 5 special pharmaceuticals. No interference with the assay was found.

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

5.50-2300 pg/mL or 0.583-244 pmol/L (defined by the Limit of Detection and the maximum of the master curve). Values below the Limit of Detection are reported as < 5.50 pg/mL (< 0.583 pmol/L). Values above the measuring range are reported as > 2300 pg/mL (> 244 pmol/L).

Lower limits of measurement

Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantitation (LoQ)

Limit of Blank = 3.50 pg/mL

Limit of Detection = 5.50 pg/mL

Limit of Quantitation = 10.0 pg/mL with a total allowable relative error of ≤ 30 %

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 relative error of ≤ 30 %

PTH (1-84)

cobas®

Parathyroid hormone (parathormone, parathyrin) - PTH, biointact = whole PTH

Dilution

Samples with PTH (1-84) concentrations above the measuring range can be diluted manually with Diluent Universal. The recommended dilution is usually 1:2 if the concentration of PTH (1-84) is > 2300 pg/mL (244 pmol/L). The concentration of the diluted sample must be > 1150 pg/mL (122 pmol/L).

After manual dilution, multiply the results by the dilution factor 2.

Expected values

Normal values in apparently healthy individuals

The normal value range was determined in a clinical study using 596 samples from apparently healthy individuals. The reference population was selected according to normal clinical chemistry parameters, normal hematology results, no vitamin D intake and normal calcium values as determined by flame photometry. The values given are only indicative and may vary from other published data.

N = 596	PTH (1-84) range	
	pg/mL	pmol/L
Mean	31.3	3.32
2.5th percentile	14.9	1.58
97.5th percentile	56.9	6.03

The subgrouping of the above cohort according to the vitamin D (25-OH) level shows the inverse relationship between the concentrations of PTH (intact) and PTH (1-84) and vitamin D (25-OH).

N	Vitamin D (25-OH)	PTH (intact) median		PTH (1-84) median	
	ng/mL	pg/mL	pmol/L	pg/mL	pmol/L
339	≤ 20	41.4	4.39	32.2	3.42
157	> 20 and < 30	37.0	3.92	29.0	3.07
100	≥ 30	33.0	3.49	24.9	2.64

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 (EP5-A2) of the CLSI (Clinical and Laboratory Standards Institute): 2 runs per day in duplication each for 21 days (n = 84). The following results were obtained:

Elecsys 2010 and **cobas e** 411 analyzers					
			Repeatability		
Sample	Mean		SD		CV
	pg/mL	pmol/L	pg/mL	pmol/L	%
Human serum 1	339	35.9	5.29	0.561	1.6
Human serum 2	1398	148	19.5	2.07	1.4
Human serum 3	13.2	1.40	0.976	0.104	7.4
Human serum 4	27.6	2.93	0.870	0.092	3.2
PreciControl Bone 1	67.3	7.13	1.58	0.168	2.4
PreciControl Bone 2	187	19.8	5.37	0.569	2.9
PreciControl Bone 3	716	75.9	9.73	1.03	1.4

Elecsys 2010 and **cobas e** 411 analyzers					
			Intermediate precision		
Sample	Mean		SD		CV
	pg/mL	pmol/L	pg/mL	pmol/L	%
Human serum 1	339	35.9	13.9	1.47	4.1
Human serum 2	1398	148	43.4	4.60	3.1
Human serum 3	13.2	1.40	1.23	0.130	9.4
Human serum 4	27.6	2.93	1.28	0.136	4.7
PreciControl Bone 1	67.3	7.13	4.09	0.443	6.1
PreciControl Bone 2	187	19.8	9.72	1.03	5.2
PreciControl Bone 3	716	75.9	46.7	4.95	6.5

MODULAR ANALYTICS E170, **cobas e** 601 and **cobas e** 602 analyzers					
			Repeatability		
Sample	Mean		SD		CV
	pg/mL	pmol/L	pg/mL	pmol/L	%
Human serum 1	6.35	0.673	0.221	0.023	3.5
Human serum 2	38.3	4.06	0.450	0.048	1.2
Human serum 3	339	35.9	2.58	0.274	0.8
Human serum 4	2028	215	14.9	1.58	0.7
PreciControl Bone 1	59.0	6.25	0.502	0.053	0.9
PreciControl Bone 2	141	15.0	1.82	0.087	1.3
PreciControl Bone 3	628	66.6	4.64	0.492	0.7

MODULAR ANALYTICS E170, **cobas e** 601 and **cobas e** 602 analyzers					
			Intermediate precision		
Sample	Mean		SD		CV
	pg/mL	pmol/L	pg/mL	pmol/L	%
Human serum 1	6.35	0.673	0.394	0.042	6.2
Human serum 2	38.3	4.06	1.16	0.123	3.0
Human serum 3	339	35.9	9.09	0.964	2.7
Human serum 4	2028	215	60.3	6.39	3.0
PreciControl Bone 1	59.0	6.25	1.43	0.152	2.4
PreciControl Bone 2	141	15.0	3.78	0.401	2.7
PreciControl Bone 3	628	66.6	14.5	1.54	2.3

Method comparison

A comparison of the Elecsys PTH (1-84) assay (y) with the Elecsys PTH assay (x) using clinical samples gave the following correlations (pg/mL):

Number of samples measured: 1347

Passing/Bablok[29]	Linear regression
y = 0.668x + 3.02	y = 0.555x + 10.2
τ = 0.927	r = 0.987

The sample concentrations were between approximately 9.38 and 2514 pg/mL (0.994 and 266 pmol/L).

Analytical specificity

- ≤ 0.1 % cross-reactivities: Osteocalcin, β-CrossLaps (collagen-fragment), and bone-specific alkaline phosphatase
- ≤ 0.1 % cross-reactivities: PTH (1-34), PTH (7-84)
- For the N-terminal PTH related peptide (PTH-RP) no cross-reactivity was found in an epitope scan with the monoclonal antibody reactive with PTH N-terminal fragment used in this assay.

PTH (1-84)

cobas®

Parathyroid hormone (parathormone, parathyrin) - PTH, biointact = whole PTH

References

1 Souberbielle JC, Friedlander G, Cormier C. Practical considerations in PTH testing. Clin Chim Acta 2006;366:81-89.

2 Segre GV, Niall HD, Habener JF, et al. Metabolism of parathyroid hormone: physiological and clinical significance. Am J Med 1974;56:774-784.

3 Silverman R, Yalow RS. Heterogeneity of parathyroid hormone: Clinical and physiologic implications. J Clin Invest 1973;52:1958-1971.

4 Flentje D, Schmidt-Gayk H, Fischer S, et al. Intact parathyroid hormone in primary hyperparathyroidism. Br J Surg 1990;77:168-172.

5 Thomas L. Parathyroid hormone (PTH). Clinical Laboratory Diagnosis. TH-Books, Frankfurt. 1st english edition 1998: 248-250.

6 Yu X, Chandrasekhar S. Parathyroid hormone (PTH 1-34) regulation of rat osteocalcin gene transcription. Endocrinology 1997;138:3085-3092.

7 Neer R, Arnaud C, Zanchetta JR, et al. Effect of parathyroid hormone (1-37) on fractures and bone mineral density in postmenopausal women with osteoporosis. N Engl J Med 2001;344:1434-1441.

8 Nussbaum S, Potts JT. Advances in Immunoassays for Parathyroid Hormone. Clinical Applications to Skeletal Disorders of Bone and Mineral Metabolism. In Bilezikian JP, Levine MA, Marcus R (eds). The Parathyroids: Basic an Clinical Concepts. Raven Press, New York 1994:157-169.

9 Berson SA, Yalow RS, Aurbach GD, et al. Immunoassay of bovine and human parathyroid hormone. Proc Natl Acad Sci USA 1963;49:613-617.

10 Bergenfelz A, Nordén NE, Ahrén B. Intraoperative fall in plasma levels of intact parathyroid hormone after removal of one enlarged parathyroid gland in hyperthyroid patients. Eur J Surg 1991;157:109-112.

11 Ohe MN, Santos RO, Kunii IS, et al. Usefulness of a rapid immunometric assay for intra-operative parathyroid hormone measurements. Braz J Med Biol Res 2003;36(6):715-721.

12 Ohe MN, Santos RO, Kunii IS, et al. Usefulness of intra-operative PTH measurement in primary and secondary hyperparathyroidism: experience with 109 patients. Arq Bras Endocrinol Metab 2006;50(5):869-875.

13 Seehofer D, Rayes N, Ulrich F, et al. Intra-operative measurement of intact parathyroid hormone in renal hyperparathyroidism by an inexpensive routine assay. Langenbecks Arch Surg 2001;386(6):440-443.

14 Seehofer D, Rayes N, Klupp J, et al. Predictive value of intact parathyroid hormone measurement during surgery for renal hyperparathyroidism. Langenbecks Arch Surg 2005;390(3):222-229.

15 Haustein SV, Mack E, Starling JR, et al. The role of intra-operative parathyroid hormone testing in patients with tertiary hyperparathyroidism after renal transplantation. Surgery 2005;138(6):1066-1071.

16 Maier GW, Kreis ME, Renn W, et al. Parathyroid hormone after adenectomy for primary hyperparathyroidism: A study of peptide hormone elimination kinetics in humans. Jour Clin Endocrinol Metab 1998;83(11):3853-3856.

17 Carter AB, Howanitz TJ. Intra-operative testing for parathyroid hormone: a comprehensive review of the use of the assay and the relevant literature. Arch Pathol Lab Med 2003;127:1424-1442.

18 Nichols JH, Christenson RH, Clarke W, et al. National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines: Evidence Based Practice for Point of Care Testing. AACC Press:2007.

19 Bergenfelz A, Isaksson A, Lindblom P, et al. Measurement of parathyroid hormone in patients with primary hyperparathyroidism undergoing first and reoperative surgery. Br J Surg 1998;85:1129-1132.

20 Yang GP, Levine S, Weigel RJ. A spike in parathyroid hormone during neck exploration may cause a false-negative intra-operative assay result. Arch Surg 2001;136:945-949.

21 Goodman WG, Salusky IB, Jüppner H. New lessons from old assays: parathyroid hormone (PTH), its receptors, and the potential biological relevance of PTH fragments. Nephrol Dial Transplant 2002;17:1731-1736.

22 National Kidney Foundation. K/DOQI clinical practice guidelines for bone metabolism and diseases in chronic kidney disease. Am J Kidney Dis 2003;42:S1-201.

23 KDIGO – Kidney Disease Improving Global Outcomes KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease-mineral and bone disorder (CKD-MBD) Kidney International 2009;76(Suppl 113).

24 Waller S, Ridout, Cantor T, et al. Differences between “intact” PTH and 1-84 PTH assays in chronic renal failure and dialysis. Pediatr Nephrol 2005;20:197-199.

25 Brossard JH, Lepage R, Cardinal H, et al. Influence of glomerular filtration rate on non-(1-84) parathyroid hormone (PTH) detected by intact PTH assays. Clin Chem 2000;46:697-703.

26 Divieti P, John MR, Juppner H, et al. Human PTH-(7–84) inhibits bone resorption in vitro via actions independent of the type 1 PTH/PTHrP receptor. Endocrinology 2002;143:171-176.

27 Tanaka M, Komaba H, Itoh K, et al. The whole-PTH/intact-PTH ratio is a useful predictor of severity of secondary hyperparathyroidism. NDT Plus 2008;1:[Suppl 3]:iii59–iii62.

28 Inaba M, Okuno S, Imanishi Y, et al. Significance of Bio-intact PTH(1–84) assay in hemodialysis patients. Osteoporos Int 2005;16:517-525.

29 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, the product information 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.

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard.

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

Significant additions or changes are indicated by a change bar in the margin.

PTH (1-84)

cobas®

Parathyroid hormone (parathormone, parathyrin) - PTH, biointact = whole PTH

CE

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com

Roche