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ADVIA Centaur® XP
ADVIA Centaur® XPT
Immunoassay Systems

Intact PTH (iPTH)

Current revision and date [a]	Rev. G, 2020-05	
Product Name	ADVIA Centaur® iPTH assay (500 tests) ADVIA Centaur iPTH assay (100 tests)	**REF** 10492369 **REF** 10492368
Systems	ADVIA Centaur XP system ADVIA Centaur XPT system	
Materials Required but Not Provided	ADVIA Centaur iPTH Calibrator (6 pack) ADVIA Centaur iPTH Calibrator (2 pack)	**REF** 10492387 **REF** 10492394
Specimen Types	EDTA Plasma, Serum	
Assay Range	2.5–1900 pg/mL (0.265–201 pmol/L)	
Reagent Storage	2–8°C	
Reagent On-System Stability	28 days	

a In Rev. B or later, a vertical bar in the margin indicates a technical update to the previous version.

Intended Use

For *in vitro* diagnostic use in the quantitative determination of intact parathyroid hormone (iPTH) in EDTA plasma or serum using the ADVIA Centaur® XP and ADVIA Centaur® XPT systems. This assay is intended to be used to aid in the differential diagnosis of hyperparathyroidism, hypoparathyroidism, or hypercalcemia of malignancy.

Summary and Explanation

Parathyroid hormone (PTH), produced by the parathyroid gland, is the major circulating factor regulating extracellular calcium concentration. Abnormally low-ionized calcium concentrations trigger the secretion of PTH. The PTH molecules bind to type 1 parathyroid hormone receptors in target tissues and initiate a sequence of reactions resulting in increased extracellular calcium concentrations. PTH stimulates osteoclastic bone resorption resulting in the release of calcium from bone. PTH stimulates transcellular calcium reabsorption from the renal tubules and stimulates the kidney to produce 1,25-dihydroxyvitamin D which acts on the intestines to increase calcium reabsorption.[1,2,3] In most clinical conditions, rising levels of extracellular calcium suppresses PTH secretion through a negative feedback mechanism.[4]

Parathyroid hormone increases the rate of bone metabolism. Depending on the age of the patient, the bones involved, and the concentrations of the hormone in circulation over time, the effect on the bone can be either catabolic or anabolic. Consistently high concentrations of parathyroid hormone generally have a catabolic effect and intermittent, slightly elevated concentrations have an anabolic effect.[2]

The intact PTH peptide (MW ~9425) consists of 84 amino acids that are sequenced and designated according to reactivity. The N-terminal or amino-terminal 1-34 region of the intact PTH molecule is biologically active. This region of the molecule contains the amino acid sequence that enables PTH to bind to the parathyroid hormone receptors in target tissues and regulate extracellular calcium concentrations. The middle and carboxy-terminal 35-84 region of the intact PTH molecule is biologically inert but possesses immunological reactivity.[5,6]

The intact PTH molecule undergoes intra- and extra-glandular proteolytic modifications that produce PTH fragments. Circulating PTH is heterogeneous, existing as both the intact PTH and PTH fragments. The PTH peptides have different rates of clearance from the circulation. Intact PTH is cleared by the kidney and liver, and it has a half-life that is less than 4 minutes. The Kupffer cells in the liver are responsible for cleaving the intact molecule into fragments and releasing them into the circulation. Very little, if any, of the amino-terminal PTH fragments are detected in circulation. The middle and carboxy-terminal PTH fragments vary in size, have longer half-lives, and are primarily cleared in the kidney by glomerular filtration. Under normal conditions, there is a greater relative concentration of circulating middle and carboxy-terminal PTH fragments. In renal insufficiency where glomerular filtration is impaired, the concentration of middle and carboxy-terminal PTH fragments is increased. The ratio of the circulating concentrations of intact PTH to middle and carboxy-terminal PTH can vary between individuals, particularly in patients with chronic renal failure.[1,2,5,6]

Quantification of circulating intact PTH assists in the differential diagnosis of hypercalcemia and hypocalcemia. In conjunction with the measurement of ionized calcium, intact PTH evaluations can be used to distinguish between patients with hyperparathyroidism, hypoparathyroidism, or hypercalcemia of malignancy. The diagnosis of primary hyperparathyroidism, a common cause of hypercalcemia, is confirmed by elevated, ionized calcium concentrations and elevated parathyroid hormone concentrations. Intact PTH levels are also used to assess and manage other metabolic bone disorders, including osteoporosis and renal osteodystrophy.[1,2,7,8] The measurement of intact PTH using two-site immunoassays provides a more accurate assessment of parathyroid tissue secretory status, especially in patients with renal impairment.[9]

The clinical utility of parathyroid hormone as a therapeutic agent has been recently investigated. Studies have shown that when slightly elevated concentrations of PTH are administered, the resulting anabolic effect on bones can protect the aging skeleton, promote fracture healing, and restore bone loss in immobilized patients. N-terminal PTH preparations are also being investigated in the treatment and prevention of osteoporosis. These preparations appear to increase bone mass and bone formation without inducing hypercalcemia.[10–12]

Principles of the Procedure

The ADVIA Centaur iPTH assay is a two-site sandwich immunoassay using direct chemiluminometric technology, which uses constant amounts of an antihuman PTH antibody in the Lite Reagent and an antihuman PTH antibody in the Solid Phase Reagent. The first antibody is a polyclonal goat antihuman PTH (N-terminal 1-34) antibody labeled with acridinium ester. The second antibody is a biotinylated polyclonal goat antihuman PTH (39-84 region) antibody. Streptavidin in the Solid Phase is covalently coupled to paramagnetic latex particles.

Reagents

Reagent	Description	Storage	Reagent Stability
ADVIA Centaur iPTH ReadyPack® primary reagent pack; Lite Reagent	5.0 mL/reagent pack acridinium ester-labeled polyclonal goat antihuman PTH (1-34 N-terminal) antibody (~1 µg/mL) in phosphate buffered saline with goat IgG, bovine gamma globulin, bovine serum albumin, and preservatives	2–8°C	**Unopened:** Stable until the expiration date on the carton **On-system:** 28 days
ADVIA Centaur iPTH ReadyPack primary reagent pack; Solid Phase Reagent	20.0 mL/reagent pack biotinylated polyclonal goat anti-human PTH (39-84 region) antibody (~3 µg/mL) and streptavidin (~0.4 mg/mL) covalently coupled to paramagnetic latex particles in phosphate buffered saline with goat IgG, bovine gamma globulin, bovine serum albumin, and preservatives	2–8°C	**Unopened:** Stable until the expiration date on the carton **On-system:** 28 days
ADVIA Centaur ReadyPack ancillary reagent pack; Multi-Diluent 11[a] M·DIL 11	5 mL/reagent pack tris buffer and goat serum with protein stabilizers and preservatives	2–8°C	**Unopened:** Stable until the expiration date on the pack label **On-system:** 28 consecutive days after accessing the ancillary reagent pack
ADVIA Centaur Multi-Diluent 11[a] M·DIL 11	10 mL/vial tris buffer and goat serum with protein stabilizers and preservatives	2–8°C	**Unopened:** Stable until the expiration date on the vial

a See *Optional Materials*

Warnings and Precautions

Safety data sheets (MSDS/SDS) available on siemens.com/healthcare.

CAUTION

This device contains material of animal origin and should be handled as a potential carrier and transmitter of disease.

Dispose of hazardous or biologically contaminated materials according to the practices of your institution. Discard all materials in a safe and acceptable manner and in compliance with prevailing regulatory requirements.

For *in vitro* diagnostic use.

Preparing Reagents

All reagents are liquid and ready to use.

Mix all primary reagent packs by hand before loading them onto the system. Visually inspect the bottom of the reagent pack to ensure that all particles are dispersed and resuspended. For detailed information about preparing the reagents for use, refer to the system operating instructions.

Note

- Discard the primary reagent packs at the end of the on-system stability interval.
- Do not use reagents beyond the expiration date.

Storing and Stability

Store the reagents upright at 2–8°C.

Protect reagent packs from all heat and light sources. Reagent packs loaded on the system are protected from light. Store unused reagent packs at 2–8°C away from heat and light sources.

All reagents are stable at 2–8°C until the expiration date on the packaging.

Specimen Collection and Handling

EDTA plasma or serum is the recommended sample type for this assay.

The following recommendations for handling and storing blood samples are furnished by the Clinical and Laboratory Standards Institute (CLSI):[13]

- Collect all blood samples observing universal precautions for venipuncture.
- Centrifuge samples at ≥ 1000 x g for 15–20 minutes.
- Keep tubes stoppered and upright at all times.
- Freeze samples only once and mix thoroughly after thawing.

Correct handling of patient samples is critical to ensure the integrity of the intact PTH molecule. Intact PTH has been demonstrated to be labile and is susceptible to fragmentation. This instability depends on both time and temperature. Patient sample stability is outlined in the following table:

Temperature	EDTA Plasma Stability	Serum Stability
Room Temperature	8 hours	4 hours
4°C	72 hours	48 hours
-70°C	8 months	Not tested

The purpose of handling and storage information is to provide guidance to users. It is the responsibility of the individual laboratory to use all available references and/or its own studies when establishing alternate stability criteria to meet specific needs.

Procedure

Materials Provided

The following materials are provided:

REF	Contents	Number of Tests
10492369	5 ReadyPack primary reagent packs containing ADVIA Centaur iPTH Lite Reagent and Solid Phase	500
	ADVIA Centaur and ADVIA Centaur CP iPTH Master Curve card	
10492368	1 ReadyPack primary reagent pack containing ADVIA Centaur iPTH Lite Reagent and Solid Phase	100
	ADVIA Centaur and ADVIA Centaur CP iPTH Master Curve card	

Materials Required but Not Provided

The following materials are required to perform this assay, but are not provided:

Item	Description	
REF 10492387	ADVIA Centaur iPTH Calibrator	6 vials of low calibrator CAL L 6 vials of high calibrator CAL H
REF 10492394	ADVIA Centaur iPTH Calibrator	2 vials of low calibrator CAL L 2 vials of high calibrator CAL H

Optional Materials

The following materials may be used to perform this assay, but are not provided:

Item	Description	
REF 05699280 (117228)	ADVIA Centaur Multi-Diluent 11 M-DIL 11	2 ReadyPack ancillary reagent packs containing 5 mL/pack
REF 03479704 (111088)	ADVIA Centaur Multi-Diluent 11 M-DIL 11	10 mL/vial
REF 10492378	ADVIA Centaur iPTH 1, 2, 3 quality control material	2 x 1 mL control 1 CONTROL 1 2 x 1 mL control 2 CONTROL 2 2 x 1 mL control 3 CONTROL 3
REF 10492373	ADVIA Centaur iPTH Master Curve Material	7 x 1 mL

Assay Procedure

For detailed instructions on performing the procedure, refer to the system operating instructions.

The system automatically performs the following actions:

- Dispenses 200 µL of sample into a cuvette.
- Dispenses 50 µL of Lite Reagent and incubates for 5.0 minutes at 37°C.
- Dispenses 200 µL of Solid Phase and incubates for 2.5 minutes at 37°C.
- Separates, aspirates, and washes the cuvettes with reagent water.

  Note For information about reagent water, refer to the system operating instructions.
- Dispenses 300 µL each of Acid Reagent and Base Reagent to initiate the chemiluminescent reaction.
- Reports results according to the selected option, as described in the system operating instructions.

A direct relationship exists between the amount of PTH present in the patient sample and the amount of relative light units (RLUs) detected by the system.

Preparing the System

Ensure that the system has sufficient primary and ancillary reagent packs. For detailed information about preparing the system, refer to the system operating instructions.

Load the ReadyPack reagent packs in the primary reagent area using the arrows as a placement guide. The system automatically mixes the primary reagent packs to maintain homogeneous suspension of the reagents. For detailed information about loading reagents, refer to the system operating instructions.

If automatic dilution of a sample is required, load ADVIA Centaur Multi-Diluent 11 in the ancillary reagent entry.

Preparing the Samples

This assay requires 200 µL of sample for a single determination. This volume does not include the unusable volume in the sample container or the additional volume required when performing duplicates or other tests on the same sample. For detailed information about determining the minimum-required volume, refer to the system operating instructions.

Note The sample volume required to perform onboard dilution differs from the sample volume required to perform a single determination. For detailed information, refer to *Dilutions*.

Before placing samples on the system, ensure that samples have the following characteristics:

- Samples are free of fibrin or other particulate matter.
- Samples are free of bubbles.

On-System Stability

The ADVIA Centaur iPTH assay reagents are stable unopened until the expiration date on the carton or onboard the system for 28 days.

Performing Calibration

For calibration of the ADVIA Centaur iPTH assay, use the ADVIA Centaur iPTH Calibrator. Perform that calibration as described in the calibrator instructions for use.

Calibration Frequency

Calibrate the assay at the end of the 14-day calibration interval.

Additionally, the ADVIA Centaur Intact PTH assay requires a two-point calibration:

- When changing lot numbers of primary reagent packs.
- When replacing system components.
- When quality control results are repeatedly out of range.

Performing Master Curve Calibration

The ADVIA Centaur Intact PTH assay requires a Master Curve calibration when using a new lot number of Lite Reagent and Solid Phase. For each new lot number of Lite Reagent and Solid Phase, use the bar-code reader or keyboard to enter the Master Curve values on the system. The Master Curve card contains the Master Curve values. For detailed information about entering calibration values, refer to the system operating instructions.

Performing Quality Control

Follow government regulations or accreditation requirements for quality control frequency.

For detailed information about entering quality control values, refer to the system operating instructions.

To monitor system performance and chart trends, as a minimum requirement, two levels of quality control material should be assayed on each day that samples are analyzed. Quality control samples should also be assayed when performing a two-point calibration. Treat all quality control samples the same as patient samples.

Siemens Healthcare Diagnostics recommends the use of iPTH quality control material or equivalent commercially available control materials with at least 2 levels (low and high). A satisfactory level of performance is achieved when the analyte values obtained are within the Acceptable Control range for the system or within your range, as determined by an appropriate internal laboratory quality control scheme.

Taking Corrective Action

If the quality control results do not fall within the Expected Values or within the laboratory's established values, do not report results. Take the following actions:

1. Determine and correct the cause of the unacceptable control results:
   a. Verify that the materials are not expired.
   b. Verify that required maintenance was performed.
   c. Verify that the assay was performed according to the instructions for use.
   d. Rerun the assay with fresh quality control samples, and confirm that quality control results are within acceptable limits before running patient samples.
   e. If the quality control results are not within acceptable limits, recalibrate the assay, and repeat step d.
   f. If necessary, contact your local technical support provider or distributor for assistance.
2. Repeat testing of patient samples before reporting results.

Perform corrective actions in accordance with your established laboratory protocol.

Results

Calculation of Results

For detailed information about how the system calculates results, refer to the system operating instructions.

The system reports intact PTH results in pg/mL (common units) or pmol/L (SI units), depending on the units defined when setting up the assay. The conversion formula is 1 pg/mL = 0.106 pmol/L.

Dilutions

The sample volume required to perform onboard dilution differs from the sample volume required to perform a single determination. Refer to the following information for the sample volume required to perform onboard dilutions:

Dilution	Sample Volume (µL)
1:5	40

The following information pertains to dilutions:

- Patient samples with intact PTH levels greater than 1900 pg/mL must be diluted and retested to obtain accurate results.
- Patient samples can be automatically diluted by the system or prepared manually.
- For automatic dilutions, ensure that ADVIA Centaur Multi-Diluent 11 is loaded and set the system parameters as follows:

  Dilution point: ≤ 1900 pg/mL

  Dilution factor: 5

  For detailed information about automatic dilutions, refer to the system operating instructions.
- Manually dilute the patient samples when patient results exceed the linearity of the assay using automatic dilution, or when laboratory protocol requires manual dilution.
- Use Multi-Diluent 11 to manually dilute patient samples, and then load the diluted sample in the sample rack, replacing the undiluted sample.
- Ensure that results are mathematically corrected for dilution. If a dilution factor is entered when scheduling the test, the system automatically calculates the result.

Interpretation of Results

Results of this assay should always be interpreted in conjunction with patient's medical history, clinical presentation and other findings.

Limitations

Results should always be interpreted in conjunction with the patient's medical history, clinical presentation, and other findings.

Interpretation of intact PTH values should always take into account serum calcium results and the interrelationship between these two elements in various disorders involving PTH and calcium. It is recommended that the intact PTH results should always be interpreted with caution and with consideration of the overall clinical manifestations even when used in conjunction with calcium values.

It should be noted that some overlap of intact PTH values does exist from patients with various parathyroid disorders.

Measurement of intact PTH is useful in differentiating between hypercalcemia due to hyperparathyroidism and hypercalcemia of malignancy. However, the assay is not intended as, and should not be relied upon as, a diagnostic indicator of malignancy.

It is also extremely important to ensure that patient samples have been handled and stored correctly. Incorrect handling of samples will result in a loss of intact PTH.

The type of specimen used (serum or EDTA plasma) may influence Intact PTH measurements.[14,15] During routine monitoring of iPTH levels, to avoid bias in the results, use the same specimen type throughout the monitoring period.

Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays.[16] Patients routinely exposed to animals or to animal serum products can be prone to this interference and anomalous values may be observed. Additional information may be required for diagnosis.

Expected Values

Results should always be interpreted in conjunction with the patient's medical history, clinical presentation, and other findings.

The reference range was established on the ACS:180® system. EDTA plasma samples were obtained from 142 apparently healthy individuals whose calcium levels ranged from 8.0 to 10.3 mg/dL. Ninety-five percent of the intact PTH values for these individuals fell in the range of 14 to 72 pg/mL (1.48 to 7.63 pmol/L) with an overall range of 11.1 to 79.5 pg/mL (1.18 to 8.43 pmol/L).

These results were confirmed for the ADVIA Centaur Intact PTH assay. Refer to *Accuracy /Method Comparison*.

As with all *in vitro* diagnostic assays, each laboratory should determine its own reference range(s) for the diagnostic evaluation of patient results.[17]

Performance Characteristics

Analytical Measuring Range

The ADVIA Centaur iPTH assay measures intact parathyroid hormone concentrations from 2.5–1900 pg/mL (0.265–201 pmol/L).

Specificity

The cross-reactivity of the ADVIA Centaur Intact PTH assay was determined by spiking samples with the PTH fragments and compounds listed below at the indicated levels. There was no significant effect on the intact PTH measurement.

Cross-reactant	Amount Added (pg/mL)	% Cross-reactivity
PTH (1-34) fragment	300	0.74
PTH (39-68) fragment	100,000	0.005
PTH (39-84) fragment	100,000	0.024
PTH (44-68) fragment	100,000	0.007
PTH (53-84) fragment	100,000	0.003
Calcitonin	100,000	0.0004

Interference testing was determined according to CLSI Document EP7-A2.[18]

Sensitivity

The ADVIA Centaur Intact PTH assay measures intact PTH concentrations up to 1900 pg/mL (201 pmol/L) with a minimum detectable concentration (analytical sensitivity) of 2.5 pg/mL (0.265 pmol/L). Analytical sensitivity is defined as the concentration of intact PTH that corresponds to the RLUs that are two standard deviations greater than the mean RLUs of 20 replicate determinations of the Intact PTH zero standard.

Precision

Three samples were assayed 12 times, in each of 12 runs, on 3 systems, (n = 144 for each sample), over a period of 4 days. The following results were obtained:

Mean (pg/mL)	Mean (pmol/L)	Within-Run % CV	Run-to-Run % CV	Total % CV
40.4	4.3	5.2	5.8	7.8
223.8	23.7	3.4	1.5	7.0
859.3	91.1	3.5	2.8	4.6

Accuracy / Method Comparison

For 185 samples in the range of 15.0 to 1908.4 pg/mL (1.58 to 202.3 pmol/L), the relationship between the ADVIA Centaur Intact PTH assay and the ACS:180 Intact PTH assay is described by the equation:

ADVIA Centaur Intact PTH = 0.95 (ACS:180 Intact PTH) + 6.48 pg/mL

Correlation coefficient (r) = 0.99

Interferences

Specimens that are . . .	Demonstrate ≤ 10% change in results up to . . .
hemolyzed	200 mg/dL of hemoglobin
lipemic	3000 mg/dL of triglycerides
icteric	40 mg/dL of bilirubin
biotin	1000 ng/mL of biotin

Dilution Recovery

Five human plasma samples in the range of 1040.2 to 1824.1 pg/mL (110.3 to 193.4 pmol/L) of intact PTH were diluted 1:2, 1:4, and 1:8 with Multi-Diluent 11 and assayed for recovery and parallelism. The recoveries ranged from 91.3 to 116.3% with a mean of 99.8%.

Sample	Dilution	Observed (pg/mL)	Expected (pg/mL)	Observed (pmol/L)	Expected (pmol/L)	Recovery %
1	—	1573.9		166.8		
	1:2	718.2	787.0	76.1	83.4	91.3
	1:4	363.1	393.5	38.5	41.7	92.3
	1:8	192.7	196.7	20.4	20.9	98.0
	Mean					93.9
2	—	1578.8		167.4		
	1:2	743.5	789.4	78.8	83.7	94.2
	1:4	362.0	394.7	38.4	41.9	91.7
	1:8	186.8	197.4	19.8	20.9	94.6
	Mean					93.5
3	—	1155.7		122.5		
	1:2	604.2	577.9	64.1	61.3	104.6
	1:4	314.0	288.9	33.3	30.6	108.7
	1:8	168.1	144.5	17.8	15.3	116.3
	Mean					109.9
4	—	1824.1		193.4		
	1:2	880.1	912.1	93.3	96.7	96.5
	1:4	438.5	456.0	46.5	48.3	96.2
	1:8	219.8	228.0	23.3	24.2	96.4
	Mean					96.4
5	—	1040.2		110.3		
	1:2	525.2	520.1	55.7	55.1	101.0
	1:4	270.4	260.1	28.7	27.6	104.0
	1:8	145.1	130.0	15.4	13.8	111.6
	Mean					105.5
Mean						**99.8**

Spiking Recovery

Varying amounts of intact PTH were added to 5 samples with endogenous intact PTH levels of 37.8 to 178.7 pg/mL (4.0 to 19.0 pmol/L). The recoveries ranged from 91.0 to 123.6% with a mean of 105.0%.

Sample	Amount Added (pg/mL)	Observed (pg/mL)	Amount Added (pmol/L)	Observed (pmol/L)	Recovery %
1	—	148.0	—	15.7	
	24	156.6	2.5	16.6	91.0
	50	192.7	5.3	20.4	97.3
	123	278.8	13.0	29.6	102.9
	292	470.9	31.0	49.9	107.0
	796	1031.2	84.4	109.4	109.2
	Mean				101.5
2	—	178.7	—	19.0	
	24	195.2	2.5	20.7	96.3
	50	218.3	5.3	23.1	95.4
	123	318.7	13.0	33.8	105.6
	292	531.1	31.0	56.3	112.8
	796	1142.2	84.4	121.1	117.2
	Mean				105.5
3	—	106.2	—	11.3	
	24	129.9	2.5	13.8	99.8
	50	162.5	5.3	17.2	104.0
	123	245.7	13.0	26.1	107.2
	292	492.3	31.0	52.2	123.6
	796	1053.4	84.4	111.7	116.8
	Mean				110.3
4	—	77.5	—	8.2	
	24	98.1	2.5	10.4	96.7
	50	121.2	5.3	12.9	95.1
	123	191.7	13.0	20.3	95.6
	292	397.6	31.0	42.2	107.6
	796	955.5	84.4	101.3	109.4
	Mean				100.9

Sample	Amount Added (pg/mL)	Observed (pg/mL)	Amount Added (pmol/L)	Observed (pmol/L)	Recovery %
5	—	37.8	—	4.0	
	24	60.0	2.5	6.4	97.1
	50	83.0	5.3	8.8	94.5
	123	173.7	13.0	18.4	108.0
	292	398.0	31.0	42.2	120.7
	796	951.9	84.4	100.9	114.2
	Mean				106.9
Mean					**105.0**

High-Dose Hook Effect

Patient samples with high intact PTH levels can cause a paradoxical decrease in the RLUs (high-dose hook effect). In this assay, patient samples with intact PTH levels as high as 100,000 pg/mL (10,600 pmol/L) do not demonstrate a paradoxical decrease in the RLUs (high-dose hook effect).

Standardization

The ADVIA Centaur Intact PTH assay standardization is maintained with internal standards manufactured using purified human PTH (1-84). The ADVIA Centaur Intact PTH assay is traceable to World Health Organization (WHO) standard preparation 79/500. The average recovery of WHO material is 73% over the full range of the assay. Assigned values for calibrators are traceable to this standardization.

Technical Assistance

For customer support, please contact your local technical support provider or distributor.

siemens.com/healthcare

References

1. Mundy GR, Guise TA. Hormonal control of calcium homeostasis. *Clin Chem*. 1999;45:1347–1352.
2. Marx SJ. Hyperparathyroid and hypoparathyroid disorders. *N Engl J Med*. 2000;343:1863–1875.
3. Friedman PA. Mechanisms of renal calcium transport. *Exp Nephrol*. 2000;8(6):343–350.
4. Akizawa T, Fukagawa M. Modulation of parathyroid cell function by calcium ion in health and uremia. *Am J Med Sci*. 1999;317(6):358–362.
5. Itani O, Tsang RC. Bone disease. In: Kaplan LA, Pesce AJ. *Clinical Chemistry: Theory, Analysis, and Correlation*, 3rd ed. St. Louis: CV Mosby; 1996:534–536.
6. Endres DB, Rude RK. Mineral and bone metabolism. In: Burtis CA. Ashwood, ER. *Tietz Textbook of Clinical Chemistry*, 2nd ed. Philadelphia: WB Saunders; 1994:1914–1922.
7. Casez J, Pfammatter R, Nguyen Q, Lippuner K, Jaeger P. Diagnostic approach to hypercalcemia: relevance of parathyroid hormone and parathyroid hormone-related protein measurements. *Euro Jour of Int Med*. 2001;12(4):344–349.
8. Johnson LR, Doherty G, Lairmore T, *et al*. Evaluation of the performance and clinical impact of a rapid intraoperative parathyroid hormone assay in conjunction with preoperative imaging and concise parathyroidectomy. *Clin Chem*. 2001;47:919–925.

9. Lepage R, Roy L, Brossard JH, *et al*. A non-(1–84) circulating parathyroid hormone (PTH) fragment interferes significantly with intact PTH commercial assay measurements in uremic samples. *Clin Chem*. 1998;44:805–809.
10. Bilezikian JP, Silverberg SJ. Parathyroid hormone. Does it have a role in the pathogenesis of osteoporosis? *Clin Lab Med*. 2000;20(3):559–567.
11. Raisz LG. Physiology and pathophysiology of bone remodeling. *Clin Chem*. 1999;45:1353–1358.
12. Morley P, Whitfield JF, Willick GE. Parathyroid hormone: an anabolic treatment for osteoporosis. *Current Pharmaceutical Design*. 2001;7(8):671–687.
13. Clinical and Laboratory Standards Institute (formerly NCCLS). *Procedures for the Handling and Processing of Blood Specimens; Approved Guideline - Third Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2004. NCCLS Document H18-A3.
14. Glendenning P, Laffer LLA, Weber HK, Musk AA, Vasikaran SD. Parathyroid hormone is more stable in EDTA plasma than in serum. *Clin Chem*. 2002;48:766–767.
15. Teal TK, Wood JL, Stevens PE, Lamb EJ. Stability of Bio-Intact (1-84) Parathyroid hormone *ex vivo* in serum and EDTA plasma from hemodialysis patients. *Clin Chem*. 2004;50:1713–1714.
16. Boscato LM, Stuart MC. Heterophilic antibodies: a problem for all immunoassays. *Clin Chem*. 1988;34:27–33.
17. Clinical and Laboratory Standards Institute (formerly NCCLS). *How to Define and Determine Reference Intervals in the Clinical Laboratory; Approved Guideline - Second Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2000. NCCLS Document C28-A2.
18. Clinical and Laboratory Standards Institute (formerly NCCLS). *Interference Testing in Clinical Chemistry; Approved Guideline - Second Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2005. NCCLS Document EP7-A2.

Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Definition	Symbol	Definition
IVD	*In vitro* diagnostic medical device	REF REF	Catalog number
	Legal manufacturer	EC REP	Authorized Representative in the European Community
CE	CE Mark	CE 0088	CE Mark with identification number of notified body
	Consult instructions for use		Biological risk
0°C	Do not freeze (> 0°C)		Temperature limitation
	Lower limit of temperature		Upper limit of temperature
	Keep away from sunlight and heat	UP	Up
	Use by	Σ (n)	Contains sufficient for (n) tests
LOT	Batch code		Shake the reagent pack vigorously. Refer to *Preparing Reagents* in the assay-specific ADVIA Centaur product instructions for detailed information.
YYYY-MM-DD	Date format (year-month-day)	Rev.	Revision
MC DEF	Master Curve Definition	CHECKSUM	Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid.
LOT DTL	Lot Details	DER GRÜNE PUNKT	Green dot
	Recycle	PRINTED WITH SOY INK	Printed with soy ink

Trademarks

ADVIA Centaur, ReadyPack, and ACS:180 are trademarks of Siemens Healthcare Diagnostics.

US Pats 5,609,822; 5,788,928

Siemens Healthcare Diagnostics Inc.
511 Benedict Avenue
Tarrytown, NY 10591 USA

Global Siemens Headquarters
Siemens AG
Wittelsbacherplatz 2
80333 Muenchen
Germany

Global Siemens Healthcare Headquarters
Siemens AG
Healthcare Sector
Henkestrasse 127
91052 Erlangen
Germany
Phone: +49 9131 84-0
www.siemens.com/healthcare

Global Division
Siemens Healthcare
Diagnostics Inc.
511 Benedict Avenue
Tarrytown, NY 10591
USA
www.siemens.com/healthcare