SIEMENS

CE 0197

ADVIA Centaur® CP
Immunoassay Systems

Intact Parathyroid Hormone (PTH)

Current revision and date[a]	Rev. 08, 2023-03	
Product Name	ADVIA Centaur® PTH (100 tests)	REF 10699154
	ADVIA Centaur PTH (500 tests)	REF 10699155
Systems	ADVIA Centaur CP system	
Materials Required but Not Provided	ADVIA Centaur Wash 1 (2 x 1500 mL)	REF 01137199 (112351)
	ADVIA Centaur Wash 1 (2 x 2500 mL)	REF 03773025
Specimen Types	Human serum, plasma (lithium heparin, sodium heparin, EDTA)	
Measuring Interval	4.6–2000 pg/mL (0.488–212 pmol/L)	
Reagent Storage	2–8°C	
Reagent On-System Stability	28 days	

[a] A vertical bar in the page margin indicates technical content that differs from the previous version.

Intended Use

The ADVIA Centaur® Intact Parathyroid Hormone (PTH) reagent is for *in vitro* diagnostic use in the quantitative determination of intact parathyroid hormone (PTH) in human serum and plasma using the ADVIA Centaur CP system. This assay is intended to be used to aid in the differential diagnosis of hyperparathyroidism, hypoparathyroidism, or disorders of calcium metabolism. This assay can be used intra-operatively.

Summary and Explanation

Parathyroid hormone (also known as parathormone or parathyrin) is secreted by the chief cells of the parathyroid glands as a polypeptide that contains 84 amino acids. PTH has a molecular weight of 9.4 kDa and is excreted through the kidneys with a half-life of approximately 4 minutes. PTH is the most important endocrine regulator of circulating calcium and phosphorus concentrations. Its contribution to calcium homeostasis is accomplished through its effects on bone, kidney, and intestine.

Abnormally low ionized calcium concentrations trigger the secretion of PTH. The hormone stimulates osteoclastic bone resorption and transcellular calcium reabsorption from the renal tubules. Additionally, PTH indirectly stimulates Ca^{++} absorption in the small intestine by stimulating synthesis of 1,25-dihydroxyvitamin D in the kidney.[1–4] Conversely, if calcium levels are abnormally elevated, the parathyroid glands reduce PTH production through a negative feedback mechanism.[4]

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 normal or elevated PTH concentrations.

Intact PTH levels are also used to assess and manage other metabolic bone disorders, including osteoporosis and renal osteodystrophy.[5,6] Additionally, intra-operative PTH measurement can be used, in conjunction with improved pre-operative localization methods (ultrasound and Sesta-MIBI scan), to control the success of parathyroidectomy for both primary and renal hyperparathyroidism.

The National Academy of Clinical Biochemistry[7] recommends the use of intra-operative parathyroid hormone testing for:

- Patients undergoing initial surgery for primary hyperparathyroidism
- Patients undergoing re-operative hyperparathyroidism
- During pre-operative localization in patients with primary hyperparathyroidism.

PTH values can vary depending on the testing procedure used. When monitoring patients over time, PTH values obtained with different methods should not be used interchangeably.

Principles of the Procedure

The ADVIA Centaur PTH assay is a 2-site sandwich immunoassay using direct chemiluminometric technology, which uses constant amounts of 2 anti-human PTH antibodies. The first antibody in the Lite Reagent is a monoclonal mouse anti-human PTH (N-terminal) antibody labeled with acridinium ester. The second antibody is a biotinylated monoclonal mouse anti-human PTH (C-terminal) antibody that is bound to streptavidin-coated paramagnetic latex particles in the Solid Phase.

Reagents

Reagent	Description	Storage	Reagent Stability
ADVIA Centaur PTH ReadyPack® primary reagent pack; Lite Reagent	10.0 mL/reagent pack Acridinium-ester-labeled mouse monoclonal anti-human PTH antibody (~0.6 mg/L) in buffered saline with mouse gamma globulin, bovine serum albumin, and preservatives	2–8°C	**Unopened:** Stable until the expiration date on the product **On-system:** 28 days
ADVIA Centaur PTH ReadyPack primary reagent pack; Solid Phase Reagent	20.0 mL/reagent pack Biotinylated mouse monoclonal anti-human PTH antibody bound to streptavidin-coated paramagnetic particles (~0.4 g/L) in buffered saline with bovine gamma globulin, bovine serum albumin, and preservatives	2–8°C	**Unopened:** Stable until the expiration date on the product **On-system:** 28 days
ADVIA Centaur PTH Calibrator	1.0 mL/vial After reconstitution, low or high levels of intact PTH synthetic peptide in buffered saline with human EDTA plasma (10%), surfactants, and preservatives	2–8°C 18–25°C ≤ -20°C	**Unopened**: Stable until the expiration date on the product **Reconstituted**: 8 hours **Reconstituted**: 60 days[a] **On-system:** 8 hours
ADVIA Centaur Wash 1[b] WASH 1	1500 mL/pack Phosphate-buffered saline with sodium azide (< 0.1%) and surfactant	2–25°C	**Unopened:** Stable until the expiration date on the product **On-system:** 1 month
ADVIA Centaur Wash 1[b] WASH 1	2500 mL/pack Phosphate-buffered saline with sodium azide (< 0.1%) and surfactant	2–25°C	**Unopened:** Stable until the expiration date on the product **On-system:** 1 month

Reagent	Description	Storage	Reagent Stability
ADVIA Centaur ReadyPack ancillary reagent pack; Multi-Diluent 13[c] M-DIL	10 mL/reagent pack Buffer with surfactant and sodium azide (< 0.1%)	2–8°C	**Unopened:** Stable until the expiration date on the product **On-system:** 28 consecutive days after the ancillary reagent pack is pierced

[a] Freeze and thaw the calibrators one time only.
[b] Refer to *Materials Required but Not Provided*.
[c] Refer to *Optional Materials*.

Warnings and Precautions

Safety data sheets (MSDS/SDS) are available on siemens-healthineers.com.

WARNING! POTENTIAL BIOHAZARD

Contains human source material.

No known test method can ensure that products derived from human source materials will not transmit infection. These materials should be handled using good laboratory practices and universal precautions.[8–10]

H412	Harmful to aquatic life with long lasting effects.
P273, P501	Avoid release to the environment. Dispose of contents and container in accordance with all local, regional, and national regulations. **Contains**: 2-methyl-2H-isothiazol-3-one hydrochloride; 5-bromo-5-nitro-1,3-dioxane (ADVIA Centaur PTH Calibrator)

Contains 2-methyl-2H-isothiazol-3-one hydrochloride. May produce an allergic reaction. (ADVIA Centaur PTH Calibrator)

Contains sodium azide as a preservative. Sodium azide can react with copper or lead plumbing to form explosive metal azides. On disposal, flush reagents with a large volume of water to prevent buildup of azides. Disposal into drain systems must be in compliance with prevailing regulatory requirements.

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.

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare professional.

For professional use.

For *in vitro* diagnostic use.

Preparing Reagents

All ADVIA Centaur PTH ReadyPack reagents are liquid and ready to use. Remove the reagents from the refrigerator, and mix the primary reagent pack by hand. Visually inspect the bottom of the reagent pack to ensure that all particles are dispersed and resuspended before loading it onto the system. 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 unopened reagents upright at 2–8°C.

Protect unopened reagent packs from all heat and light sources. Reagent packs loaded on the system are protected from light.

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

Specimen Collection and Handling

Human serum and plasma (lithium heparin, sodium heparin, EDTA) are the recommended specimen types for this assay.

Collecting the Specimen

- Serum and plasma can be collected using recommended procedures for collection of diagnostic blood specimens by venipuncture.[11]
- Follow the instructions provided with your specimen collection device for use and processing.[12]
- For serum specimens, complete clot formation should take place before centrifugation. Serum should be physically separated from cells as soon as possible with a maximum limit of 2 hours from the time of collection.[13]
- Centrifuge samples at ≥ 1000 x g for 15–20 minutes.
- Keep tubes stoppered and upright at all times.

Storing the Specimen

- 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:

		Plasma Stability		
Temperature	**Serum Stability**	**EDTA**	**Lithium Heparin**	**Sodium Heparin**
25°C	8 hours	25 hours	9 hours	9 hours
2–8°C	8 hours	14 days	72 hours	72 hours
Frozen	1 month @ -20°C	Not recommended	Not recommended	Not recommended

- Thawed frozen specimens must be clarified by centrifugation prior to testing.

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.

Transporting the Specimen

Package and label samples for shipment in compliance with applicable federal and international regulations covering the transport of clinical samples and etiological agents.

Procedure

Materials Provided

The following materials are provided:

REF	Contents	Number of Tests
10699154	1 ReadyPack primary reagent pack containing ADVIA Centaur PTH Lite Reagent and Solid Phase Reagent 1 vial ADVIA Centaur PTH low calibrator CAL L 1 vial ADVIA Centaur PTH high calibrator CAL H ADVIA Centaur PTH Calibrator Assigned Value Card and barcode labels ADVIA Centaur PTH Master Curve Card	100
10699155	5 ReadyPack primary reagent packs containing ADVIA Centaur PTH Lite Reagent and Solid Phase Reagent 2 vials ADVIA Centaur PTH low calibrator CAL L 2 vials ADVIA Centaur PTH high calibrator CAL H ADVIA Centaur PTH Calibrator Assigned Value Card and barcode labels ADVIA Centaur PTH Master Curve Card	500

Materials Required but Not Provided

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

Item		Description	
REF	01137199 (112351)	ADVIA Centaur Wash 1 WASH 1	2 x 1500 mL/pack
REF	03773025	ADVIA Centaur Wash 1 WASH 1	2 x 2500 mL/pack

Optional Materials

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

Item		Description	
REF	10699156	ADVIA Centaur PTH Quality Control	2 x 1 mL control 1 CONTROL 1 2 x 1 mL control 2 CONTROL 2 2 x 1 mL control 3 CONTROL 3
		Lot-specific assigned value card and barcode labels	
REF	10698597	ADVIA Centaur PTH Master Curve Material	5 x 1 mL
		Lot-specific value sheet	
REF	10492364	ADVIA Centaur Multi-Diluent 13 M-DIL	2 ReadyPack ancillary reagent packs that contain 10 mL/pack

Assay Procedure

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

The system automatically performs the following actions:

1. Dispenses 50 µL of sample into a cuvette.
2. Dispenses 100 µL of Lite Reagent and 200 µL of Solid Phase, and incubates for 10.0 minutes at 37°C.
3. Separates, aspirates, and washes the cuvettes with ADVIA Centaur Wash 1.
4. Dispenses 300 µL of ADVIA Centaur Acid Reagent and 300 µL of ADVIA Centaur Base Reagent to initiate the chemiluminescent reaction.
5. Reports results according to the selected option, as described in the system operating instructions.

A direct relationship exists between the amount of intact 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 reagent packs. For detailed information about preparing the system, refer to the system operating instructions.

Load the ReadyPack primary 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 13 in the ancillary reagent entry.

Preparing the Samples

This assay requires 50 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.

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.

Note Remove particulates by centrifugation according to CLSI guidance and the collection device manufacturer's recommendations.[13]

On-System Stability

The ADVIA Centaur PTH assay reagents are stable onboard the system for 28 days and are stable unopened until the expiration date on the product. Discard reagents at the end of the on-system stability interval. Do not use products beyond the expiration date printed on the product labeling.

Defining the Master Curve

The ADVIA Centaur PTH assay requires that you define the master curve when using a new reagent lot number. Use the barcode 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 defining the master curve, refer to the system operating instructions.

Performing Calibration

For calibration of the ADVIA Centaur PTH assay, use the ADVIA Centaur PTH Calibrators provided with each kit.

Note The low and high calibrators provided in this kit are matched to the ReadyPack primary reagent pack. Do not mix calibrator lots with different lots of reagent packs.

Each assay kit contains a Calibrator Assigned Value Card to facilitate entering the calibrator values on the system. Enter the values using the barcode scanner or the keyboard. For detailed information about entering calibrator values, refer to the system operating instructions.

Preparing the Calibrators

Prepare calibrators using the following steps:

1. Add 1.0 mL of reagent water into each calibrator vial using a volumetric or precision pipet.

Note For information about reagent water, refer to the system operating instructions.

2. Let the calibrators stand for 30 minutes at room temperature to allow the lyophilized material to dissolve.
3. Gently swirl and invert the vials until homogeneous.

Note After reconstitution, calibrators are stable for 8 hours at room temperature (18–25°C). For longer storage, store at ≤ -20°C for up to 60 days. Freeze and thaw the calibrators one time only.

Calibration Procedure

For detailed information about processing calibrators, refer to the system operating instructions.

Perform the calibration using the following steps:

1. Ensure that the appropriate master curve values are entered on the system. Refer to *Defining the Master Curve*.
2. Enter the calibrator assigned values found on the ADVIA Centaur PTH Calibrator Assigned Value Card into the system.
3. Ensure that the required reagents are loaded for the assay.
4. Schedule the calibrators to the worklist.
5. Label 2 sample cups with ADVIA Centaur PTH Calibrator barcode labels: 1 cup for the low calibrator and 1 cup for the high calibrator. Place the barcode label on each sample cup with the readable characters oriented vertically.

Note Calibrator barcode labels are lot-number-specific. Do not use barcode labels from one lot of calibrators with any other lot of calibrators.

6. Gently mix the low and high calibrators, and dispense a sufficient volume of each calibrator into the appropriate sample cups. Avoid bubbles.

Note Refer to the system operator's guide for sample volume requirements.

7. Load the calibrator sample cups in the sample rack.
8. Load the rack in the sample compartment.
9. Ensure that the reagents and other materials required to perform the assay are loaded.
10. At the main menu, open the Reagent Compartment Screen.
11. Select the assay to calibrate.
12. Select **Calibrate**.

Note Dispose of any calibrator that remains in the sample cups after 8 hours. Do not refill sample cups when the contents are depleted; if required, dispense fresh calibrators.

Calibration Frequency

Calibrate the assay at the end of the 21-day calibration interval.

Additionally, this assay requires a 2-point calibration:

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

Performing Quality Control

Siemens Healthcare Diagnostics recommends the use of ADVIA Centaur PTH Quality Control (REF 10699156) or an equivalent commercially available control.

Quality control samples should be assayed at least once on each day that samples are analyzed to monitor system performance and chart trends. Quality control samples should also be assayed when performing a 2-point calibration.

Additional quality control material can be used at the discretion of the laboratory. Use the quality control material in accordance with the quality control instructions for use.

In addition, perform quality control:

- Following a valid calibration
- With use of a new lot of reagent
- When troubleshooting test results that do not match clinical conditions or symptoms

Follow government regulations or accreditation requirements for quality control frequency. Individual laboratory quality control programs and procedures may require more frequent quality control testing.

Acceptable performance is achieved when the analyte values obtained are within the expected control interval for the system, as indicated by the manufacturer of the control material or within the interval determined by an internal laboratory quality control procedure.

Follow your laboratory's quality control procedures if the results obtained do not fall within the acceptable limits. For information about entering quality control definitions, refer to the system online help.

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:

- Verify that the materials are not expired.
- Verify that required system maintenance was performed.
- Verify that the assay was performed according to the instructions for use.
- Rerun the assay with fresh quality control samples.
- If necessary, contact your local technical support provider or distributor for assistance.
- Repeat testing of patient samples before reporting results.

Perform corrective actions in accordance with your established laboratory protocol.

Results

Calculation of Results

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.

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

Dilutions

Refer to the following information for the sample volume required to perform onboard dilutions:

Dilution	Sample Volume (µL)
1:5	50

Perform an onboard dilution to obtain accurate results for patient samples that have intact PTH levels > 2000 pg/mL (> 212 pmol/L).

- Ensure that ADVIA Centaur Multi-Diluent 13 is loaded on the system.
- For automatic dilutions, set the system parameters as follows:

  Dilution point: ≤ 2000 pg/mL (≤ 212 pmol/L)

  Dilution factor: 5
- When diluted samples result in intact PTH concentrations > 10,000 pg/mL (> 1060 pmol/L), report results as > 10,000 pg/mL (> 1060 pmol/L).

For detailed information about automatic dilutions, refer to the system operating instructions.

Interpretation of Results

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

Limitations

The following information pertains to limitations of the assay:

- Interpretation of intact PTH values should always take into account serum calcium results and the interrelationship between these 2 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.
- Some overlap of intact PTH values does exist for 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 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 ADVIA Centaur PTH assay will detect non-intact PTH, such as PTH fragment (7-84). In patients with abnormal renal function, interpret the PTH result with caution, and do not make patient management decisions on the PTH result alone. A study of characterized PTH fragments is provided in Lopez *et al* "Selected Reaction Monitoring- Mass Spectrometric Immunoassay Responsive to Parathyroid Hormone and Related Variants."[14]
- Patient samples may contain heterophilic antibodies that could react in immunoassays to give falsely elevated or depressed results.[15] This assay is designed to minimize the interference from heterophilic antibodies.

Expected Values

The reference range was established on the ADVIA Centaur XP system. Matched EDTA plasma and serum samples were obtained from 142 apparently healthy individuals with normal levels of calcium, creatinine, vitamin D, and TSH.

The expected results (from 95% of the values) are:

- Plasma: 18.4–80.1 pg/mL (1.95–8.49 pmol/L)
- Serum: 18.5–88.0 pg/mL (1.96–9.33 pmol/L)

As with all *in vitro* diagnostic assays, each laboratory should determine its own reference range(s) for the diagnostic evaluation of patient results.[16]

Performance Characteristics

Measuring Interval

The ADVIA Centaur PTH assay measures intact parathyroid hormone concentrations from 4.6–2000 pg/mL (0.488–212 pmol/L). The lower end of the assay range is defined by the Limit of Quantitation (LoQ).

Report results below the measuring interval as < 4.6 pg/mL (< 0.488 pmol/L). When samples exceed the measuring interval, refer to *Dilutions*.

Specificity

Interference was determined according to CLSI Document EP07-A2[17] using the ADVIA Centaur XP system.

The cross-reactivity of the ADVIA Centaur PTH assay was determined by spiking samples with the PTH fragments and compounds listed below at the indicated levels. The following results were obtained:

	Amount Added	Cross-reactivity
Cross-reactant	**(pg/mL)**	**(%)**
PTH (1-34) fragment	12,000	< 0.1
PTH (39-68) fragment	100,000	< 0.1
PTH (39-84) fragment	100,000	< 0.1
PTH (44-68) fragment	100,000	< 0.1
PTH (53-84) fragment	100,000	< 0.1
PTH (7-84) fragment[a]	300	37.4
Beta-Cross Laps	10,000	< 0.1
Calcitonin	100,000	< 0.1
Osteocalcin	50,000	< 0.1
PTH RP (1-34)	100,000	< 0.1

[a] Refer to *Limitations*

Detection Capability

The Limit of Blank (LoB), the Limit of Detection (LoD), and the Limit of Quantitation (LoQ) were determined as described in CLSI protocol EP17-A2.[18] The assay is designed to have an LoB of < 6.0 pg/mL, an LoD of ≤ 6.0 pg/mL, and an LoQ of ≤ 6.0 pg/mL.

Representative detection capability data are shown below. Assay results obtained at individual laboratories may vary from the data presented.

The LoB is defined as the highest measurement result that is likely to be observed for a blank sample. The ADVIA Centaur PTH assay has an LoB of 1.5 pg/mL (0.160 pmol/L).

The LoD is defined as the lowest concentration of intact PTH that can be detected with 95% probability. The ADVIA Centaur PTH assay has an LoD of 3.2 pg/mL (0.339 pmol/L).

The LoQ is defined as the lowest concentration of intact PTH that can be detected at a total CV of 20%. The ADVIA Centaur PTH assay has an LoQ of 4.6 pg/mL (0.488 pmol/L).

Precision

The ADVIA Centaur PTH assay is designed to meet the following repeatability and within-lab precision requirements:

Intact PTH Level		Design Requirements	
(pg/mL)	(pmol/L)	Repeatability (Within-Run) % CV	Within-Lab (Total Precision) % CV
10.0–20.0	1.06–2.12	≤ 8.0	≤ 10.0
> 20.0–700	> 2.12–74.2	≤ 6.0	≤ 8.0
> 700	> 74.2	≤ 8.0	≤ 10.0

Precision was evaluated according to the CLSI protocol EP05-A3.[19] Six EDTA plasma samples were assayed 2 times per day in replicates of 2, for 20 days (n = 80 replicates per sample) using the ADVIA Centaur PTH assay. The following results were obtained:

	Mean		Repeatability (Within-Run)			Within-Lab (Total Precision)		
Sample	(pg/mL)	(pmol/L)	SD (pg/mL)	SD (pmol/L)	% CV	SD (pg/mL)	SD (pmol/L)	% CV
Sample 1	13.1	1.39	0.5	0.06	4.02	1.0	0.11	7.90
Sample 2	47.7	5.05	1.2	0.13	2.51	2.0	0.22	4.27
Sample 3	142.3	15.09	3.3	0.35	2.31	4.4	0.46	3.08
Sample 4	415.6	44.05	11.9	1.26	2.86	17.2	1.82	4.13
Sample 5	591.8	62.73	13.6	1.44	2.29	18.2	1.93	3.08
Sample 6	1113.2	118.00	25.7	2.72	2.31	44.1	4.68	3.96
ADVIA Centaur PTH Quality Controls								
Control 1	38.5	4.08	1.3	0.14	3.35	2.0	0.21	5.16
Control 2	235.8	25.00	5.1	0.54	2.14	7.1	0.75	3.00
Control 3	896.8	95.06	21.7	2.30	2.41	33.8	3.58	3.77

Based on internal testing on the ADVIA Centaur CP system, the overall reproducibility is estimated to be ≤ 15% CV for samples tested and includes multiple reagent lots, instruments, days, and replicates. Performance of the assay at individual laboratories may vary.

Accuracy / Method Comparison

The ADVIA Centaur PTH assay is designed to have a correlation coefficient ≥ 0.95 when compared to a commercial intact PTH assay. Typical data obtained showed 0.99.

For 248 EDTA plasma samples within the range of 16.0–1931.0 pg/mL (1.70–204.7 pmol/L), the relationship between the ADVIA Centaur PTH assay using the ADVIA Centaur CP system (y), and the ADVIA Centaur PTH assay using the ADVIA Centaur XP system (x) is described using Passing-Bablok regression:

ADVIA Centaur PTH (y) = 0.99 (x) - 0.88 pg/mL (0.09 pmol/L), r = 0.998

The correlation of the assay may vary depending on the study design, comparable method, and sample population. Results obtained at individual laboratories may vary from the data presented.

Specimen Collection Tube Comparison

The ADVIA Centaur PTH assay was evaluated using different specimen matrices and tube collection types. The assay is designed to have a correlation of coefficient ≥ 0.95, and a slope of test tube type vs. reference of 1.0 ± 0.1.

A total of 56 matched dipotassium EDTA plasma, serum, serum separator tube, lithium heparin, and sodium heparin samples that span the range of the assay were examined. The following results were obtained using the ADVIA Centaur XP system:

Comparison[a]	Regression Equation (pg/mL)	r
Serum vs. dipotassium EDTA plasma	Serum = 0.99 EDTA - 1.85	0.996
Serum separator tube vs. dipotassium EDTA plasma	Serum separator tube = 1.03 EDTA + 0.20	0.996
Lithium heparin vs. dipotassium EDTA plasma	Lithium heparin = 0.99 EDTA + 1.95	0.998
Sodium heparin vs. dipotassium EDTA plasma	Sodium heparin = 1.00 EDTA + 1.03	0.997

[a] This study was performed using Becton Dickinson tubes. Siemens recommends that laboratories evaluate performance when using other manufacturers' tubes.

Interferences

Potential interference in this assay from the interferents listed below is designed to be ≤ 10%. Interfering substances at the levels indicated in the table below were tested as described in CLSI Document EP07-A2[17] using the ADVIA Centaur PTH assay when run on the ADVIA Centaur XP system.

Interferent	Highest Concentration Tested	Observed Interference (%)
Aliskiren	200 µg/mL	5.3
Bilirubin (conjugated)	60 mg/dL	5.9
Bilirubin (unconjugated)	60 mg/dL	-2.2
Biotin	3500 ng/mL	-2.8
Caffeine	308 µmol/L	2.3
Calcitrol	360 pg/mL	2.5
Cholesterol	500 mg/dL	-6.5
EDTA	9 mg/mL	1.6
Enalaprilat	0.86 µmol/L	-2.6
Epoetin alfa	15 mU/L	-1.2
Fosrenol	20 ng/mL	3.4
Furosemide	181 µmol/L	-2.6
Hemoglobin	500 mg/dL	-4.5
Heparin	75 U/mL	-1.8
IgG	6 g/dL	1.3
Total Protein (high)	12 g/dL	-4.2
Total Protein (low)	6 g/dL	-7.5
Triglycerides	3275 mg/dL	-0.4

Six human plasma samples containing human anti-mouse antibodies (HAMA) were tested at 2 PTH concentrations. Samples at a PTH concentration of 60 pg/mL (6.36 pmol/L) demonstrated a difference of -11.5% to 3.2% from the expected values. Samples at a PTH concentration of 340 pg/mL (36.04 pmol/L) demonstrated a difference of -3.8% to 2.4% from the expected values. Refer to *Limitations*.

Assay results obtained at individual laboratories may vary from the data presented.

Linearity

The ADVIA Centaur PTH assay is linear from 4.6–2000 pg/mL (0.488–212 pmol/L).

Linearity was evaluated according to the CLSI Document EP06-A.[20] An EDTA plasma sample containing a high concentration of intact PTH was mixed with an assay-specific diluent (ADVIA Centaur Multi-Diluent 13, REF 10492364). The resulting sample mixtures were tested with the ADVIA Centaur PTH assay.

Dilution Recovery

This assay is designed to have a mean dilution recovery of 90%–110%.

A low sample pool (~29 pg/mL PTH) was spiked with a commercially available synthetic PTH peptide to reach levels of approximately 3000 pg/mL (318 pmol/L), 6000 pg/mL (636 pmol/L), and 9000 pg/mL (954 pmol/L). Each sample was diluted 1:5 with ADVIA Centaur Multi-Diluent 13 onboard the ADVIA Centaur CP system. The following results were obtained:

Sample	Observed Mean[a] (pg/mL)	Expected (pg/mL)	Observed Mean[a] (pmol/L)	Expected (pmol/L)	Recovery (%)
1	3144.4	3027.5	333.4	321.0	103.9
2	6277.8	6026.1	665.7	639.0	104.2
3	9531.1	9024.7	1010.7	957.0	105.6
Mean					**104.5**

[a] Each value in this column is the mean of 3 onboard dilution results.

Spiking Recovery

This assay is designed to have a mean spiking recovery of 90%–110%.

Varying amounts of intact PTH were added to 4 human plasma samples with endogenous intact PTH levels of 28.4–78.1 pg/mL (3.01–8.28 pmol/L). The recoveries ranged from 96.9%–102.6% with a mean of 99.3%.

Sample	Observed (pg/mL)	Expected (pg/mL)	Observed (pmol/L)	Expected (pmol/L)	Recovery (%)
1	73.3	74.7	7.77	7.92	98.1
	731.1	755.7	77.50	80.10	96.7
Mean					**97.4**
2	120.4	122.4	12.76	12.97	98.4
	795.4	807.5	84.31	85.60	98.5
Mean					**98.4**
3	81.9	80.3	8.68	8.34	102.0
	772.3	762.1	81.86	78.23	101.3
Mean					**101.7**

Sample	Observed (pg/mL)	Expected (pg/mL)	Observed (pmol/L)	Expected (pmol/L)	Recovery (%)
4	121.5	118.4	12.88	12.55	102.6
	771.5	798.7	81.78	84.66	96.6
Mean					**99.6**
Mean					**99.3**

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) are reported as > 2000 pg/mL (> 212 pmol/L).

Standardization

The ADVIA Centaur PTH assay standardization is maintained with internal standards using purified human PTH (1-84). Assigned values for calibrators are traceable to this standardization.

Technical Assistance

According to EU regulation 2017/746, any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the EU Member State in which the user and/or patient is established.

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

siemens-healthineers.com

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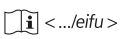
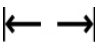
Trademarks

Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Symbol Title	Source	Symbol	Symbol Title	Source
	Manufacturer	5.1.1[a]		Authorized representative in the European Community	5.1.2[a]
	Use-by date	5.1.4[a]		Authorized representative in Switzerland	Proprietary
	Catalog number	5.1.6[a]		Batch code	5.1.5[a]
	Consult Instructions for Use	5.4.3[a]		Contains sufficient for <n> tests	5.5.5[a]
	Internet URL address to access the electronic instructions for use	Proprietary		Version of Instructions for Use	Proprietary
	*In vitro* diagnostic medical device	5.5.1[a]		Revision	Proprietary
RxOnly	Prescription device (US only)	FDA[c]		Unique Device Identifier	5.7.10[b]
	CE Marking with Notified Body	EU IVDR[d]		CE Marking	EU IVDR[d]
	Temperature limit	5.3.7[a]		Keep away from sunlight	5.3.2[a]
	Upper limit of temperature	5.3.6[a]		Lower limit of temperature	5.3.5[a]
	Do not re-use	5.4.2[a]		Do not freeze	Proprietary
	Recycle	1135[e]		This way up	0623[e]
	Biological risks	5.4.1[a]		Caution	5.4.4[a]
	Common Units	Proprietary		Document face up[f]	1952[e]
YYYY-MM-DD	Date format (year-month-day)	N/A		International System of Units	Proprietary
	Target	Proprietary	**YYYY-MM**	Date format (year-month)	N/A
				Interval	Proprietary

Symbol	Symbol Title	Source	Symbol	Symbol Title	Source
	Handheld barcode scanner	Proprietary	CHECKSUM	Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid.	Proprietary
LOT DTL	Lot details	Proprietary	MC DEF	Master Curve definition	Proprietary
CAL LOT VAL	Calibrator lot value	Proprietary	CONTROL LOT VAL	Quality control lot value	Proprietary

a International Standard Organization (ISO). ISO 15223-1 Medical Devices- Symbols to be used with medical device labels, labelling and information to be supplied.

b ISO 15223-1:2020-04

c Federal Register. Vol. 81, No 115. Wednesday, June 15, 2016. Rules and Regulations: 38911.

d IVDR REGULATION (EU) 2017/746

e International Standard Organization (ISO). ISO 7000 Graphical symbols for use on equipment.

f Indicates Assay-eNote

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