BECKMAN COULTER

CE 2797

ACCESS
Immunoassay Systems

Instructions For Use

Access Intact PTH
Parathyroid Hormone, Intact

REF A16972

FOR PROFESSIONAL USE ONLY

Rx Only

Routine Mode (~30 minutes)
Intraoperative Mode (~15 minutes)

For use on Access 2, DxC 500i, UniCel DxC 600i, UniCel DxI 600, UniCel DxI 800, UniCel DxC 880i, UniCel DxC 860i, UniCel DxC 680i, and UniCel DxC 660i systems

PRINCIPLE

INTENDED USE

The Access Intact PTH assay is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of intact parathyroid hormone (parathyrin, PTH) levels in human serum and plasma using the Access Immunoassay Systems. It is indicated to aid in the differential diagnosis of hyperparathyroidism, hypoparathyroidism, or hypercalcemia of malignancy and can be used intraoperatively. Assay results should be used in conjunction with other clinical data to assist the clinician in making individual patient management decisions.

SUMMARY AND EXPLANATION

Parathyroid hormone (PTH) is synthesized by the chief cells of the parathyroid glands and stored into dense neuroendocrine-type secretory granules, awaiting secretion. Intact PTH is an 84 amino acid polypeptide with a molecular mass of approximately 9.43 kilodaltons. After secretion PTH undergoes rapid proteolysis to generate various circulating C-terminal fragments. Some of these fragments re-enter the bloodstream and are cleared primarily by glomerular filtration, an important route for PTH clearance. The intact and biologically active peptide has a half-life in the circulation of less than 5 minutes.[1]

PTH plays a crucial role in maintaining calcium homeostasis and its measurement is an important aid in the diagnosis of calcium related disorders. In healthy individuals, PTH secretion responds to small alterations in plasma ionized calcium concentration within seconds. Abnormally low ionized calcium concentrations trigger PTH secretion, whereas rising levels of extracellular calcium reduce PTH secretion through a negative feedback mechanism.

PTH regulates calcium levels by concerted effect on three principal organs: bone, intestinal mucosa and kidney. The effect of PTH on intestinal calcium is indirect, resulting from renal production of the intestinally active vitamin D metabolite, 1,25-dihydroxyvitamin D. In the kidney, PTH stimulates calcium reabsorption and inhibition of phosphate reabsorption from the renal tubules. Eventually PTH promotes osteoclastic bone resorption and release of calcium and phosphate from bone.[2]

In patients with disorders of calcium metabolism, quantitative determination of circulating PTH may assist in the differential diagnosis of hypercalcemia and hypocalcemia.[3] In hypercalcemia due to primary hyperparathyroidism or ectopic PTH secretion (pseudo hyperparathyroidism), most patients have increased PTH levels. By contrast in hypercalcemia due to malignancy or other causes, the concentration of PTH in the circulation is typically low, either below or towards the low end of the reference range for apparently healthy individuals.[4]

Secondary hyperparathyroidism is a compensatory hyperfunctioning of the parathyroid glands caused by hypocalcemia or peripheral resistance to PTH. It is typically caused by renal failure and leads to elevated PTH levels.[3] Chronic overproduction of PTH in renal failure contributes to the spectrum of bone disease, which is also termed renal osteodystrophy.[2] The National Kidney Foundation (NKF) has published clinical practice guidelines addressing bone metabolism for the management of chronic kidney disease. It recommends that serum levels of calcium, phosphorus and PTH be measured periodically in all patients with chronic kidney disease.[5] Since this condition is a complex and multifactorial disease, PTH results should be interpreted in light of all the information available to the clinician.

Hypoparathyroidism is an uncommon congenital or acquired condition in which PTH secretion is deficient or absent. In most cases, hypoparathyroidism follows parathyroidectomy or thyroidectomy. Pseudohypoparathyroidism is a rare disorder and describes hereditary conditions that cause end organ resistance to PTH.[2]

Rapid intraoperative PTH measurement in patients undergoing parathyroidectomy has also been described.[6,7,8] Based on a review of the literature, the National Academy of Clinical Biochemistry has published laboratory medicine practice guidelines for the use of intraoperative PTH measurements.[9] These guidelines recommend use of intraoperative PTH testing for patients undergoing surgery for primary hyperparathyroidism and strongly recommends use in minimally invasive or directed procedures.

METHODOLOGY

The Access Intact PTH assay is a two-site immunoenzymatic (“sandwich”) assay. A sample is added to a reaction vessel, along with a monoclonal anti-PTH antibody conjugated to alkaline phosphatase, TRIS buffered saline with proteins and paramagnetic particles coated with a goat polyclonal anti-PTH antibody. After incubation in a reaction vessel, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. Then, the chemiluminescent substrate is added to the vessel and light generated by the reaction is measured with a luminometer. The light production is directly proportional to the concentration of PTH in the sample. The amount of analyte in the sample is determined from a stored, multi-point calibration curve.

SPECIMEN

SPECIMEN COLLECTION AND PREPARATION

1. Serum and plasma (heparin and EDTA) are the recommended samples.
2. Observe the following recommendations for handling, processing, and storing blood samples:[10]
    - Collect all blood samples observing routine precautions for venipuncture.
    - Allow serum samples to clot completely before centrifugation.
    - Keep tubes stoppered at all times.
    - Physically separate serum or plasma from contact with cells as soon as possible.
    - For plasma (heparin and EDTA) samples:
        - Store samples tightly stoppered at room temperature (15 to 30°C) for no longer than eight hours.
        - If the assay will not be completed within 8 hours, refrigerate samples at 2 to 8°C for no longer than 48 hours.
        - If the assay will not be completed within 48 hours, or for shipment of samples, freeze at -20°C or colder for no longer than 6 months.
    - For serum samples:
        - Store samples tightly stoppered at room temperature (15 to 30°C) for no longer than 4 hours.
        - If the assay will not be completed within 4 hours, refrigerate samples at 2 to 8°C for no longer than 8 hours.
        - If the assay will not be completed within 8 hours, or for shipment of samples, freeze at -20°C or colder for no longer than 6 months.
3. Use the following guidelines when preparing specimens:

- Ensure residual fibrin and cellular matter have been removed prior to analysis.
- Thaw frozen sample and centrifuge prior to analysis.
- Follow blood collection tube manufacturer's recommendations for centrifugation.

4. Each laboratory should determine the acceptability of its own blood collection tubes and serum separation products. Variations in these products may exist between manufacturers and, at times, from lot-to-lot.
5. Thaw samples no more than three times. Avoid assaying lipemic or hemolyzed samples.

REAGENTS

PRODUCT INFORMATION

Access Intact PTH Reagent Pack

Ref. No. A16972: 100 determinations, 2 packs, 50 tests/pack

- Used for both the Routine and Intraoperative modes.
- Provided ready to use.
- Store upright and refrigerate at 2 to 10°C.
- Refrigerate at 2 to 10°C for a minimum of two hours before use on the instrument.
- Stable until the expiration date stated on the label when stored at 2 to 10°C.
- Stable at 2 to 10°C for 28 days after initial use.
- Signs of possible deterioration are a broken elastomeric layer on the pack or control values out of range.
- If the reagent pack is damaged (i.e., broken elastomer), discard the pack.
- All antisera are polyclonal unless otherwise indicated.

Well	Contents	Ingredients
R1a:	3.25 mL	Paramagnetic particles coated with goat anti-PTH antibody suspended in TRIS buffered saline with bovine serum albumin (BSA), surfactant, < 0.1% sodium azide, 0.1% ProClin* 300.
R1b:	3.1 mL	TRIS buffered saline with block ACE, protein (mouse, goat), surfactant, < 0.1% sodium azide, 0.1% ProClin 300.
R1c:	3.1 mL	Mouse monoclonal anti-PTH alkaline phosphatase conjugate in ACES buffered saline with BSA, surfactant, < 0.1% sodium azide, 0.1% ProClin 300.

*ProClin is a trademark of LANXESS Corp.

WARNING AND PRECAUTIONS

- For *in vitro* diagnostic use.
- Patient samples and blood-derived products may be routinely processed with minimum risk using the procedure described. However, handle these products as potentially infectious according to universal precautions and good clinical laboratory practices, regardless of their origin, treatment, or prior certification. Use an appropriate disinfectant for decontamination. Store and dispose of these materials and their containers in accordance with local regulations and guidelines.
- For hazards presented by the product refer to the following sections: REACTIVE INGREDIENTS and GHS HAZARD CLASSIFICATION.

REACTIVE INGREDIENTS

> ⚠ **CAUTION**
>
> **Sodium azide preservative may form explosive compounds in metal drain lines. See NIOSH Bulletin: Explosive Azide Hazard (8/16/76).**
> **To avoid the possible build-up of azide compounds, flush wastepipes with water after the disposal of undiluted reagent. Sodium azide disposal must be in accordance with appropriate local regulations.**

GHS HAZARD CLASSIFICATION

Paramagnetic Particles (Compartment R1a)	WARNING	
		
	H317	May cause an allergic skin reaction.
	H412	Harmful to aquatic life with long lasting effects.
	P273	Avoid release to the environment.
	P280	Wear protective gloves, protective clothing and eye/face protection.
	P333+P313	If skin irritation or rash occurs: Get medical advice/attention.
	P362+P364	Take off contaminated clothing and wash it before use.
		reaction mass of: 5-chloro-2-methyl-4-isothiazolin -3-one [EC# 247-500-7] and 2-methyl-4-isothiazolin-3-one [EC# 220-239-6](3:1) < 0.05%
Reagent (Compartment R1b)	WARNING	
		
	H317	May cause an allergic skin reaction.
	H412	Harmful to aquatic life with long lasting effects.
	P273	Avoid release to the environment.
	P280	Wear protective gloves, protective clothing and eye/face protection.
	P333+P313	If skin irritation or rash occurs: Get medical advice/attention.
	P362+P364	Take off contaminated clothing and wash it before use.
		reaction mass of: 5-chloro-2-methyl-4-isothiazolin -3-one [EC# 247-500-7] and 2-methyl-4-isothiazolin-3-one [EC# 220-239-6](3:1) < 0.05%
Conjugate (Compartment R1c)	WARNING	

H317	May cause an allergic skin reaction.
H412	Harmful to aquatic life with long lasting effects.
P273	Avoid release to the environment.
P280	Wear protective gloves, protective clothing and eye/face protection.
P333+P313	If skin irritation or rash occurs: Get medical advice/attention.
P362+P364	Take off contaminated clothing and wash it before use.
	reaction mass of: 5-chloro-2-methyl-4-isothiazolin -3-one [EC# 247-500-7] and 2-methyl-4-isothiazolin-3-one [EC# 220-239-6](3:1) < 0.05%

SDS	Safety Data Sheet is available at beckmancoulter.com/techdocs

MATERIALS NEEDED BUT NOT SUPPLIED WITH REAGENT KIT

1. Access Intact PTH Calibrators
   Provided at zero and approximately 10, 60, 300, 1,500 and 3,500 pg/mL (1.1, 6.4, 31.8, 159.0 and 371.0 pmol/L).
   Ref. No. A16953
2. Quality Control (QC) materials: commercial control material.
3. Access Sample Diluent A
   Vial Ref. No. 81908
   Diluent Pack Ref. No. A79783 (For use with the UniCel DxI system onboard dilution feature.)
4. Access Substrate
   Ref. No. 81906
5. Access Wash Buffer II, Ref. No. A16792
   UniCel DxI Wash Buffer II, Ref. No. A16793

EQUIPMENT AND MATERIALS

R1	Access Intact PTH Reagent Packs

CALIBRATION

CALIBRATION INFORMATION

An active calibration curve is required for all tests. For the Access Intact PTH assay, calibration is required every 28 days. Refer to the appropriate system manuals and/or Help system for information on calibration theory, configuring calibrators, calibrator test request entry, and reviewing calibration data.

QUALITY CONTROL

Quality control materials simulate the characteristics of patient samples and are essential for monitoring the system performance of immunochemical assays. Because samples can be processed at any time in a “random access” format rather than a “batch” format, quality control materials should be included in each 24-hour time period.[11] Include commercially available quality control materials that cover at least two levels of analyte. More frequent use of controls or the use of additional controls is left to the discretion of the user based on good laboratory practices or laboratory accreditation requirements and applicable laws. Follow manufacturer's instructions for reconstitution and storage. Each laboratory should establish mean values and acceptable ranges to assure proper performance. Quality control results that do not fall within acceptable ranges may indicate invalid test results. Examine all test results generated since obtaining the last acceptable quality control test point for this analyte. Refer to the appropriate system manuals and/or Help system for information about reviewing quality control results.

TESTING PROCEDURE(S)

PROCEDURAL COMMENTS

1. Refer to the appropriate system manuals and/or Help system for a specific description of installation, start-up, principles of operation, system performance characteristics, operating instructions, calibration procedures, operational limitations and precautions, hazards, maintenance, and troubleshooting.
2. Mix contents of new (unpunctured) reagent packs by gently inverting pack several times before loading on the instrument. Do not invert open (punctured) packs.
3. Use fifty-five (55) µL of sample for each determination in addition to the sample container and system dead volumes. Use fifty (50) µL of sample in addition to the sample container and system dead volumes for each determination run with the DxI system onboard dilution feature. Refer to the appropriate system manuals and/or Help system for the minimum sample volume required.
4. The system default unit of measure for sample results is pg/mL. To change sample reporting units to the International System of Units (SI units), pmol/L, refer to the appropriate system manuals and/or Help system. To manually convert concentrations to the International System, multiply pg/mL by multiplication factor 0.106.

PROCEDURE

Refer to the appropriate system manuals and/or Help system for information on managing samples, configuring tests, requesting tests, and reviewing test results.

Use **PTH** as the test name for the Access Intact PTH assay Routine Mode, and use **PTHIO** as the test name for the Access Intact PTH assay Intraoperative Mode. The same reagent pack is used for both modes.

RESULTS INTERPRETATION

Patient test results are determined automatically by the system software. The amount of analyte in the sample is determined from the measured light production by means of the stored calibration data. Patient test results can be reviewed using the appropriate screen. Refer to the appropriate system manuals and/or Help system for complete instructions on reviewing sample results.

REPORTING RESULTS

EXPECTED RESULTS

1. Each laboratory should establish its own reference ranges to assure proper representation of specific populations.
2. It is well documented that PTH concentrations are influenced by several factors known to synergistically affect calcium homeostasis. Age, gender, geographic latitude, season of the year, skin pigmentation, sunlight exposure, vitamin D supplementation, kidney function and vitamin D insufficiency have all been reported to potentially affect PTH metabolism and impact reference values and decision thresholds.[12] To establish a reference range, PTH

concentrations were measured in 289 matched human EDTA plasma and serum samples from apparently healthy male and female subjects aged 19-67 years. Because of significant seasonal variations of 25-hydroxyvitamin D, the samples were collected during three time periods in two geographic latitudes: June 2005 in the northern United States and September 2005 in the southern United States, and February 2006 in both the northern and southern United States. Additional testing was performed to exclude individuals with abnormal serum calcium, creatinine or 25-hydroxyvitamin D. Median values and 95% non parametric reference intervals are described below. Routine and Intraoperative Mode reference intervals are equivalent.

n	Median age	Age Range	Median Value	Reference Interval
289	40	19-67	37.8 pg/mL (4.0 pmol/L)	12-88 pg/mL (1.3-9.3 pmol/L)

PROCEDURAL NOTES

LIMITATIONS

1. **For Routine Mode:**

   Samples can be accurately measured within the analytical range of the lower limit of detection and the highest calibrator value (approximately 3,500 pg/mL [371 pmol/L]).

   - If a sample contains less than the analytical sensitivity for the assay, report the results as less than that value (i.e., < 1 pg/mL [< 0.1 pmol/L]). Additional information on the functional sensitivity for the Intact PTH assay can be found in the Specific Performance Characteristics section of this insert. When the DxI system onboard dilution feature is used, the system will report results as less than 2,975 pg/mL (316 pmol/L).
   - If a sample contains more than the stated value of the highest Access Intact PTH Calibrator (S5), report the result as greater than that value (i.e., > 3,500 pg/mL [> 371 pmol/L]). Alternatively, dilute one volume of sample with nine volumes of Access Sample Diluent A. Refer to the appropriate system manuals and/or Help system for instructions on entering a sample dilution in a test request. The system reports the results adjusted for the dilution.
     The DxI system onboard dilution feature automates the dilution process, using one volume of sample with nine volumes of Access Sample Diluent A, allowing samples to be quantitated up to approximately 35,000 pg/mL (3,714 pmol/L). The system reports the results adjusted for the dilution.

     For Intraoperative Mode:

     Samples can be accurately measured within the analytical range of the lower limit of detection and the highest calibrator value (approximately 3,500 pg/mL [371 pmol/L]).

   - If a sample contains less than the analytical sensitivity for the assay, report the results as less than that value (i.e., < 6 pg/mL [< 0.6 pmol/L]). When the DxI system onboard dilution feature is used, the system will report results as less than 2,975 pg/mL (316 pmol/L).
   - If a sample contains more than the stated value of the highest Access Intact PTH Calibrator (S5), report the result as greater than that value (i.e., > 3,500 pg/mL [> 371 pmol/L]). Alternatively, dilute one volume of sample with nine volumes of Access Sample Diluent A. Refer to the appropriate system manuals and/or Help system for instructions on entering a sample dilution in a test request. The system reports the results adjusted for the dilution. The DxI system onboard dilution feature automates the dilution process, using one volume of sample with nine volumes of Access Sample Diluent A, allowing samples to be quantitated up to approximately 35,000 pg/mL (3,714 pmol/L). The system reports the results adjusted for the dilution.

2. For assays employing antibodies, the possibility exists for interference by heterophile antibodies in the patient sample. Patients who have been regularly exposed to animals or have received immunotherapy or diagnostic procedures utilizing immunoglobulins or immunoglobulin fragments may produce antibodies, e.g. HAMA, that interfere with immunoassays. Additionally, other heterophile antibodies such as human anti-goat antibodies may

be present in patient samples.[13,14] Such interfering antibodies may cause erroneous results. Carefully evaluate the results of patients suspected of having these antibodies.

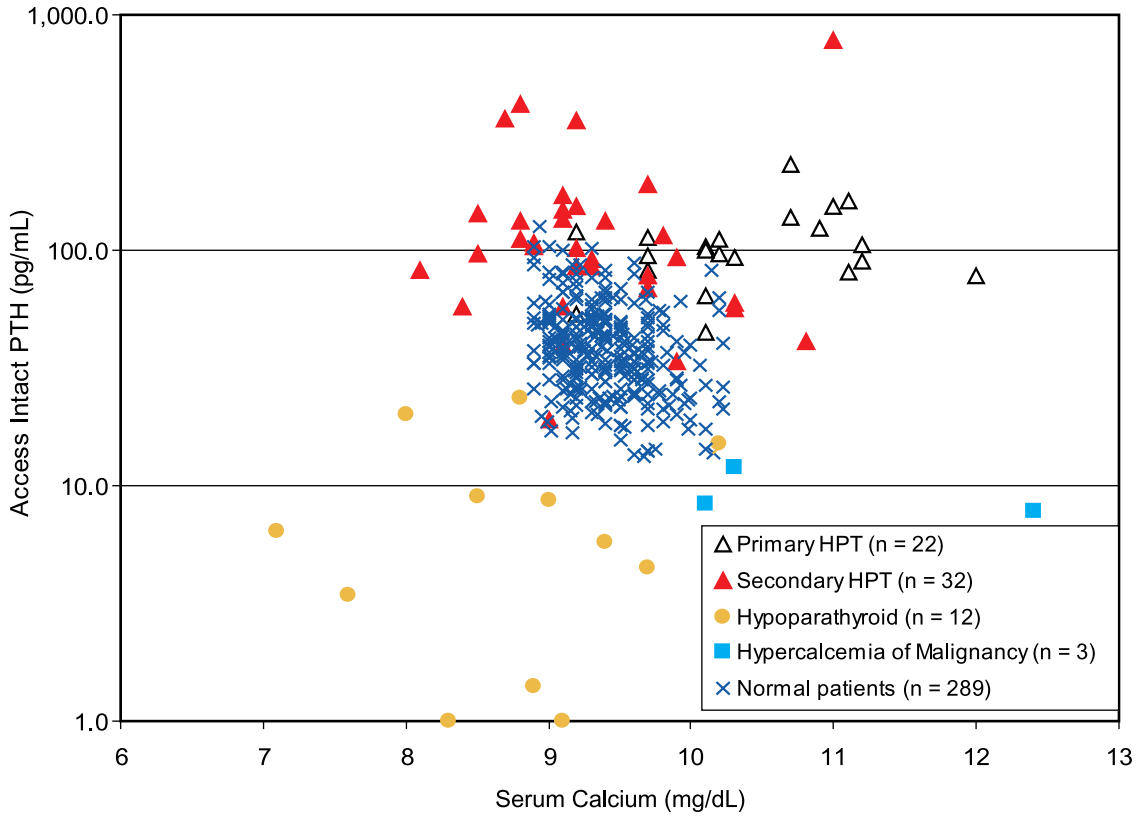
3. The Access Intact PTH results should be interpreted in light of the total clinical presentation of the patient, including: symptoms, clinical history, data from additional tests, and other appropriate information.
4. The Access Intact PTH assay does not demonstrate any “hook” effect up to 250,000 pg/mL (26,500 pmol/L).
5. Pediatric reference ranges (expected values) for the Access Intact PTH assay have not been established.
6. The Intraoperative Mode of the Access Intact PTH assay is not recommended for use in routine PTH testing. Performance characteristics for cross reactivity with metabolized forms of PTH have not been established.
7. For Intraoperative Mode testing with the Access Intact PTH assay in patients undergoing parathyroidectomy for primary hyperparathyroidism, the following practices are recommended:[9]
   - Baseline samples should be drawn at pre-operation/exploration and pre-excision.
   - Samples should be drawn at 5 and 10 minutes post-resection of the hyperfunctioning parathyroid tissue. Additional samples may be necessary.
   - At least a 50% reduction in PTH value should be observed when the highest baseline sample is compared to the post-resection samples.

PERFORMANCE CHARACTERISTICS

PERFORMANCE CHARACTERISTICS

Clinical Performance - Routine Mode

Intact PTH was also measured in patients with various disorders of calcium metabolism. The figure below illustrates the relationship between each patient's serum calcium concentration and their corresponding intact PTH plotted on a log scale. The following patient populations were included in this study: apparently healthy individuals (n=289), surgically confirmed primary hyperparathyroidism (n=22), secondary hyperparathyroidism (n=32), hypoparathyroidism (n=12), and hypercalcemia of malignancy (n=3).



Methods Comparison - Routine Mode

A comparison of 500 values using the Access Intact PTH assay Routine Mode on the Access Immunoassay system and a commercially available immunoassay system gave the following statistical data using Deming calculations:

n	Range of Observations pg/mL (pmol/L)	Intercept pg/mL (pmol/L)	Slope	Correlation Coefficient (r)
500	16-2,627 (1.7-278.5)	-11.48 (-1.22)	1.09	0.99

Dilution Recovery (Linearity) - Routine Mode

EDTA plasma samples with elevated PTH concentrations were diluted in Access Sample Diluent A. The recovery results are summarized in the following table:

Sample 1	Expected Concentration pg/mL (pmol/L)	Determined Concentration pg/mL (pmol/L)	Recovery (%)
Neat	3,185 (337.6)	3,185 (337.6)	N/A
1/1.1	2,942 (311.9)	2,847 (301.8)	97
1/1.3	2,624 (278.1)	2,510 (266.1)	96
1/1.5	2,228 (236.2)	2,103 (222.9)	94
1/1.8	1,770 (187.6)	1,718 (182.1)	97

Sample 1	Expected Concentration pg/mL (pmol/L)	Determined Concentration pg/mL (pmol/L)	Recovery (%)
1/2.3	1,417 (150.2)	1,383 (146.6)	98
1/3.0	1,064 (112.8)	997 (105.7)	94
1/4.5	709 (75.2)	660 (70.0)	93
1/9.0	356 (37.7)	317 (33.6)	89
		Mean % Recovery	**95**

Sample 2	Expected Concentration pg/mL (pmol/L)	Determined Concentration pg/mL (pmol/L)	Recovery (%)
Neat	3,081 (326.6)	3,081 (326.6)	N/A
1/1.1	2,845 (301.6)	2,848 (301.9)	100
1/1.3	2,540 (269.2)	2,486 (263.5)	98
1/1.5	2,164 (229.4)	2,066 (219.0)	95
1/1.8	1,713 (181.6)	1,803 (191.1)	105
1/2.3	1,370 (145.2)	1,325 (140.5)	97
1/3.0	1,027 (108.9)	966 (102.4)	94
1/4.5	684 (72.5)	640 (67.8)	94
1/9.0	345 (36.6)	327 (34.7)	95
		Mean % Recovery	**97**

Sample 3	Expected Concentration pg/mL (pmol/L)	Determined Concentration pg/mL (pmol/L)	Recovery (%)
Neat	992.7 (105.2)	992.7 (105.2)	N/A
1/1.375	722.0 (76.5)	712.6 (75.5)	98.7
1/2.75	361.1 (38.3)	358.6 (38.0)	99.3
1/5.5	180.6 (19.1)	178.0 (18.9)	98.6
1/11	90.4 (9.6)	83.7 (8.9)	92.6
1/27.5	36.2 (3.8)	31.6 (3.3)	87.2
1/220	4.6 (0.5)	3.4 (0.4)	73.3
		Mean % Recovery	**91.6**

Imprecision - Routine Mode

This assay exhibits total imprecision ≤ 8% at concentrations greater than 12 pg/mL (1.3 pmol/L). One study, using human EDTA plasma based control material, performed with one instrument and during one calibration cycle, generating a

total of 20 assays, 2 replicates per assay, over 22 days provided the following data, analyzed via analysis of variance (ANOVA).[15]

Human EDTA Plasma Sample	Mean Dose pg/mL (pmol/L)	Within Run (%CV)	Between Run (%CV)	Total Imprecision (%CV)
Level 1	12.1 (1.3)	2.6	5.8	6.4
Level 2	144 (15.3)	1.6	3.2	3.6
Level 3	1,439 (152.5)	2.2	2.8	3.5

Analytical Specificity/Interferences - Routine Mode

The following drugs/interferents were added to an EDTA plasma sample pool containing approximately 60 pg/mL (6.4 pmol/L) PTH. Each drug/interferent was tested at a minimum of the concentration listed below. All PTH values obtained in the presence of each drug/interferent were within ± 10% of the control values, indicating that these substances do not interfere with the assay.

Drug/interferent	Concentration tested	% Interference
Bilirubin, conjugated	20 mg/dL	-3.2
Bilirubin, unconjugated	20 mg/dL	-2.5
Triolein	3,000 mg/dL	4.8
Cholesterol	500 mg/dL	-1.1
Hemoglobin	500 mg/dL	4.3
Human serum albumin	49 g/L	-5.6
Acetaminophen	20 mg/dL	0.2
D-biotin	100 µg/L	0.0
Heparin	8,000 IU/dL	0.0
Ibuprofen	40 mg/dL	-2.2
Pamidronate	10 µg/mL	0.6
Propofol	2 µg/mL	-1.3
Salicylic acid	50 mg/dL	1.9

Each of the following potential cross-reacting fragments was added to Access Intact PTH Calibrator S0 and assayed in replicates of five.

Substance	Analyte Added pg/mL (pmol/L)	Cross-reactivity (%)
PTH 1-84	4,713 (500)	100
PTH 7-84	4,391 (500)	72
PTH 44-68	5,672 (2,000)	< 0.1
PTH 53-84	7,022 (2000)	< 0.1
PTH 39-84	9,970 (2000)	< 0.1
PTHrp 1-34	8,036 (2000)	< 0.1

Analytical Sensitivity - Routine Mode

The lowest detectable level of PTH distinguishable from zero (Access Intact PTH Calibrator S0) with 95% confidence is 1 pg/mL (0.1 pmol/L). This value is determined by processing a complete six point calibration curve, controls, and 10 replicates of the zero calibrator in multiple assays. The analytical sensitivity value is calculated from the curve at the point that is two standard deviations from the mean measured zero calibrator signal.

Functional Sensitivity - Routine Mode

The term functional sensitivity was originally used to define the lowest point in a TSH assay measuring range where results could be derived with a consistently attainable total imprecision of 20% CV.[16] The functional sensitivity, as determined by total imprecision of 20% CV, was found to be < 4 pg/mL (< 0.4 pmol/L).

Methods Comparison - Intraoperative Mode

A comparison of 393 values using the Access Intact PTH assay Intraoperative Mode on the Access Immunoassay system and a commercially available immunoassay system gave the following statistical data using Deming calculations:

n	Range of Observations pg/mL (pmol/L)	Intercept pg/mL (pmol/L)	Slope	Correlation Coefficient (r)
393	8.0-2,453 (0.8-260.0)	0.13 (0.014)	0.87	1.00

A comparison of 493 values using the Access Intact PTH assay Routine Mode and the Intraoperative Mode on the Access Immunoassay system gave the following statistical data using Deming calculations:

n	Range of Observations pg/mL (pmol/L)	Intercept pg/mL (pmol/L)	Slope	Correlation Coefficient (r)
493	13-2,848 (1.4-301.9)	9.69 (1.03)	0.94	1.00

Dilution Recovery (Linearity) - Intraoperative Mode

EDTA plasma samples obtained with elevated PTH concentrations were diluted in Access Sample Diluent A. The recovery results are summarized in the following table:

Sample 1	Expected Concentration pg/mL (pmol/L)	Determined Concentration pg/mL (pmol/L)	Recovery (%)
Neat	3,054 (323.7)	3,054 (323.7)	N/A
1/1.1	2,823 (299.2)	2,818 (298.7)	100
1/1.3	2,518 (266.9)	2,522 (267.3)	100
1/1.5	2,142 (227.1)	2,093 (221.9)	98
1/1.8	1,699 (180.1)	1,731 (183.5)	102
1/2.3	1,357 (143.8)	1,357 (143.8)	100
1/3.0	1,020 (108.1)	987 (104.6)	97
1/4.5	680 (72.1)	639 (67.7)	94

Sample 1	Expected Concentration pg/mL (pmol/L)	Determined Concentration pg/mL (pmol/L)	Recovery (%)
1/9.0	343 (36.4)	319 (33.8)	93
		Mean % Recovery	**98**

Sample 2	Expected Concentration pg/mL (pmol/L)	Determined Concentration pg/mL (pmol/L)	Recovery (%)
Neat	3,050 (323.3)	3,050 (323.3)	N/A
1/1.1	2,813 (298.2)	2,700 (286.2)	96
1/1.3	2,501 (265.1)	2,408 (255.2)	96
1/1.5	2,130 (225.8)	1,945 (206.2)	91
1/1.8	1,697 (179.9)	1,611 (170.8)	95
1/2.3	1355 (143.6)	1,244 (131.9)	92
1/3.0	1,018 (107.9)	931 (98.7)	91
1/4.5	678 (71.9)	576 (61.1)	85
1/9.0	343 (36.4)	290 (30.7)	85
		Mean % Recovery	**91**

Sample 3	Expected Concentration pg/mL (pmol/L)	Determined Concentration pg/mL (pmol/L)	Recovery (%)
Neat	737 (78.1)	737 (78.1)	N/A
1/5	148 (15.7)	138 (14.6)	93
1/10	75 (8.0)	63 (6.7)	84
1/25	31 (3.3)	26 (2.8)	85
1/50	16 (1.7)	14 (1.5)	88
1/100	8.6 (0.9)	7.8 (0.8)	90
		Mean % Recovery	**88**

Imprecision - Intraoperative Mode

This assay exhibits total imprecision ≤ 12% at concentrations greater than 12 pg/mL (1.3 pmol/L). One study, using human EDTA plasma based control material, performed with one instrument and during one calibration cycle, generating a total of 20 assays, 2 replicates per assay, over 22 days provided the following data, analyzed via analysis of variance (ANOVA).[15]

Human EDTA Plasma Sample	Mean Dose pg/mL (pmol/L)	Within Run (%CV)	Between Run (%CV)	Total Imprecision (%CV)
Level 1	11.4 (1.2)	6.8	8.1	10.6
Level 2	144 (15.3)	2.8	3.3	4.4
Level 3	1,433 (151.9)	3.2	3.0	4.4

Analytical Specificity/Interferences - Intraoperative Mode

The following drugs/interferents were added to an EDTA plasma sample pool containing approximately 60 pg/mL (6.4 pmol/L) PTH. Each drug/interferent was tested at a minimum of the concentration listed below. All PTH values obtained in the presence of each drug/interferent were within ± 10% of the control values indicating that these substances do not interfere with the assay.

Drug/interferent	Concentration tested	% Interference
Bilirubin, conjugated	20 mg/dL	1.1
Bilirubin, unconjugated	20 mg/dL	2.2
Triolein	3,000 mg/dL	6.1
Cholesterol	500 mg/dL	5.3
Hemoglobin	500 mg/dL	-0.3
Human serum albumin	49 g/L	-9.9
Acetaminophen	20 mg/dL	-0.3
D-biotin	100 µg/L	-1.3
Heparin	8,000 IU/dL	-2.0
Ibuprofen	40 mg/dL	0.2
Pamidronate	10 µg/mL	-0.2
Propofol	2 µg/mL	-4.0
Salicylic acid	50 mg/dL	2.0

Analytical Sensitivity - Intraoperative Mode

The lowest detectable level of PTH distinguishable from zero (Access Intact PTH Calibrator S0) with 95% confidence is 6 pg/mL (0.6 pmol/L). This value is determined by processing a complete six point calibration curve, controls, and 10 replicates of the zero calibrator in multiple assays. The analytical sensitivity value is calculated from the curve at the point that is two standard deviations from the mean measured zero calibrator signal.

Functional Sensitivity - Intraoperative Mode

The term functional sensitivity was originally used to define the lowest point in a TSH assay measuring range where results could be derived with a consistently attainable total imprecision of 20% CV.[16] The functional sensitivity, as determined by total imprecision of 20% CV, was found to be < 8 pg/mL (< 0.8 pmol/L).

ADDITIONAL INFORMATION

For a patient/user/third party in the European Union and in countries with identical regulatory regime (Regulation 2017/746/EU on In vitro Diagnostic Medical Devices); if, during the use of this device or as a result of its use, a serious

incident has occurred, please report it to the manufacturer and/or its authorized representative and to your national authority.

REVISION HISTORY

Revision A

New release of IVDR compliant IFU.

Revision B

Added Translations.

Revision C

Updated ProClin trademark statement.

Revision D

Added Translations.

Revision E

Updated "For Use" section.

Revision F

Updated Translations.

SYMBOLS KEY

Glossary of Symbols is available at beckmancoulter.com/techdocs (document number C02724).

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