



ARCHITECT

SYSTEM

en

Intact PTH

IVD

REF 8K25

84-6434/R5


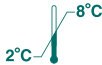


Read Highlighted Changes
Revised November, 2008

Intact PTH

Customer Service
United States: 1-877-4ABBOTT
International: Call your Abbott Representative

This package insert must be read carefully before product use. Package insert instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

Key to symbols used

| | | | |
|---|---|-------------------------|------------------|
| REF | List Number | REACTION VESSELS | Reaction Vessels |
| IVD | <i>In Vitro</i> Diagnostic Medical Device | SAMPLE CUPS | Sample Cups |
| LOT | Lot Number | SEPTUM | Septum |
|  | Expiration Date | REPLACEMENT CAPS | Replacement Caps |
|  | Store at 2-8°C | REAGENT LOT | Reagent Lot |
|  | Consult instructions for use | ASSAY CD-ROM | Assay CD-ROM |
| SN | Serial Number | CONTROL NO. | Control Number |
|  | Manufacturer | | |

See **REAGENTS** section for a full explanation of symbols used in reagent component naming.

NAME

ARCHITECT Intact PTH

INTENDED USE

The ARCHITECT Intact PTH assay is an *in vitro* chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of intact parathyroid hormone (PTH) in human serum and plasma on the ARCHITECT *i* System.

SUMMARY AND EXPLANATION OF TEST

PTH is a single chain polypeptide of 84 amino acids produced by the parathyroid gland. Intact PTH1-84 is secreted into the blood stream and undergoes extensive proteolytic modifications. In contrast to its degradation products, the concentration of intact PTH is relatively independent of glomerular filtration rate and reflects the biologically active portion of the hormone.¹

The primary role of PTH is to regulate the blood calcium level. PTH synthesis and secretion are stimulated within a few minutes by low concentrations of ionized calcium (Ca_i). The biological activity of PTH is to increase absorption of dietary calcium, decrease renal clearance and mobilize skeletal calcium stores. Abnormally high Ca_i concentrations suppress secretion of PTH.¹

In conjunction with serum calcium levels, the PTH assay may be used as an aid in the differential diagnosis of hypercalcemia, hypocalcemia and parathyroid disorders. PTH determination is important in monitoring dialysis patients to manage renal osteodystrophy.

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT Intact PTH assay is a two-step sandwich immunoassay for the quantitative determination of intact PTH in human serum and plasma using CMIA technology with flexible assay protocols, referred to as Chemiflex.

In the first step, sample, assay diluent, and anti-PTH coated paramagnetic microparticles are combined. Intact PTH present in the sample binds to the anti-PTH coated microparticles. After washing, anti-PTH acridinium-labeled conjugate is added to create a reaction mixture in the second step. Following another wash cycle, pre-trigger and trigger solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light units (RLUs).

A direct relationship exists between the amount of intact PTH in the sample and the RLUs detected by the ARCHITECT *i* System optics.

For additional information on system and assay technology, refer to the ARCHITECT System Operations Manual, Section 3.

REAGENTS

Reagent Kit

NOTE: Some kit sizes are not available in all countries. Please contact your local distributor.

ARCHITECT Intact PTH Reagent Kit (8K25)

- **MICROPARTICLES** 1 or 4 Bottle(s) (6.6 mL each) Anti-PTH (goat, polyclonal) coated microparticles in TRIS buffer. Preservative: sodium azide.
- **CONJUGATE** 1 or 4 Bottle(s) (5.9 mL each) Anti-PTH (goat, polyclonal) acridinium-labeled conjugate in MES buffer with protein (bovine, goat) stabilizer. Preservative: sodium azide.
- **ASSAY DILUENT** 1 or 4 Bottle(s) (10.0 mL each) Intact PTH Assay Diluent containing phosphate buffer with protein (bovine, goat) stabilizer. Preservative: sodium azide.

Assay Diluent

ARCHITECT *i* Multi-Assay Manual Diluent (7D82-50)

- **MULTI-ASSAY MANUAL DILUENT** 1 Bottle (100 mL) ARCHITECT *i* Multi-Assay Manual Diluent containing phosphate buffered saline solution. Preservative: antimicrobial agent.

Other Reagents

ARCHITECT *i* Pre-Trigger Solution

- **PRE-TRIGGER SOLUTION** Pre-Trigger Solution containing 1.32% (w/v) hydrogen peroxide.

ARCHITECT *i* Trigger Solution

- **TRIGGER SOLUTION** Trigger Solution containing 0.35 N sodium hydroxide.

ARCHITECT *i* Wash Buffer

- **WASH BUFFER** Wash Buffer containing phosphate buffered saline solution. Preservative: antimicrobial agent.

WARNINGS AND PRECAUTIONS

- **For *In Vitro* Diagnostic Use.**


Safety Precautions

- **CAUTION:** This product requires the handling of human specimens. It is recommended that all human sourced materials be considered potentially infectious and handled in accordance with the OSHA Standard on Bloodborne Pathogens.² Biosafety Level 2³ or other appropriate biosafety practices^{4,5} should be used for materials that contain or are suspected of containing infectious agents.
- This product contains sodium azide. For a specific listing, refer to the **REAGENTS** section of this package insert. Contact with acids liberates very toxic gas. This material and its container must be disposed of in a safe way.
- For product not classified as dangerous per European Directive 1999/45/EC as amended - Safety data sheet available for professional user on request.
- For a detailed discussion of safety precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 8.

Handling Precautions

- Do not use reagent kits beyond the expiration date.
- **Do not pool reagents within a reagent kit or between reagent kits.**
- Before loading the ARCHITECT Intact PTH Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend the microparticles that have settled during shipment. For microparticle mixing instructions, refer to the **PROCEDURE, Assay Procedure** section of this package insert.
- **Septums MUST be used to prevent reagent evaporation and contamination, and to ensure reagent integrity. Reliability of assay results cannot be guaranteed if septums are not used according to the instructions in this package insert.**
 - To avoid contamination, wear clean gloves when placing a septum on an uncapped reagent bottle.
 - Once a septum has been placed on an open reagent bottle, **do not invert the bottle** as this will result in reagent leakage and may compromise assay results.
 - Over time, residual liquids may dry on the septum surface. These are typically dried salts, which have no effect on assay efficacy.
- For a detailed discussion of handling precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 7.

Storage Instructions

-  The ARCHITECT Intact PTH Reagent Kit must be stored at 2-8°C in an upright position and may be used immediately after removal from 2-8°C storage.
- When stored and handled as directed, reagents are stable until the expiration date.
- The ARCHITECT Intact PTH Reagent Kit may be stored on board the ARCHITECT *i* System for a maximum of 30 days. After 30 days, the reagent kit must be discarded. For information on tracking onboard time, refer to the ARCHITECT System Operations Manual, Section 5.
- Reagents may be stored on or off the ARCHITECT *i* System. If reagents are removed from the system, store them at 2-8°C (with septums and replacement caps) in an upright position. For reagents stored off the system, it is recommended that they be stored in their original trays and boxes to ensure they remain upright. **If any bottle does not remain upright (with a septum installed) while in refrigerated storage off the system, the reagent kit must be discarded.** After reagents are removed from the system, initiate a reagent scan to update the onboard stability timer.

Indications of Reagent Deterioration

When a control value is out of the specified range, it may indicate deterioration of the reagents or errors in technique. Associated test results are invalid and samples must be retested. Assay recalibration may be necessary. For troubleshooting information, refer to the ARCHITECT System Operations Manual, Section 10.

INSTRUMENT PROCEDURE

- The ARCHITECT Intact PTH assay file (assay number 581) must be installed on the ARCHITECT *i* System from the ARCHITECT *i* Assay CD-ROM Addition E before performing the assay.
- The ARCHITECT Intact PTH STAT assay file (assay number 585) must be installed on the ARCHITECT *i* System with *STAT* protocol capability from the ARCHITECT *i* Assay CD-ROM Addition E before performing the assay.
- The Routine assay may not be available on all ARCHITECT *i* Systems.
- For detailed instructions on the assay file installation and on viewing and editing assay parameters, refer to the ARCHITECT System Operations Manual, Section 2.
- For information on printing assay parameters, refer to the ARCHITECT System Operations Manual, Section 5.
- For a detailed description of system procedures, refer to the ARCHITECT System Operations Manual.
- The default result unit for the ARCHITECT Intact PTH assay is pg/mL. An alternate result unit, pmol/L, may be selected for reporting results by editing assay parameter "Result concentration units" to pmol/L. The conversion factor used by the system is 0.106.
- Conversion formula: (Concentration in pg/mL) x (0.106) = pmol/L.

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

The specimen collection tubes listed below were verified to be used with the ARCHITECT Intact PTH assay.

- Human serum (use of serum separator tubes may result in a decrease in concentration).
- Human plasma collected in:
 - Lithium Heparin
 - Sodium Heparin
 - Potassium EDTA
- Liquid anticoagulants may have a dilution effect resulting in lower concentrations for individual patient specimens.
- The ARCHITECT *i* System does not provide the capability to verify specimen type. It is the responsibility of the operator to verify that the correct specimen types are used in the ARCHITECT Intact PTH assay.
- Sodium Citrate, Sodium Fluoride/Potassium Oxalate, and Ammonium Heparin tubes cannot be used with the ARCHITECT Intact PTH assay.

Specimen Conditions

- Do not use specimens with the following conditions:
 - heat-inactivated
 - pooled
 - grossly hemolyzed (> 500 mg/dL)
 - obvious microbial contamination
 - cadaver specimens or any other body fluids
- For accurate results, serum and plasma specimens should be free of fibrin, red blood cells or other particulate matter. Serum specimens from patients receiving anticoagulant or thrombolytic therapy may contain fibrin due to incomplete clot formation.
- Use caution when handling patient specimens to prevent cross contamination. Use of disposable pipettes or pipette tips is recommended.
- For optimal results, inspect all specimens for bubbles. Remove bubbles with an applicator stick before analysis. Use a new applicator stick for each specimen to prevent cross contamination.

Preparation for Analysis

- Follow the tube manufacturer's processing instructions for serum and plasma collection tubes. Gravity separation is not sufficient for specimen preparation.
- Mix thawed specimens thoroughly by low speed vortexing or by inverting 10 times. Visually inspect the specimens. If layering or stratification is observed, continue mixing until specimens are visibly homogeneous.

- To ensure consistency in results, specimens must be transferred to a centrifuge tube and centrifuged at $\geq 10,000$ RCF (Relative Centrifugal Force) for 10 minutes before testing if
 - they contain fibrin, red blood cells, or other particulate matter, or
 - they require repeat testing.Transfer clarified specimens to a sample cup or secondary tube for testing.
- Centrifuged specimens with a lipid layer on the top must be transferred to a sample cup or secondary tube. Care must be taken to transfer only the clarified specimens without the lipemic material.

Storage

- Specimens may be stored on or off the clot, or red blood cells for up to 2 days refrigerated at 2-8°C.
- If testing will be delayed more than 2 days, remove serum or plasma from the clot, or red blood cells and store frozen.
- Specimens stored frozen for 6 months showed no performance difference. Avoid more than 5 freeze/thaw cycles.

Shipping

- Before shipping specimens, it is recommended that specimens be removed from the clot or red blood cells.
- When shipping specimens, package and label specimens in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances.
- Specimens may be shipped on wet ice or on dry ice. Do not exceed the storage time limitations listed above.

PROCEDURE

Materials Provided

- 8K25 ARCHITECT Intact PTH Reagent Kit

Materials Required but not Provided

- ARCHITECT *i* System
- 1L66 ARCHITECT *i* **ASSAY CD-ROM** - WW (excluding US) - Addition E
- 8K25-01 ARCHITECT Intact PTH Calibrators
- 8K25-10 ARCHITECT Intact PTH Controls
- 7D82-50 ARCHITECT *i* **MULTI-ASSAY MANUAL DILUENT**
- ARCHITECT *i* **PRE-TRIGGER SOLUTION**
- ARCHITECT *i* **TRIGGER SOLUTION**
- ARCHITECT *i* **WASH BUFFER**
- ARCHITECT *i* **REACTION VESSELS**
- ARCHITECT *i* **SAMPLE CUPS**
- ARCHITECT *i* **SEPTUM**
- ARCHITECT *i* **REPLACEMENT CAPS**
- Pipettes or pipette tips (optional)

For information on materials required for maintenance procedures, refer to the ARCHITECT System Operations Manual, Section 9.

Assay Procedure

- Before loading the ARCHITECT Intact PTH Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend the microparticles that have settled during shipment. After the first time the microparticles have been loaded, no further mixing is required.
 - **Invert the microparticle bottle 30 times.**
 - Visually inspect the bottle to ensure microparticles are resuspended. If microparticles remain adhered to the bottle, continue inverting the bottle until the microparticles have been completely resuspended.
 - **If the microparticles do not resuspend, DO NOT USE. Contact your local Abbott representative.**
- Once the microparticles have been resuspended, place a septum on the bottle. For instructions on placing septums on bottles, refer to the **Handling Precautions** section of this package insert.

- Load the ARCHITECT Intact PTH Reagent Kit on the ARCHITECT *i* System or the ARCHITECT *i* System with *STAT* protocol capability.
 - Verify that all necessary assay reagents are present.
 - Ensure that septums are present on all reagent bottles.
- Order calibration, if necessary.
 - For information on ordering calibrations, refer to the ARCHITECT System Operations Manual, Section 6.
- Order tests.
 - For information on ordering patient specimens and controls and for general operating procedures, refer to the ARCHITECT System Operations Manual, Section 5.
- The minimum sample cup volume is calculated by the system and is printed on the Orderlist report. No more than 9 replicates may be sampled from the same sample cup. To minimize the effects of evaporation, verify adequate sample cup volume is present before running the test.
 - Priority: 200 µL for the first ARCHITECT Intact PTH test plus 150 µL for each additional ARCHITECT Intact PTH test from the same sample cup.
 - ≤ 3 hours on board: 200 µL for the first ARCHITECT Intact PTH test plus 150 µL for each additional ARCHITECT Intact PTH test from the same sample cup.
 - > 3 hours on board: additional sample volume is required. For information on sample evaporation and volumes, refer to the ARCHITECT System Operations Manual, Section 5.
 - If using primary or aliquot tubes, use the sample gauge to ensure sufficient patient specimen is present.
- Prepare calibrators and controls.
 - Mix ARCHITECT Intact PTH Calibrators and Controls by gentle inversion before use.
 - To obtain the recommended volume requirements for the ARCHITECT Intact PTH Calibrators and Controls, hold the bottles **vertically** and dispense 15 drops of each calibrator or 10 drops of each control into each respective sample cup.
- Load samples.
 - For information on loading samples, refer to the ARCHITECT System Operations Manual, Section 5.
- Press RUN.
- For additional information on principles of operation, refer to the ARCHITECT Operations Manual, Section 3.
- For optimal performance, it is important to perform routine maintenance as described in the ARCHITECT System Operations Manual, Section 9. When a laboratory requires more frequent maintenance, follow those procedures.

Specimen Dilution Procedures

Specimens with an intact PTH concentration of > 3000.0 pg/mL (Routine protocol) or > 2500.0 pg/mL (STAT protocol) will be flagged as “> 3000.0 pg/mL” or “> 2500.0 pg/mL” and may be diluted with the Manual Dilution Procedure.

- Manual dilutions should be performed as follows:
 - The suggested dilution for the ARCHITECT Intact PTH assay is 1:2.
 - Add 150 µL of the patient specimen to 150 µL of ARCHITECT *i* Multi-Assay Manual Diluent.
 - The operator must enter the dilution factor in the Patient or Control order screen. The system will use this dilution factor to automatically calculate the concentration of the sample before dilution and report the result. The result (before dilution factor is applied) should be greater than 1.0 pg/mL.
- For detailed information on ordering dilutions, refer to the ARCHITECT System Operations Manual, Section 5.

Calibration

- To perform an ARCHITECT Intact PTH calibration, test calibrators A, B, C, D, E, and F in replicates of two. A single sample of each Intact PTH control level must be tested to evaluate the assay calibration. Ensure that assay control values are within the concentration ranges specified in the control package insert. Calibrators should be priority loaded.
- Calibration Range:
 - Routine protocol: 0.0 – 3000.0 pg/mL
 - STAT protocol: 0.0 – 2500.0 pg/mL
- Once an ARCHITECT Intact PTH calibration is accepted and stored, all subsequent samples may be tested without further calibration unless:
 - A reagent kit with a new lot number is used.
 - Controls are out of range.
- For detailed information on how to perform an assay calibration, refer to the ARCHITECT System Operations Manual, Section 6.

QUALITY CONTROL PROCEDURES

The recommended control requirement for the ARCHITECT Intact PTH assay is that a single sample of each control be tested once every 24 hours each day of use. If laboratory quality control procedures require more frequent use of controls to verify test results, follow those procedures.

The ARCHITECT Intact PTH Control values must be within the acceptable ranges specified in the control package insert. If a control is out of its specified range, the associated test results are invalid and samples must be retested. Recalibration may be indicated.

Verification of Assay Claims

For protocols to verify package insert claims, refer to the ARCHITECT System Operations Manual, Appendix B. The ARCHITECT Intact PTH assay belongs to method group 1. ARCHITECT Intact PTH Calibrators may be used when MasterCheck is not available. Refer to the ARCHITECT System Operations Manual, Appendix B.

RESULTS

Calculation

The ARCHITECT Intact PTH assay uses a point to point data reduction method to generate a calibration curve.

Flags

- Some results may contain information in the Flags field. For a description of the flags that may appear in this field, refer to the ARCHITECT System Operations Manual, Section 5.

Measurement Range (Reportable Range)

The measurement range for the ARCHITECT Intact PTH assay is

- STAT protocol: 4.0 pg/mL to 2500.0 pg/mL

- Routine protocol: 3.0 pg/mL to 3000.0 pg/mL

Results below the range of measurement should be reported as < 4.0 pg/mL or < 3.0 pg/mL, respectively.

LIMITATIONS OF THE PROCEDURE

- If the Intact PTH results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.
- For diagnostic purposes, the results should be used in conjunction with other data; e.g., symptoms, results of other tests, clinical impressions, etc.
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays.⁶ 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

It is recommended that each laboratory establish its own reference range, which may be unique to the population it serves depending on the geographical, dietary, or environmental factors.

A study was performed for the ARCHITECT Intact PTH assay to establish the reference range using plasma specimens from apparently healthy adults. Data from this study are summarized in the following table.*

| | n | Intact PTH (pg/mL) | | |
|----------------|-----|--------------------|------------------------------|-------------------------------|
| | | Median | 2.5 th percentile | 97.5 th percentile |
| Healthy Adults | 143 | 35.6 | 15.0 | 68.3 |

* Representative performance data are shown. Results obtained at individual laboratories may vary.

SPECIFIC PERFORMANCE CHARACTERISTICS

Precision

The ARCHITECT Intact PTH assay is designed to have precision of $\leq 9\%$ total CV for the Low Control and of $\leq 7\%$ total CV for the Medium and High Control. A study was performed for the ARCHITECT Intact PTH assay, based on guidance from the National Committee for Clinical Laboratory Standards Institute (NCCLS) Protocol EP5-A.7 Multiple ARCHITECT Intact PTH control lots were assayed using two lots of reagents in replicates of two at two separate times per day for 20 days at one site on two instruments using the STAT protocol and at a second site on two instruments using the Routine protocol.

In addition, a second precision study was performed, where two lots of reagents were assayed in four replicates per run at two separate times per day over 10 days on one instrument at a third site using the STAT protocol and on one instrument at a fourth site using the Routine protocol. Each reagent lot used a single calibration curve throughout the study. Data from both studies are summarized in the following tables.*

ARCHITECT Intact PTH Precision Using STAT Protocol

| Sample | n | Mean Conc. (pg/mL) | Within Run | | Total ^a | |
|----------------|-----|--------------------|------------|-----|--------------------|-----|
| | | | SD | %CV | SD | %CV |
| Low Control | 878 | 8.5 | 0.74 | 8.7 | 0.74 | 8.7 |
| Medium Control | 880 | 56.5 | 2.34 | 4.1 | 2.35 | 4.2 |
| High Control | 880 | 208.9 | 8.62 | 4.1 | 8.62 | 4.1 |

ARCHITECT Intact PTH Precision Using Routine Protocol

| Sample | n | Mean Conc. (pg/mL) | Within Run | | Total ^a | |
|----------------|-----|--------------------|------------|-----|--------------------|-----|
| | | | SD | %CV | SD | %CV |
| Low Control | 880 | 10.7 | 0.65 | 6.1 | 0.69 | 6.4 |
| Medium Control | 880 | 69.6 | 2.28 | 3.3 | 2.31 | 3.3 |
| High Control | 880 | 255.8 | 7.40 | 2.9 | 7.56 | 3.0 |

^a Total assay variability contains within run, run to run and day to day variability.

* Representative performance data are shown. Results obtained at individual laboratories may vary.

Recovery

The ARCHITECT Intact PTH assay is designed to have a mean recovery of $100 \pm 10\%$. A study was performed where known concentrations (0, 4.8, 24, 120, 600 pg/mL) of intact PTH were added to 10 aliquots of human plasma with endogenous levels ranging from 22.9 pg/mL to 162.8 pg/mL of intact PTH. The concentration of intact PTH and the percent recovery were calculated for each sample. The percent recovery of the ARCHITECT Intact PTH assay resulted in a mean of 101%. Data are representative performance data, but results obtained at individual laboratories may vary.

Linearity

The ARCHITECT Intact PTH assay is designed to recover diluted specimens within $\pm 10\%$ of the expected result in the dilution range from 20% to 80%. A dilution linearity study was performed using specimens with undiluted intact PTH values that ranged between 65.6 pg/mL and 2257.0 pg/mL. These specimens were diluted manually using ARCHITECT *i* Multi-Assay Manual Diluent at various dilution factors (0.2 to 0.8) to result in 80% to 20% of the endogenous intact PTH level. Data from this study are summarized in the following tables.*

| Sample | Dilution Factor | Observed Values (pg/mL) | % Mean Recovery ^a |
|--------|-----------------|-------------------------|------------------------------|
| 1 | undiluted | 65.6 | – |
| | 0.2 to 0.8 | 53.8 to 12.4 | 97 |
| 2 | undiluted | 779.9 | – |
| | 0.2 to 0.8 | 644.7 to 163.2 | 103 |
| 3 | undiluted | 2257.0 | – |
| | 0.2 to 0.8 | 1860.5 to 435.2 | 98 |

In addition, a dilution study was performed using specimens with different high and low intact PTH concentration values ranging between 19.1 pg/mL and 2038.8 pg/mL. The low level sample was used to dilute the high level sample to different concentrations (dilution factors of 0.25, 0.50 and 0.75). Data from this study are summarized in the following table.*

| Sample | Undiluted Concentration Level (pg/mL) | Diluted Concentration Range (pg/mL) | % Mean Recovery ^a |
|--------|---------------------------------------|-------------------------------------|------------------------------|
| 1 | Low 19.1 | 168.3 to | 101 |
| | High 615.0 | 477.1 | |
| 2 | Low 21.5 | 339.5 to | 104 |
| | High 1271.9 | 989.4 | |
| 3 | Low 22.8 | 522.6 to | 102 |
| | High 2038.8 | 1580.8 | |

$$^a \text{ \% Recovery} = \frac{\text{Observed Value (pg/mL)}}{\text{Expected Value (pg/mL)}} \times 100$$

% Mean Recovery = Mean of % Recovery of all dilutions of a sample

* Representative performance data are shown. Results obtained at individual laboratories may vary.

Functional Sensitivity

The ARCHITECT Intact PTH assay is designed to have a functional sensitivity of ≤ 5 pg/mL at a total CV of 20%. A study was performed using human samples with concentrations targeted at 3 pg/mL, 4 pg/mL and 5 pg/mL of intact PTH. Those samples were tested in replicates of two over 10 days using two reagent lots on two instruments using the STAT protocol and on one instrument using the Routine protocol. Functional sensitivity was determined to be ≤ 4 pg/mL* for the STAT protocol and ≤ 3 pg/mL* for the Routine protocol.

* Representative performance data are shown. Results obtained at individual laboratories may vary.

Analytical Sensitivity

The ARCHITECT Intact PTH assay is designed to have an analytical sensitivity of ≤ 1 pg/mL. Analytical sensitivity is defined as the concentration at two standard deviations above the calibrator A (0.0 pg/mL). In a study (n = 12 runs, 20 replicates of calibrator A and 10 replicates of calibrator B, using three instruments and two reagent lots), the analytical sensitivity was calculated to be 0.23 pg/mL* using the Routine protocol and 0.31 pg/mL* using the STAT protocol at a 95% level of confidence.

* Representative performance data are shown. Results obtained at individual laboratories may vary.

Specificity

The specificity of the ARCHITECT Intact PTH assay is designed to have a cross-reactivity of $\leq 0.01\%$ when tested with structurally similar compounds listed in the table below. A study was performed with the ARCHITECT Intact PTH assay based on guidance from NCCLS Protocol EP7-A.8 Aliquots of ARCHITECT Intact PTH Calibrator A were supplemented with potential cross-reactants at the concentrations listed and tested for intact PTH. Data from this study are summarized in the following table.*

| PTH fragment | Concentrations | % Cross-Reactivity ^a |
|--------------|----------------|---------------------------------|
| 1-34 | 100000 pg/mL | 0.00 |
| 39-68 | 100000 pg/mL | 0.00 |
| 53-84 | 100000 pg/mL | 0.00 |
| 44-68 | 100000 pg/mL | 0.00 |
| 39-84 | 100000 pg/mL | 0.00 |

$$^a \text{ \% Cross-Reactivity} = \frac{\text{Mean Value spiked} - \text{Mean Value non spiked (pg/mL)}}{\text{Concentration of Cross-Reactant (pg/mL)}} \times 100$$

* Representative performance data are shown. Results obtained at individual laboratories may vary.

Interference

Potential interference in the ARCHITECT Intact PTH assay from hemoglobin, bilirubin, triglycerides, and protein at the levels indicated below is designed to be $\leq 10\%$. Interference was demonstrated by a study based on guidance from the NCCLS Protocol EP7-A.⁸ There was no significant interference observed since the % mean recovery is within $\pm 10\%$ of the expected value. Data from this study are summarized in the following table.*

Potentially Interfering

| Substance | Concentration | % Mean Recovery ^a |
|---------------------------------|---------------|------------------------------|
| Hemoglobin | 500 mg/dL | 102 |
| Bilirubin | 20 mg/dL | 98 |
| Triglycerides | 5000 mg/dL | 105 |
| Protein low | 4 g/dL | 106 |
| Protein high | 9.5 g/dL | 93 |
| Protein high (Routine protocol) | 10.5 g/dL | 94** |

$$^a \text{ \% Recovery} = \frac{\text{Observed Value (pg/mL)}}{\text{Expected Value (pg/mL)}} \times 100$$

% Mean Recovery = Mean of % Recovery of all tested samples

* Representative performance data are shown. Results obtained at individual laboratories may vary.

** For using the STAT protocol, interference with high levels of protein may be observed.

Method Comparison

The ARCHITECT Intact PTH assay is designed to have a correlation coefficient of ≥ 0.95 when evaluated against a comparison assay. A study was performed with the ARCHITECT Intact PTH assay, where regression analysis was performed using the Passing-Bablok and Least Squares regression methods. Data from this study are summarized in the following table.*

| ARCHITECT Intact PTH vs. Comparison Assay | | | | |
|---|-----|-------|-----------|-------------------------|
| Regression Method | n | Slope | Intercept | Correlation Coefficient |
| Passing-Bablok ^a | 199 | 1.02 | 0.61 | 0.99 |
| Least Squares | 199 | 0.98 | 9.00 | |

^a A linear regression method with no special assumptions regarding the distribution of samples and measurement errors.⁹

In this evaluation, specimen concentrations ranged from 5.9 pg/mL to 1277.0 pg/mL with the ARCHITECT Intact PTH assay and from 7.5 pg/mL to 1344.3 pg/mL with the comparison assay.

Another study was performed comparing the ARCHITECT Intact PTH assay to a diagnostic assay commercially available. In the study 709 specimens were analyzed resulting in a correlation coefficient of 0.99*. The specimen concentrations ranged from 1.5 to 2326.9 pg/mL with the ARCHITECT Intact PTH assay and from 1.2 to 1813.0 pg/mL with the commercially available diagnostic kit. The specimen categories included in the study are as follows: normal adults (285), series of intraoperative measurements of parathyroidectomy (32), Hypoparathyroidism (20), Primary Hyperparathyroidism (39), Chronic Renal Failures (93), Hypercalcemia of malignancies (40), randomized PTH levels (200).

* Representative performance data are shown. Variables such as differences in sampling size and sample population may impact the correlation of the assay, therefore, results obtained at individual laboratories may vary from these data.

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