CPAL
Central **P**ennsylvania **A**lliance
Laboratory

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Intact PTH
- Testing System Change –

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Affected Tests:

Mnemonics:	PTH GP (PTH, Calcium and Nomogram)	PTH PLUS (PTH, Calcium, Creatinine, Phosphorous and Nomogram)
Test Name:	PTH Intact Group	PTH Intact, Plus
Test Number:	1750033	1750032
Specimen:	1.0 mL Serum, frozen within 8 hours (-20^{o}C)	

Effective Date: Testing will begin on January 26, 2015 with samples received in the afternoon on January 23, 2015.

Performed: Monday through Friday

Reference Range: 9 - 72 pg/mL

Method Change:
Parathyroid hormone will be moved from the Siemens Immulite to the Abbott Architect i2000, as the Immulite is being phased out.

Background:
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.

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. In conjunction with serum calcium levels, the Architect Intact 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**.**

Principle of Test:
The Architect Intact PTH assay is a two-step sandwich immunoassay for the quantitative determination of intact PTH in human serum 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.

Results Interpretation:
Old Reference range: 12 - 65 pg/mL
New Reference range: 9 - 72 pg/mL

Note: The following comment and interpretive guide will appear on reports:

Effective 1/24/2015: The previous plotted nomogram has been replaced with Guidelines for the Interpretation of PTH and Calcium results. Please refer to these guidelines to evaluate patient results.

Generalized Guidelines for Interpretation of PTH and Calcium Results

Classification	Definition PTH (pg/mL)	Definition Calcium (mg/dL)
Normal	9 to 72	8.6 to 10.3
Primary or Tertiary hyperparathyroidism	>72	>10.3
Secondary hyperparathyroidism	>72	<=10.3
Hypoparathyroidism	<9	<9.0
Non parathyroid Hypercalcemia	<72	>10.3

A definitive clinical diagnosis should not be based upon the result of a single diagnostic method, but should only be made by the physician after all clinical and laboratory findings have been evaluated.

Limitations:

1. For diagnostic purposes, results should be used in conjunction with other data; e.g., symptoms, results of other tests, clinical impressions, etc.
2. If the Intact PTH results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.
3. Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays. 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.
4. This assay has not been clinically validated for intraoperative use.

Validation Data:

Precision

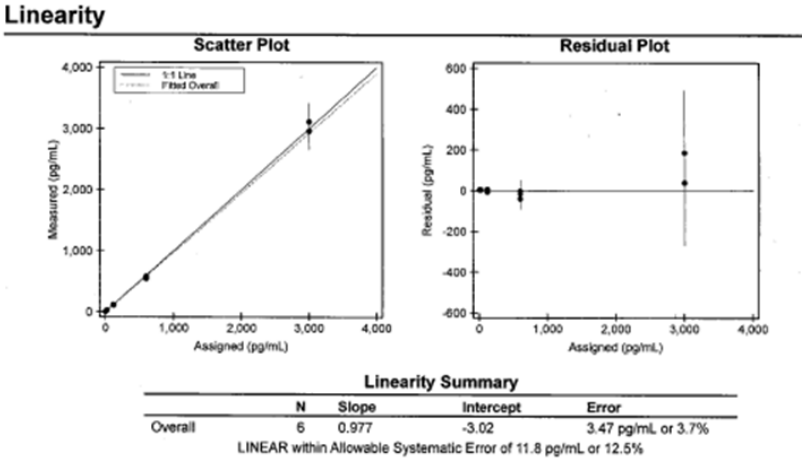
Precision was analyzed using two levels of PTH controls, with 10 replicates in each run for two days. The CVs fall within the Manufacturer's claims of ≤ 9% for the low control and ≤ 7% for the high control. Criteria were met for both within run and between run precision (Table 1).

Table 1		**PTH Precision**					
Within Run Precision				**Between Run Precision**			
pg/mL	**%CV**	**pg/mL**	**%CV**	**pg/mL**	**%CV**	**pg/mL**	**%CV**
9.6	5.51%	240.4	4.68%	9.25	6.12%	238.45	4.12%

Linearity

To verify the analytical measurement range of the assay, 6 levels of known standard materials were used, spanning the analytical measurement range of 3.0 pg/mL to 3000 pg/mL. Linear regression analysis yielded a slope is 0.977 with an intercept of -3.02 with an error of 3.47 pg/mL or 3.7%. The assay is linear within Allowable Systematic Error of 11.8 pg/mL or 12.5. (Figure 1)

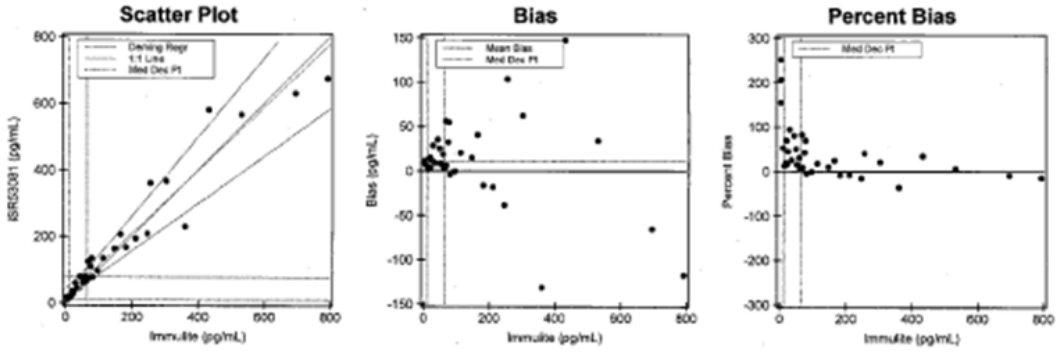
Figure 1: PTH Linearity (pg/mL)



Method Comparison

A total of 39 specimens were split and processed utilizing the Siemens Immulite 2000 assay and the Abbott Architect i2000 assay. Quantitative analysis yielded a correlation coefficient (R) of 0.9677 with a slope of 0.950 and an intercept of 17.90. Overall bias for the Architect i2000 vs the Immulite was 10.48%. Medical decision point analysis showed the manufacturer's stated range of 9 - 72 pg/mL fell within the calculated 95% confidence intervals, with only 1 interpretive outlier of 39 specimens. A separate reference range validation confirmed this range utilizing 20 normal specimens.

Figure 2: PTH Method Comparison (Architect vs Immulite)



Regression Analysis

	Deming	Regular
Slope	0.950 (0.867 to 1.033)	0.921 (0.839 to 1.003)
Intercept	17.90 (-2.03 to 37.82)	22.23 (2.45 to 42.01)
Std Err Est	46.92	46.58

95% Confidence Intervals are shown in parentheses

References:

1. Architect System Intact PTH package insert; 04/13.
2. Architect System Intact PTH Calibrators package insert; 12/06.