510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

k133601

B. Purpose for Submission:

Modified polyclonal antibody

C. Measurand:

Intact Parathyroid Hormone (iPTH)

D. Type of Test:

Quantitative Immunoassay

E. Applicant:

Siemens Healthcare, Inc.

F. Proprietary and Established Names:

ADVIA Centaur Intact Parathyroid Hormone (iPTH) Assay

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
CEW	II	862.1545 Parathyroid hormone test system	75 (Chemistry)

H. Intended Use:

1. Intended use(s):

   See indications for use below

2. Indication(s) for use: The ADVIA Centaur Intact Parathyroid (iPTH) assay is for in vitro diagnostic use in the quantitative determination of intact parathyroid hormone (iPTH) in EDTA plasma or serum using the ADVIA Centaur and ADVIA Centaur XP systems. This assay is intended to be used to aid in the differential diagnosis of hyperparathyroidism and hypoparathyroidism.

3. Special conditions for use statement(s):

   For prescription use only.

4. Special instrument requirements:

   Siemens ADVIA Centaur and ADVIA Centaur XP systems.

I. Device Description:

The device consists of the following two reagents:

1. Lite Reagent 5.0 mL/ reagent pack - The Lite Reagent contains acridinium ester-labeled polyclonal goat antihuman PTH (1-34 N-terminal) antibody (~1 µg/mL) in phosphate buffered saline with goat IgG, bovine gamma globulin, bovine serum albumin, and preservatives
2. Solid Phase 20.0 mL/ reagent pack - The Solid Phase reagent contains biotinylated polyclonal goat anti-human PTH (39-84 region) antibody (~3 µg/mL) and streptavidin (~0.4 mg/mL) covalently coupled to paramagnetic latex particles in phosphate buffered saline with goat IgG, bovine gamma globulin, bovine serum albumin, and preservatives

J. Substantial Equivalence Information:

Reagent Similarities and Differences		
Item	Candidate Device: ADVIA Centaur Intact Parathyroid Hormone (iPTH)	Predicate Device: ADVIA Centaur Intact Parathyroid Hormone (iPTH) k121981
Intended Use/Indications for Use	The ADVIA Centaur Intact Parathyroid (iPTH) assay is for in vitro diagnostic use in the quantitative determination of intact parathyroid hormone (iPTH) in EDTA plasma or serum using the ADVIA Centaur and ADVIA Centaur XP systems. This assay is intended to be used to aid in the differential diagnosis of hyperparathyroidism and hypoparathyroidism.	Same

Sample Type	EDTA Plasma, Serum	same
Measurement	Quantitative	same
Operating Principle	Sandwich Immunoassay	same
Technology	Chemiluminescence	same
Detection Antibody	Goat polyclonal antibody conjugated to Acridium Ester	New goat polyclonal antibody conjugated to Acridium Ester
Capture Antibody	Goat polyclonal antibody conjugated to biotin directly coupled to streptavidin magnetic particles	New goat polyclonal antibody conjugated to biotin directly coupled to streptavidin magnetic particles
Assay Range	6.3 – 1900 pg/mL	5.5 – 1900 pg/mL
Sample Volume	200 µL	same
Calibrators	Siemens iPTH Calibrators	same
Calibration	2 Point	same
Number of calibrators	Two (2) levels	same
Expected Values	13.8 – 85.0 pg/mL (plasma) 12.4 – 76.8 pg/mL (serum)	same

K. Standard/Guidance Document Referenced (if applicable):

- CLSI Guideline EP5-A2: Evaluation of Precision Performance of Qualitative
- Measurement Methods
- CLSI Guideline EP17-A2: Evaluation of Detection Capability for Clinical
- Laboratory Measurement Procedures
- CLSI Guideline EP6-A: Evaluation of the Linearity of Qualitative Measurement
- Methods
- CLSI Guideline C28-A3c: Defining, Establishing, and Verifying Reference
- Intervals in the Clinical Laboratory; Approved Guideline
- CLSI Guideline EP7-A2: Interference Testing in Clinical Chemistry; Approved
- Medical devices – Application of risk management to medical devices; (ANSI/AAMI/ISO 14971:2007/(R) 2010)

L. Test Principle:

The ADVIA Centaur Intact PTH assay is a two-site sandwich immunoassay using direct chemiluminometric technology. PTH in the sample reacts with the first antibody (in the Lite Reagent) which is a polyclonal goat anti-human PTH (N-terminal 1–34) antibody labeled with acridinium ester. This complex is then captured by the solid phase (a second antibody which is a biotinylated polyclonal goat anti-human PTH (39–84 region) antibody that is preformed to streptavidin coated paramagnetic latex particles [Solid Phase]). Unbound materials are then removed by washing. Acid Reagent and Base Reagent are then added to initiate the chemiluminescent reaction. A direct relationship exists between the amount of PTH present in the patient sample and the amount of relative light units (RLUs) detected by the system.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   Assay imprecision (within run and total) was performed as recommended in CLSI EP5-A2. Seven samples (4 human plasma and 3 controls) with concentrations that spanned the measuring range of the device were tested in duplicate using two runs per day for twenty days. The results are summarized below.

Sample	Conc. (pg/mL)	Within run %CV	Total %CV
Pool 1	16.1	7.1	7.7
Control 1	38.7	3.6	4.7
Pool 2	62.8	2.7	3.7
Control 2	185	2.4	3.2
Control 3	663	2.2	2.8
Pool 3	839	3.0	3.9
Pool 4	1698	2.3	3.2

   b. Linearity/assay reportable range:

   Linearity was evaluated following the guidelines of CLSI EP06-A. High and low concentration samples were mixed to prepare samples at 12 test concentrations and tested with the device. Results are summarized below:

Level	Observed (pg/mL)	Expected (pg/mL)	Linear Fit (pg/mL)	Non-linearity (pg/mL)	% Non-Linearity
1	4.4	4.4	-0.6	5.1	N/A
2	16.6	20.2	14.9	1.7	10.4
3	59.1	67.5	61.3	-2.1	-3.6
4	117	131	123	-6.0	-5.1
5	244	257	247	-2.5	-1.0
6	513	509	495	18.5	3.6
7	728	761	742	-14.6	-2.0
8	1025	1013	990	35.8	3.5
9	1241	1265	1237	4.0	0.3
10	1521	1517	1485	36.3	2.4
11	1754	1769	1733	21.0	1.2
12	2021	2021	1980	41.4	2.0

The regression statistics for the linearity study were as follows:

y= 0.98x – 4.98, R = 1.00

These results demonstrate linearity across the claimed measuring range of the device (6.3 – 1900 pg/mL).

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

The ADVIA Centaur Intact PTH assay standardization is maintained with internal standards manufactured using purified human iPTH (1-84); values have been assigned to correlate to a commercially available iPTH assay.

Calibrators and controls were previously cleared in k020217

On-board stability for the ADVIA Centaur Intact PTH assay was established by real time studies on the ADVIA Centaur XP system. The stability study protocol and the acceptance criteria have been found acceptable. The on board stability of the reagent is 28 days with a calibration interval of 14 days. The ADVIA Centaur Intact PTH assay reagent is stable until the date printed on the label when stored at 2-8˚C.

d. *Detection limit:*

The Limit of Blank (LoB), Limit of Detection (LoD), and the Limit of Quantitation (LoQ) were calculated per CLSI EP17-A2. The LoB was calculated nonparametrically. The LoQ was estimated as the dose corresponding to 20% Total CV using the precision profile method.
A single experimental design was used to generate the data for LoB, LoD & LoQ. Five test samples were prepared by spiking analyte into diluent and/or

diluting plasma samples to obtain the following approximate concentrations: 1, 2, 5, 10, and 15 pg/mL. These samples were tested at n=6 x 2 instruments x 5 days for a total of n=60 per reagent lot (2 reagents lots were used). Results were as follows:

LoB	LoD	LoQ
0.1 pg/mL	2.7 pg/mL	6.3 pg/mL

e. Analytical specificity:

Interference

Interference testing for endogenous substances and biotin was performed following the guidelines of CLSI EP07-A2. Two patient plasma pools, with endogenous iPTH concentrations of ~20 pg/mL and ~200 pg/mL were spiked with each interferent. Neat samples and spiked samples were tested at the concentrations shown in the results table below. The sponsor defines non-significant interference as a difference of less than or equal to 10% between the spiked and the control samples. Results of non-significant interference are summarized in the table below.

Interfering Substance	Highest Concentration with non-significant interference
Hemoglobin	500 mg/mL
Triglycerides	3,000 mg/mL
Conjugated Bilirubin	40 mg/dL
Unconjugated Bilirubin	40 mg/mL
Biotin	1,000 mg/dL

Cross Reactivity

Cross reactants were tested by spiking each compound into a sample without iPTH and a sample with endogenous iPTH concentration between 20- 70 pg/mL. The compounds tested, concentrations, tested, and % cross reactivity calculated are summarized below:

Cross-reactant	Concentration tested	% cross reactivity
PTH (1-34) fragment	300	0.1
PTH (39-68) fragment	100,000	0.0
PTH (39-84) fragment	100,000	0.0
PTH (44-68) fragment	100,000	0.0
PTH (53-84) fragment	100,000	0.0
PTH (7-84) fragment	300	51
Calcitonin	100,000	0.0
Beta-cross Laps	1,000	0.2
Osteocalcin	100,000	0.0

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

The modified assay was compared to the unmodified (predicate) device by evaluating 106 EDTA plasma samples and 105 serum samples with concentrations that spanned the claimed measuring range. Study was performed on the ADVIA Centaur XP system. Samples were run in singlicate and Passing & Bablok Regression analysis was performed. The results are summarized below.

Y	N	Regression Equation	R	Sample range (pg/mL)
Plasma	106	y=0.98x+10.6	1.00	11.8 – 1862
Serum	105	y=1.00x+5.0	1.00	9.8 - 1868

b. Matrix comparison:

The sponsor claims serum and EDTA plasma as acceptable sample types. See method comparison study above.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

The reference range previously cleared in 510(k) submission number k121981 was verified following the guidelines of CLSI C28-A3c. Forty (40) EDTA plasma and 40 serum samples obtained from apparently healthy individuals (calcium and inorganic phosphorus results within their respective reference ranges) were tested. The samples were tested using 2 reagent lots across 4 different instruments and verified that the reference range is unchanged with the modified device.

The package insert states the following for expected values:

The Expected Results (from 95% of the values) are:

For plasma: 13.8 to 85.0 pg/mL (1.46 to 9.01 pmol/L)

For serum: 12.4 to 76.8 pg/mL (1.31 to 8.14 pmol/L)

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.