510(k) Summary of Safety and Effectiveness for the MAR 2 1 2013

ADVIA® Centaur Intact Parathyroid (iPTH) Assay

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

A. 510(k) Number: K121981

B. Date of Preparation: March 8, 2013

C. Proprietary and Established Names:

ADVIA® Centaur Intact Parathyroid Hormone (iPTH) Assay

D. Applicant:

Siemens Healthcare Diagnostics Inc.,
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E. Regulatory Information:

1. Regulation section: 21 CFR § 862.1545
2. Classification: Class II
3. Product Code: CEW, Parathyroid Hormone Test System
4. Panel: Clinical Chemistry

F. Predicate Device:

The ADVIA® Centaur iPTH Assay is substantially equivalent to the Abbott Architect Intact PTH Assay cleared under 510(k) k063232

G. Device Description:

The ADVIA Centaur iPTH assay is a two-site sandwich immunoassay using direct chemiluminometric technology, which uses constant amounts of an antihuman PTH antibody in the Lite Reagent and an antihuman PTH antibody in the Solid Phase Reagent. The first antibody is a polyclonal goat antihuman PTH (N-terminal 1-34) antibody labeled with acridinium ester. The second antibody is a biotinylated polyclonal goat antihuman PTH (39-84 region) antibody that is preformed to streptavidin coated paramagnetic latex particles in the Solid Phase reagent.

The ADVIA Centaur iPTH reagent kit contains the following:

- ReadyPack® primary reagent pack containing ADVIA Centaur Lite and Solid Phase Reagent)
- ADVIA Centaur iPTH Master Curve card

Materials Required but Not Provided

- iPTH Calibrator

Optional Reagents

- ADVIA Centaur Multi-Diluent 11
- iPTH 1, 2, 3 quality control material
- iPTH Master Curve Material

H. Intended Use / Indications for Use:

The ADVIA Centaur 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 XP system. This assay is intended to be used to aid in the differential diagnosis of hyperparathyroidism and hypoparathyroidism.

I. Substantial Equivalence Information:

Both the ADVIA Centaur iPTH assay (New Device) and Abbott Architect Intact PTH assay (Predicate Device cleared under k063232) employ prepackaged reagents for use on automated test systems. A comparison of the important similarities and differences of these assays is shown in the following tables:

Similarities:

Item	New Device: ADVIA Centaur Intact PTH Assay	Predicate Device: Abbott Architect Intact PTH Assay
Intended Use	For *in vitro* diagnostic use in the quantitative determination of intact parathyroid hormone (iPTH) in EDTA plasma or serum using the ADVIA Centaur systems	For *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
Indications for Use	This assay is intended to be used to aid in the differential diagnosis of hyperparathyroidism and hypoparathyroidism.	In conjunction with serum calcium levels, this assay may be used as an aid in the differential diagnosis of hypercalcemia, hypocalcemia, or parathyroid disorders.
Sample type	EDTA Plasma, Serum	Serum and Plasma
Measurement	Quantitative	Same
Operating Principle	Sandwich immunoassay	Same
Technology	Chemiluminescence	Same
Detection Antibody	Goat polyclonal antibody conjugated to Acridium Ester	Goat polyclonal antibody conjugated to Acridium
Capture Antibody	Goat polyclonal antibody conjugated to biotin directly coupled to streptavidin magnetic particles	Goat polyclonal antibody coated to microparticles
Interference	No significant interference by hemolysis, icterus (bilirubin),	No significant interference from hemoglobin, bilirubin, triglycerides or

Item	New Device: ADVIA Centaur Intact PTH Assay	Predicate Device: Abbott Architect Intact PTH Assay
	triglycerides, or biotin at tested levels	protein at tested levels
Expected Values	13.8 – 85.0 pg/mL (plasma) 12.4 – 76.8 pg/mL (serum)	8.7 – 77.1 pg/mL
Calibration	2 Point	6 Point
Calibrators	Siemens iPTH Calibrators	ARCHITECT Intact PTH Calibrators
Number of calibrators	Two (2) levels	Six (6) levels
Use of Controls	Yes (recommended)	Same
Number of controls	Three levels	Same
Detection Antibody	Goat polyclonal antibody conjugated to Acridium Ester	Same

Differences:

Item	New Device: ADVIA Centaur Intact PTH Assay	Predicate Device: Abbott Architect Intact PTH Assay
Assay Range	5.5 – 1900 pg/mL	3.0 – 3000 pg/mL (Routine) 4.0 – 2500 pg/mL (STAT)
Sample Volume	200 µL	150 µL
Calibrators	Siemens iPTH Calibrators	ARCHITECT Intact PTH Calibrators
Calibration	2 Point	6 Point
Number of calibrators	Two (2) levels	Six (6) levels

J. 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 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). 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.

K. Performance Characteristics

Substantial equivalence was demonstrated by testing several performance characteristics including imprecision, interfering and cross-reacting substances, and method comparison.

a. Precision

Precision estimates were computed according to CLSI document EP05-A2, Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline. Within run and total imprecision were evaluated by testing one EDTA plasma (patient) pool, five (5) Medical Decision Pools (iPTH spiked into human EDTA plasma pools), two levels of calibrators, and 3 levels of commercial control materials. Each sample was assayed in 2 replicates per run, 2 runs per day for 20 days for a total of 80 replicates.

		Within Run		Total	
Sample	MEAN pg/mL	SD	%CV	SD	%CV
Patient Pool	16.7	0.8	4.6	1.5	9.2
Low Calibrator	33.0	2.0	6.0	2.3	6.9
Control 1	45.2	2.0	4.4	3.2	7.0
Medical Decision Pool 1	47.3	1.4	2.9	2.3	4.8
Medical Decision Pool 2	97.3	2.8	2.9	3.9	4.0
Medical Decision Pool 3	175.6	4.8	2.7	10.5	6.0
Control 2	196.6	6.8	3.5	8.3	4.2
Control 3	691.0	17.8	2.6	24.5	3.5
Medical Decision Pool 4	699.8	20.1	2.9	24.4	3.5
High Calibrator	807.7	23.1	2.9	37.7	4.7
Medical Decision Pool 5	1802.9	46.7	2.6	57.7	3.2

b. Interfering Substances

Interference by hemoglobin, triglycerides (Intralipids), bilirubin, and biotin was evaluated in the ADVIA Centaur iPTH assay at three levels of PTH. There was no indication of interference (≤ 10% effect) up to the interferent levels claimed.

Interferent	[Interf] mg/dL	Patient 1 Dose (pg/mL)	Patient 1 Bias (%)	Patient 2 Dose (pg/mL)	Patient 2 Bias (%)	Patient 3 Dose (pg/mL)	Patient 3 Bias (%)
Hemoglobin	500	11.16	-3.19%	52.35	-0.22%	182.15	-9.59%
	250	10.58	-8.26%	51.41	-2.03%	191.19	-5.10%
	0	11.53		52.47		201.48	
Bilirubin (unconjugated)	40	27.26	6.33%	64.48	-3.78%	126.70	-2.27%
	20	26.09	1.76%	64.64	-3.55%	122.52	-5.49%
	0	25.64		67.02		129.64	
Bilirubin (conjugated)	40	25.29	-7.19%	64.49	-2.85%	116.18	-3.72%
	20	26.35	-3.32%	62.57	-5.75%	116.28	-3.64%
	0	27.25		66.38		120.67	

Interferent	[Interf] mg/dL	Patient 1 Dose (pg/mL)	Patient 1 Bias (%)	Patient 2 Dose (pg/mL)	Patient 2 Bias (%)	Patient 3 Dose (pg/mL)	Patient 3 Bias (%)
Triglycerides	3000	23.70	2.50%	80.56	7.14%	115.71	6.11%
	1500	22.34	-3.38%	72.37	-3.75%	111.29	2.06%
	0	23.13		75.19		109.05	
Biotin	0.10	25.29	3.35%	85.09	7.54%	120.45	-1.45%
	0.05	24.77	1.24%	78.16	-1.22%	118.13	-3.35%
	0.00	24.47		79.12		122.23	

c. Cross-reactivity

Cross reactivity was evaluated in the ADVIA Centaur iPTH immunoassay using a normal EDTA plasma sample and an assay specific Multi-diluent 11 (buffered goat serum with **no analyte**). No cross reactivity was observed at the highest levels tested with the exception of the PTH 7 – 84 fragment (~ 51%) – this will be reported in the Labeling.

Protein	[Interf] pg/mL	Multi-Dil 11 iPTH Dose (pg/mL)	%Cross React.	Plasma Sample iPTH Dose (pg/mL)	%Cross React.
PTH 1-34	300	0.00	0.00%	45.17	0.09%
PTH 39-68	100,000	0.00	0.00%	32.25	-0.01%
PTH 39-84	100,000	0.42	0.00%	26.23	-0.02%
PTH 44-68	100,000	0.00	0.00%	34.52	-0.01%
PTH 53-84	100,000	1.32	0.00%	29.61	-0.02%
Calcitonin	100,000	0.00	0.00%	43.56	0.00%
PTH 7-84	300	152.21	50.74%	203.70	51.39%
Beta-Cross Laps	1000	0.00	0.00%	33.44	0.17%
Osteocalcin	50,000	0.00	0.00%	32.67	0.00%

d. Method Comparison

Method Comparison studies were done with EDTA plasma samples to demonstrate equivalence to the Predicate (Abbott Architect Intact PTH assay). The ADVIA Centaur iPTH assay shows good correlation in sample results compared to the Predicate.

System (y)	N	Regression Equation*	R**	Mean (Median) Bias (%)	Sample Range (pg/mL)
ADVIA Centaur iPTH (EDTA Plasma)	177	y = 1.03x – 3.32	0.991	-2.0 (-1.5)	10.5 -1882

x =Predicate (Abbott Architect Intact PTH assay)

* Passing & Bablok

** Least Squares Linear regression

e. Serum Plasma Matrix Equivalency

EDTA plasma and serum samples were compared in the ADVIA Centaur iPTH assay. Correlation results for EDTA plasma and serum demonstrate that the matrices are equivalent using the ADVIA Centaur iPTH assay.

	N	Regression Equation*	R	Sample Range (pg/mL)
ADVIA Centaur iPTH	79	0.98x + 3.72	0.992	11.1 – 1791

x = EDTA plasma, y = Serum
* Weighted Linear regression

f. Expected Values

Matched serum and plasma samples from apparently healthy donors were tested with the ADVIA Centaur iPTH to confirm that the Expected Values or reference range is comparable to the Predicate Device. 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)

L. Conclusions

Comparative testing of the ADVIA Centaur iPTH assay is substantially equivalent in principle and performance to the Predicate Device, Architect Intact PTH assay, cleared under 510(k) k063232.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-002

March 21, 2013

Siemens Healthcare Diagnostics
c/o Philip Liu, Ph.D.
511 Benedict Avenue
Tarrytown, New York 10591

Re: k121981
Trade/Device Name: ADVIA® Centaur Intact Parathyroid (iPTH) Assay
Regulation Number: 21 CFR 862.1545
Regulation Name: Parathyroid Hormone Test System
Regulatory Class: Class II
Product Code: CEW
Dated: February 14, 2013
Received: February 15, 2013

Dear Dr. Liu:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostics and Radiological Health at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Carol C. Benson -S for

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of *In Vitro* Diagnostics and Radiological Health
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): k121981

Device Name:

ADVIA® Centaur Intact Parathyroid (iPTH) Assay

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 XP system. This assay is intended to be used to aid in the differential diagnosis of hyperparathyroidism and hypoparathyroidism.

Prescription Use X (21 CFR Part 801 Subpart D) And/Or Over the Counter Use ____. (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostics and Radiological Health (OIR)

Ruth A. Chesler-S

Division Sign-Off
Office of In Vitro Diagnostics and Radiological Health

510(k) k121981