



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

I Background Information:

A 510(k) Number

K250250

B Applicant

Siemens Healthcare Diagnostics, Inc.

C Proprietary and Established Names

ADVIA Centaur Anti-Thyroid Peroxidase II (aTPOII)

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
JZO	Class II	21 CFR 866.5870 - Thyroid Autoantibody Immunological Test System	IM - Immunology

II Submission/Device Overview:

A Purpose for Submission:

New device

B Measurand:

Autoantibodies against thyroid peroxidase (TPO)

C Type of Test:

Quantitative, chemiluminescent immunoassay

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The ADVIA Centaur Anti-Thyroid Peroxidase II (aTPOII) assay is for in vitro diagnostic use in the quantitative measurement of autoantibodies against thyroid peroxidase in human serum and plasma (EDTA and lithium heparin) using the ADVIA Centaur XP system.

Anti-thyroid peroxidase (aTPO) measurements are used, in conjunction with a clinical assessment, as an aid in the diagnosis of autoimmune thyroiditis and Graves' Disease.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

ADVIA Centaur XP System

IV Device/System Characteristics:

A Device Description:

The ADVIA Centaur Anti-Thyroid Peroxidase II (aTPOII) assay is available in a 100-test kit and in a 500-test kit. Both versions of the assay include:

- aTPOII ReadyPack primary reagent pack consisting of:
 - Lite Reagent: 10.0 mL/reagent pack; Recombinant TPO (~90 ng/mL) complexed with mouse monoclonal anti-TPO antibody (~30 ng/mL) labeled with acridinium ester in phosphate buffer; blocker (bovine and mouse); surfactant; sodium azide (< 0.1%); preservatives
 - Solid Phase: 20.0 mL/reagent pack; Streptavidin-coated paramagnetic microparticles (~0.3 mg/mL) with biotinylated mouse monoclonal anti-TPO antibody (~6 µg/mL) in phosphate buffer; blocker (bovine and mouse); surfactant; sodium azide (< 0.1%); preservatives Tg ReadyPack primary reagent pack
- ADVIA Centaur aTPOII master curve card
- aTPOII CAL low calibrator: lyophilized anti-TPO antibodies in defibrinated human plasma; sodium azide (< 0.1%); preservatives; 1.0 mL/vial
- aTPOII CAL high calibrator: lyophilized anti-TPO antibodies in defibrinated human plasma; sodium azide (< 0.1%); preservatives; 1.0 mL/vial
- ADVIA Centaur aTPOII CAL calibrator assigned value cards and barcode labels

B Principle of Operation:

The ADVIA Centaur aTPOII assay is a fully automated 1-step competitive immunoassay using acridinium ester (AE) chemiluminescent technology. The assay employs two anti-TPO antibodies and a recombinant TPO antigen. The first antibody, in the Solid Phase, is a biotinylated mouse monoclonal anti-TPO antibody that is bound to streptavidin-coated paramagnetic microparticles. The second antibody is a mouse monoclonal anti-TPO antibody labeled with acridinium ester in a preformed complex with unlabeled recombinant thyroid peroxidase (rTPO). Successful bridging of the Solid Phase antibody with the AE-labeled antibody and rTPO in the Lite Reagent will result in signal generation. Anti-TPO autoantibodies present in the sample will compete with the Solid Phase biotinylated anti-TPO monoclonal antibody for binding to rTPO and reduce the signal. An inverse relationship exists between the amount of anti-TPO antibody present in the patient sample and the amount of relative light units (RLUs) detected by the system.

V Substantial Equivalence Information:

A Predicate Device Name(s):

ARCHITECT Anti-TPO Immunoassay, Calibrators & Controls

B Predicate 510(k) Number(s):

K052407

C Comparison with Predicate(s):

Device & Predicate Device(s):	<u>K250250</u> (Candidate Device)	<u>K052407</u> (Predicate Device)
Device Trade Name	ADVIA Centaur aTPOII	ARCHITECT Anti-TPO Immunoassay
General Device Characteristic Similarities		
Intended Use/ Indications For Use	The ADVIA Centaur Anti-Thyroid Peroxidase II (aTPOII) assay is for in vitro diagnostic use in the quantitative measurement of autoantibodies against thyroid peroxidase in human serum and plasma (EDTA and lithium heparin) using the ADVIA Centaur XP system. Anti-thyroid peroxidase (aTPO) measurements are used, in conjunction with a clinical assessment, as an aid in the diagnosis of autoimmune thyroiditis and Graves' Disease.	Architect Anti-TPO is a chemiluminescent microparticle Immunoassay (CMIA) for the quantitative determination of the IgG class of thyroid peroxidase autoantibodies (anti-TPO) in human serum and plasma (EDTA and Heparin) on the Architect i System. The Architect Anti-TPO assay is intended for use as an aid in the diagnosis of autoimmune thyroid disease.
Assay Technology	Chemiluminescent	Same

Sample Matrices	Serum, K2-EDTA plasma, Lithium heparin plasma	Same
Traceability	Traceable to NIBSC 66/387	Same
Measurement	Quantitative	Same
General Device Characteristic Differences		
Assay Range	4.6 – 400.0 IU/mL	0.5 – 1000.0 IU/mL
Cut-off	10.4 IU/mL	5.6 IU/mL
Instrument	ADVIA Centaur XP System	ARCHITECT i System

VI Standards/Guidance Documents Referenced:

The following Clinical and Laboratory Standards Institute (CLSI) guidelines were used:

- CLSI EP05-A3, Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition
- CLSI EP06-Ed2, Evaluation of the Linearity of Quantitative Measurement Procedures – Second Edition
- CLSI EP07-A3, Interference Testing in Clinical Chemistry – Third Edition
- CLSI EP09c 3rd Edition, Measurement Procedure Comparison and Bias Estimation Using Patient Samples
- CLSI EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition
- CLSI EP25-A, Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline
- CLSI EP28-A3c, Defining Establishing and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline – Third Edition
- CLSI EP35, Assessment of Equivalence or Suitability of Specimen Types for Medical Laboratory Measurement Procedures – First Edition
- CLSI EP37, Supplemental Tables for Interference Testing in Clinical Chemistry – First Edition

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Precision and reproducibility studies were conducted following the recommendations in CLSI EP05-A3.

Within-Laboratory Precision:

Within-laboratory precision was assessed using six native human serum samples, one contrived sample (Serum A), and two levels of control materials. Two replicates each of the samples were run on one (1) ADVIA Centaur XP system for 20 days, two runs per day using one aTPOII reagent lot for a total of 80 replicates per sample. The data were analyzed for repeatability (within-run), between-run, between-day, and within-laboratory precision. The mean (IU/mL), standard deviation (SD) (IU/mL) and % of coefficient of variation (%CV) are summarized in the table below:

Sample	Mean (IU/mL)	Within-Run (Repeatability)		Between-Run		Between-Day		Within-Laboratory	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
Serum A	6.0	0.56	9.3	0.56	9.3	0.32	5.3	0.86	14.2
Serum B	12.8	1.17	9.1	0	0	0.18	1.4	1.18	9.2
Serum C	17.1	1.76	10.3	0.57	3.3	0.66	3.9	1.97	11.5
Serum D	26.2	1.67	6.4	0.78	3.0	0	0	1.84	7.0
Serum E	124.4	5.73	4.6	0	0	2.4	1.9	6.21	5.0
Serum F	170.0	8.99	5.3	2.78	1.6	2.53	1.5	9.74	5.7
Serum G	362.4	22.12	6.1	0	0	0	0	22.12	6.1
Control 1	25.3	1.35	5.3	0.43	1.7	1.03	4.1	1.75	6.9
Control 2	175.4	8.51	4.9	5.33	3.0	6.54	3.7	11.99	6.8

Lot-to-Lot Precision:

The lot-to-lot precision was evaluated using three reagent lots on the ADVIA Centaur XP system. Eight serum samples at different concentrations and two levels of control materials were tested with five replicates per run, one run per day over five days, resulting in N=75 datapoints per sample on one instrument. The same study was also performed on two additional instruments. The data was analyzed for within-run, between-day, and between-reagent lot, and total precision. The lot-to-lot precision data on one representative instrument are summarized in the table below.

Sample	Mean (IU/mL)	Within-Run		Between-Day		Between-Lot		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
Serum A	5.4	0.66	12.2	0.64	11.9	0.46	8.5	1.03	19.1
Serum B	9.9	0.78	7.9	0.00	0.0	0.60	6.1	0.98	9.9
Serum C	16.4	1.30	7.9	0.00	0.0	0.67	4.1	1.47	9.0
Serum D	23.3	1.71	7.3	0.76	3.3	1.51	6.5	2.41	10.3
Serum E	28.2	1.90	6.7	0.00	0.0	2.40	8.5	3.06	10.9
Serum F	130.8	7.05	5.4	3.01	2.3	10.90	8.3	13.32	10.2
Serum G	168.5	9.80	5.8	1.43	0.8	17.75	10.5	20.33	12.1
Serum H	359.6	16.43	4.6	8.44	2.3	20.05	5.6	27.26	7.6
Control 1	29.6	1.83	6.2	1.80	6.1	0.80	2.7	2.69	9.1
Control 2	203.6	8.21	4.0	6.54	3.2	0.00	0.0	10.50	5.2

Instrument-to-Instrument Precision:

The instrument-to-instrument precision was evaluated using three reagent lots on three ADVIA Centaur XP systems. Eight (8) serum samples and two levels of control materials at different concentrations were tested with five replicates per run, one run per day over five days, resulting in N=75 datapoints per sample using one lot. The same study was also performed on two additional instruments. The data was analyzed for within-run, between-day, and between-instrument, and total precision. The instrument-to-instrument precision data on one representative lot are summarized in the table below.

Sample	Mean (IU/mL)	Within-Run		Between-Day		Between-Instrument		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
Serum A	5.6	0.79	14.1	0.70	12.5	0.31	5.5	1.10	19.6
Serum B	10.3	0.78	7.6	0.28	2.7	0.79	7.7	1.14	11.1
Serum C	15.8	1.32	8.4	0.25	1.6	2.01	12.7	2.42	15.3
Serum D	23.8	1.47	6.2	0.33	1.4	1.37	5.8	2.04	8.6
Serum E	27.9	2.01	7.2	0.76	2.7	0.74	2.7	2.28	8.2
Serum F	132.2	6.69	5.1	1.65	1.2	3.00	2.3	7.51	5.7
Serum G	182.0	9.80	5.4	4.23	2.3	1.92	1.1	10.85	6.0
Serum H	344.0	15.40	4.5	5.24	1.5	6.89	2.0	17.66	5.1
Control 1	28.6	1.86	6.5	1.23	4.3	0.84	2.9	2.39	8.4
Control 2	198.1	7.52	3.8	2.97	1.5	3.59	1.8	8.84	4.5

2. Linearity:

The linearity of the ADVIA Centaur aTPOII was determined in accordance with CLSI EP06-ED2. Linearity samples were prepared by mixing high and low samples in known ratios. Two sets of overlapping dilutions were created; Sample Set 1 was prepared by combining a low/negative human serum sample with a moderately positive aTPOII sample, while Sample Set 2 was prepared by combining a different moderately positive aTPOII sample with a high aTPOII positive sample. Each dilution was tested in quadruplicate. The results are summarized in the table below:

Sample Set	Range (IU/mL)	Slope (95% CI)	Intercept (95% CI)	r	% Deviation from Linearity
1	0.13–159.3	1.05 (1.01–1.08)	0 (-0.54–1.09)	0.999	-4.3%–6.6%
2	154.7 – 412.0	1.08 (1.05–1.11)	0 (-30.3–32.57)	0.989	-7.7%–6.7%
Combined	0.13 – 412.0	1.07 (1.04–1.09)	0 (-0.78–0.91)	0.997	-7.5%–8.4%

All dilutions were within $\pm 10\%$ deviation from the linearity. The data supports a linearity of the claimed analytical measuring interval (AMI) of 4.6–400.0 IU/mL for the ADVIA Centaur aTPOII.

3. Analytical Specificity/Interference:

Interference:

Interference studies were performed in accordance with the CLSI guidelines EP07 3rd Edition and CLSI EP37 1st Edition to determine if endogenous and exogenous substances interfere with the test results of the ADVIA Centaur aTPOII assay. Three samples representing the assay cut-off and low positives ($\geq 10.4 - \leq 20.0$ IU/mL), a moderate positive ($> 20.0 - \leq 40.0$ IU/mL), and a high positive ($\geq 130.0 - \leq 270.0$ IU/mL) were tested in ≥ 5 replicates for each substance with one aTPOII reagent lot on one ADVIA Centaur XP analyzer. The mean results were determined from the replicates tested. Interferents were analyzed using a paired difference method. No significant interference ($< 10\%$ difference for the moderate and high positive, $< \pm 4.0$ IU/mL for the low positive) was observed for the ADVIA Centaur aTPOII to the following concentration for each endogenous and exogenous substance tested:

a) Endogenous Substances:

Substance	Concentration
Bilirubin, conjugated	60 mg/dL
Bilirubin, unconjugated	60 mg/dL
Hemoglobin	1000 mg/dL
Human anti-mouse antibody (HAMA)	67 ng/mL
Immunoglobulin G (IgG)	6 g/dL
Lipemia (Intralipid)	3500 mg/dL
Rheumatoid factor (RF)	750 IU/mL

b) Exogenous Substances:

Substance	Concentration	Substance	Concentration
Acetaminophen	20 mg/dL	Losartan potassium	0.2 mg/dL
Acetylcysteine	15 mg/dL	Methimazole	8 mg/dL
Acetylsalicylic acid*	65 mg/dL	Methyldopa	2.25 mg/dL
Ampicillin sodium	7.5 mg/dL	Methylprednisolone	0.783 mg/dL
Ascorbic acid	5.25 mg/dL	Metoprolol tartrate	0.15 mg/dL
Atorvastatin calcium	0.075 mg/dL	Metronidazole	12.3 mg/dL
Biotin	3500 ng/mL	Octreotide	0.03 mg/dL
Carbimazole	3 mg/dL	Omeprazole	0.84 mg/dL
Cefoxitin	660 mg/dL	Phenylbutazone	32.1 mg/dL
Cholesterol	400 mg/dL	Prednisone	9.9 µg/dL
Cyclosporine	0.18 mg/dL	Propranolol Hydrochloride	24 mg/dL
Dexamethasone	1.2 mg/dL	Propylthiouracil	30 mg/dL
Doxycycline	1.8 mg/dL	Rifampicin	4.8 mg/dL
EDTA, tripotassium	425 mg/dL	Silwet L720 **	0.03 mg/dL
Ibuprofen	50 mg/dL	Theophylline	6 mg/dL
Iodide	38 mg/dL	Thyroxine	1000 µg/mL

Substance	Concentration	Substance	Concentration
Levodopa	0.75 mg/dL	Total protein	12 g/dL
Liothyronine	0.0075 mg/dL		

* Aspirin

** Octamethyl-cyclotetrasiloxane

Cross-reactivity:

Closely related analytes were tested to determine if they cross-react in the ADVIA Centaur aTPOII assay. Each cross-reactant was tested at a single concentration. Three samples representing the assay cut-off and low positives ($\geq 10.4 - \leq 20.0$ IU/mL), a moderate positive ($> 20.0 - \leq 40.0$ IU/mL), and a high positive ($\geq 130.0 - \leq 270.0$ IU/mL) were tested in six replicates for each substance with one ADVIA Centaur aTPOII reagent lot on one analyzer. No-significant cross reactivity was observed for the ADVIA Centaur aTPOII to the following concentration for each substance tested:

Substance	Test Concentration
Anti-thyroglobulin antibody (TgAb)	2000 IU/mL
Thyroglobulin (Tg)	700 ng/mL
Thyroid-stimulating immunoglobulin (TSI)	113 IU/mL

4. Assay Reportable Range:

The assay reportable range for the ADVIA Centaur aTPOII assay is 4.6 –400.0 IU/mL.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

a) Traceability:

The ADVIA Centaur aTPOII assay is traceable to NIBSC 66/387 Human Anti-thyroid Microsome Serum reference standard.

b) Stability:

Kit stability:

Shelf-life stability: A Real Time stability study was conducted at 3-month intervals using three lots of reagents stored at 2–8°C. At each timepoint, three samples representing the assay cut-off and low positives ($\geq 10.4 - \leq 20.0$ IU/mL), a moderate positive ($> 20.0 - \leq 40.0$ IU/mL), and a high positive ($\geq 130.0 - \leq 270.0$ IU/mL) were tested at time 0, 3, 6, 9, 12, 15, 18, 21, 24, and 25-months. The results support a 24-month stability claim.

In-use reagent stability:

In-use stability of the ADVIA Centaur aTPOII kit was evaluated by testing three samples representing the assay cut-off and low positives ($\geq 10.4 - \leq 20.0$ IU/mL), a

moderate positive ($>20.0 - \leq 40.0$ IU/mL), and a high positive ($\geq 130.0 - \leq 270.0$ IU/mL) for the reagent study and using two lots which were opened and stored on the ADVIA Centaur XP system for the duration of the study, which included at least five timepoints and at least two replicates per sample. The results support a claim for reagent onboard stability of 42 days.

Sample stability:

The stability of specimens stored under different conditions was evaluated by testing a panel of samples collected into Serum Separator tubes (SST), Lithium Heparin (LiHep) tubes and dipotassium EDTA (K2 EDTA) tubes spiked with anti-TPO positive samples to make samples across the assay range. The data supported the following storage conditions for all three tested sample matrices:

Sample Stability Attribute:	Stability Claims
Room Temperature (RT):	8 hours
Refrigerated (2 – 8°C)	7 days
Frozen (-20°C)	6 months
On the clot - RT	8 hours
Freeze-thaw	2 cycles
Time to centrifugation	8 hours

6. Detection Limit:

The Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantitation (LoQ) for the ADVIA Centaur aTPOII were determined based on the CLSI guideline EP17-A2.

a) LoB:

The LoB was determined by testing four independent human serum samples using three different reagent lots of the ADVIA Centaur aTPOII. These samples were obtained from patients who had undergone thyroidectomy over 10 years ago and were confirmed to be negative for anti-thyroid peroxidase (aTPO) antibodies using the predicate ARCHITECT aTPO assay. Ten replicates of each sample were run on two ADVIA Centaur XP systems, one run per day for three days yielding 240 datapoints per reagent lot (120 rep per system per lot). The claimed LoB is 2.3 IU/mL.

b) LoD:

The LoD was determined by testing four low-level pooled samples using three different reagent lots of the ADVIA Centaur aTPO II. Each pooled sample was prepared by combining a unique aTPO positive sample with a unique negative sample. Ten replicates of each pooled sample were tested on two ADVIA Centaur XP systems, with one run per day over three days, resulting in a total of 240 datapoints per reagent lot (120 rep per system per lot). The claimed LoD is 4.6 IU/mL.

c) LoQ:

The LoQ was determined using six native samples and two pooled samples, with concentrations ranging from 3 to 15 IU/mL. Four replicates of each sample were tested on two ADVIA Centaur XP systems over five days using two different reagent lots

ADVIA Centaur aTPOII, resulting in 40 replicates per sample per reagent lot. The claimed LoQ is 4.6 IU/mL.

7. Assay Cut-Off:

The assay cut-off is 10.4 IU/mL.

B Comparison Studies:

1. Method Comparison with Predicate Device:

A method comparison was conducted for the ADVIA Centaur aTPOII assay (candidate device) against the Abbott ARCHITECT aTPO assay (predicate device), using prospectively and retrospectively collected samples. The samples included autoimmune thyroid disease (AITD), non-autoimmune thyroid disease control samples (NAITD), and disease control samples. Results outside the AMR (analytical measurement range) of either assay were excluded from the final analysis and positive percent agreement (PPA) and negative percent agreement (NPA), with 95% confidence intervals were calculated:

		Predicate		Total
		Positive	Negative	
ADVIA Centaur aTPOII	Positive	199	1	200
	Negative	28	52	80
	Total	227	53	280

PPA: 87.7% (199/227) (95% CI: 82.8–91.3%)

NPA: 98.1% (52/53) (95% CI: 90.1–99.7%)

2. Matrix Comparison:

To demonstrate that Li-Heparin plasma and K2-EDTA plasma samples yield results comparable to results obtained with serum samples, 56 sample sets that cover the AMI for the ADVIA Centaur aTPOII assay were tested and analyzed by Passing-Bablok regression. The results are summarized in the following table:

	Range (IU/mL)	Slope (95% CI)	Intercept (95% CI)	r
Li-Heparin vs. Serum	6.4–398.0	0.94 (0.92–0.98)	0.1 (-2.2–1.5)	0.987
K2-EDTA vs. Serum	6.4–380.9	0.99 (0.94–1.04)	-0.9 (-7.2–2.4)	0.975

C Clinical Studies:

1. Clinical Sensitivity and Specificity:

A total of 666 samples were evaluated in two cohorts. In a clinical study, 364 samples, of which 207 samples were clinically confirmed autoimmune thyroiditis (also known as

Hashimoto's thyroiditis) and Graves' disease (collectively, autoimmune thyroid disease, AITD), were prospectively collected across six sites in the United States. Definitive diagnoses were made by endocrinologists in accordance with the American Thyroid Association's guidelines^{1,2} The samples were collected from subjects who presented with clinical signs or symptoms and are suspected of, or have been diagnosed with, Graves' disease or autoimmune thyroiditis or were pregnant and postpartum (within one year postpartum from pregnancy) female subjects with clinical signs or symptoms of thyroid disease. Subjects could enroll if they had not started treatment, or who started antithyroid medications or hormone replacement therapy treatment less than or equal to six (6) months from the date of collection and were ≥ 22 years of age. The samples were defined as AITD or not-AITD (NAITD) and not further characterized except for multinodular goiter.

		Clinical Diagnosis			
		Autoimmune Thyroiditis	Graves' Disease	NAITD*	Total
ADVIA Centaur aTPOII	Positive	60	88	17	165
	Negative	40	19	140	199
	Total	100	107	157	364

* The NAITD cohort included 62 multinodular goiter patients.

Autoimmune Thyroiditis	Sensitivity:	60.0% (60/100) (95% CI: 50.2–69.1%)
	Specificity:	89.2% (140/157) (95% CI: 83.3–93.1%)

Graves' Disease	Sensitivity:	82.2% (88/107) (95% CI: 73.9–88.3%)
	Specificity:	89.2% (140/157) (95% CI: 83.3–93.1%)

An additional 262 samples were retrospectively obtained from pregnant subjects and patients with various other disease states that could be considered in the differential diagnosis of AITD and added to the prospective cohort. The clinical sensitivity and specificity for the ADVIA Centaur aTPOII were determined and shown in the table below:

		Clinical Diagnosis			
		Autoimmune Thyroiditis	Graves' Disease	Controls	Total
ADVIA Centaur aTPOII	Positive	60	88	84	231
	Negative	40	19	375	435
	Total	100	107	459	666

Autoimmune Thyroiditis	Sensitivity:	60.0% (60/100) (95% CI: 50.2–69.1%)
	Specificity:	81.7% (375/459) (95% CI: 77.9–85.0%)

Graves' Disease	Sensitivity:	82.2% (88/107) (95% CI: 73.9–88.3%)
	Specificity:	81.7% (375/459) (95% CI: 77.9–85.0%)

¹ Ross DS et al. 2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis. *Thyroid*. 2016; 26:1343. doi: 10.1089/thy.2016.0229.

² Jonklaas J et al. American Thyroid Association Task Force on Thyroid Hormone Replacement. Guidelines for the treatment of hypothyroidism: prepared by the American thyroid association task force on thyroid hormone replacement. *Thyroid*. 2014; 24:1670. doi: 10.1089/thy.2014.0028.

Distribution of target and differential disease samples and antibody positivity rates are shown in the table below:

		ADVIA Centaur aTPOII	Predicate
	N	n POS (%)	n POS (%)
Target conditions			
Graves' Disease	100	60 (60%)	60 (60%)
Autoimmune Thyroiditis	107	88 (82.2%)	89 (83.2%)
Total	207	148 (71.5%)	149 (72.0%)
Differential diagnosis controls			
Multinodular goiter	62	2 (3.2%)	4 (6.5%)
Non-autoimmune thyroid disease (NAITD) and all other diseases*	95	15 (15.8%)	21 (22.1%)
Thyroid Carcinoma	20	4 (20.0%)	4 (20.0%)
Silent Painless Thyroiditis	20	7 (35.0%)	8 (40.0%)
Subacute Thyroiditis	10	0 (0.0%)	0 (0.0%)
Hepatitis C virus (HCV)	20	0 (0.0%)	0 (0.0%)
Hepatitis B virus (HBV)	20	7 (35.0%)	7 (35.0%)
Human immunodeficiency virus (HIV)	20	1 (5.0%)	5 (25.0%)
iabetes Type 1	10	2 (20.0%)	3 (30.0%)
Sjogren's Syndrome	10	1 (10.0%)	1 (10.0%)
Primary Biliary Cholangitis	10	9 (90.0%)	9 (90.0%)
Systemic Sclerosis	10	4 (40.0%)	4 (40.0%)
Pernicious Anemia	10	1 (10.0%)	2 (20.0%)
Rheumatoid Arthritis	10	0 (0.0%)	0 (0.0%)
Systemic Lupus Erythematosus (SLE)	10	1 (10.0%)	2 (20.0%)
Addison's Disease	10	0 (0.0%)	2 (20.0%)
Miscarriage	20	20 (100.0%)	20 (100.0%)
Pregnancy – 1st Trimester	31	1 (3.2%)	2 (6.5%)
Pregnancy – 2nd Trimester	30	7 (23.3%)	7 (23.3%)
Pregnancy – 3rd Trimester	31	2 (6.5%)	4 (12.9%)
Total	459	84 (18.3%)	105 (22.9%)

* Prospective cohort not further diagnosed

D Clinical Cut-Off:

The clinical cut-off is 10.4 IU/mL.

E Expected Values/Reference Range:

A reference interval for apparently healthy adults using the ADVIA Centaur aTPOII was established non-parametrically in accordance with CLSI Document EP28-A3c. Samples were collected prospectively from 261 euthyroid male and female adult subjects ≥ 22 years of age with normal TSH levels, no evidence of goiter, and tested on three lots of the ADVIA Centaur

aTPOII. The 95th percentile of Lot 2 was below the LoQ while the 95th percentile of Lot 1 and Lot 3 were 4.8 and 6.5 IU/mL. A small percentage of samples were above the clinical cut-off of 10.4 IU/mL; Lot 1, 3.1% (8 samples); Lot 2, 3.8% (10 samples); Lot 3, 3.4% (9 samples). The reference range claim is defined as < 10.4 IU/mL.

The sponsor recommends each laboratory should determine its own reference interval for the diagnostic evaluation of patient results.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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