510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K240996

B Applicant

Beckman Coulter, Inc.

C Proprietary and Established Names

Access Thyroglobulin Antibody II

D Regulatory Information

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

II Submission/Device Overview:

A Purpose for Submission:

Modification of the previously cleared device – the change of substrate for the assay on the DxI 9000 Immunoassay Analyzer

B Measurand:

Anti-Thyroglobulin autoantibody

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 Access Thyroglobulin Antibody II assay is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of thyroglobulin antibody levels in human serum and plasma using the Access Immunoassay Systems. The measurement of thyroid autoantibodies may aid in the diagnosis of Hashimoto's disease, nontoxic goiter, and Graves' disease.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only
For In Vitro Diagnostic Use

D Special Instrument Requirements:

DxI 9000 Access Immunoassay Analyzer (K221225)

IV Device/System Characteristics:

A Device Description:

Each Access Thyroglobulin Antibody II (TgAb II) reagent kit contains two reagent packs (100 determinations, 50 tests/pack). Each pack contains the following:

- R1a (3.25 mL): Paramagnetic particles coated with streptavidin and coupled to biotinylated human thyroglobulin, suspended in a TRIS buffer with protein (bovine) and preservatives
- R1b (13.25 mL): Human thyroglobulin alkaline phosphatase (bovine) conjugate in a TRIS buffer with protein (bovine) and preservatives
- R1c (4.5 mL): TRIS buffer with bovine protein and preservatives
- R1d (3.1 mL): TRIS buffer with blocking polymer and preservatives

<u>Materials needed but not supplied with reagent kit.</u>

- Access Thyroglobulin Antibody II Calibrators: at 0, 50, 250, 500, 1000, and 2500 IU/mL
- Quality Control (QC) materials: commercial control material
- Substrate: Lumi-Phos PRO
- UniCel DxI Wash Buffer II

The modification of the Access Thyroglobulin Antibody II is to replace substrate (Lumi-Phos 530) with a new substrate, Lumi-Phos PRO, on the DxI 9000 Access Immunoassay Analyzer.

B Principle of Operation:

The Access Thyroglobulin Antibody II assay is a sequential two-step immunoenzymatic ("sandwich") assay. A sample is added to a reaction vessel with paramagnetic particles coated with the thyroglobulin protein. The TgAb in the sample binds to the thyroglobulin coated on the

particles. After incubation, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. The thyroglobulin-alkaline phosphatase conjugate is added and binds to the TgAb. After a second incubation, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. Then the chemiluminescent substrate is added to the vessel and light generated by the reaction is measured with a luminometer. The light production is directly proportional to the concentration of analyte in the sample. Analyte concentration is automatically determined from a stored calibration.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Access Thyroglobulin Antibody II

B Predicate 510(k) Number(s):

K213517

C Comparison with Predicate:

Device & Predicate Device(s):	K240996 (Candidate)	K213517 (Predicate)
Device Trade Name	Access Thyroglobulin Antibody II	Access Thyroglobulin Antibody II
General Device Characteristic Similarities		
Intended Use/ Indications For Use	The Access Thyroglobulin Antibody II assay is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of thyroglobulin antibody levels in human serum and plasma using the Access Immunoassay Systems. The measurement of thyroid autoantibodies may aid in the diagnosis of Hashimoto's disease, nontoxic goiter, and Graves' disease.	Same
Analyte	Thyroglobulin antibody (TgAb)	Same
Methodology	Chemiluminescent immunoassay	Same
Sample Type	Human serum and plasma (EDTA or lithium heparin)	Same
Sample Volume	10 µL	Same
Calibration	6-level multipoint calibration curve	Same
Measuring Interval	1.5−2500 IU/mL	Same

General Device Characteristic Differences		
Instrument	DxI 9000 Access Immunoassay Analyzer	Access 2 Immunoassay System; UniCel DxI 800 Immunoassay System; UniCel DxI 600 Immunoassay System
Substrate	Lumi-Phos PRO substrate	Access Substrate

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, 2nd Edition, Evaluation of Linearity of Quantitative, Measurement Procedures
- 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

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

All results presented below met the manufacturer's pre-determined acceptance criteria.

1. Precision/Reproducibility:

   Precision testing was performed in accordance with CLSI Guideline EP05-A3.

   a) Within-Laboratory Precision:

   The studies were performed at a single site using one lot of the modified Access Thyroglobulin Antibody II (TgAb II) reagent on one DxI 9000 Access Immunoassay Analyzer. Five samples (four native serum sample pools and one contrived serum sample) were run in duplicate per run, two runs daily over 20 days, resulting in 80 datapoints for each sample. The data were analyzed by ANOVA methods for within-run (repeatability), between-run, between-day, and within-laboratory precision. The mean (IU/mL), standard deviation (SD, IU/mL), and percent coefficient of variation (%CV) for each sample are summarized in table below:

Sample	Mean (IU/mL)	N	Within-Run		Between-Run		Between-Day		Within-Laboratory	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	2.4	80	0.1	4.2	0.1	2.5	0.1	2.0	0.1	5.2
2	188	80	6.6	3.5	0.0	0.0	3.9	2.1	7.6	4.1
3	727	80	22.0	3.0	0.0	0.0	21.3	2.9	30.6	4.2
4	1493	80	35.5	2.4	39.9	2.7	51.2	3.4	74.0	5.0
5	1925	80	53.5	2.8	56.9	3.0	80.9	4.2	112.5	5.8

b) *Instrument-to-Instrument Precision:*

The study was performed using three individual DxI 9000 Access Immunoassay Analyzers with a single lot of the modified Access TgAb II reagent. Five samples (four native serum sample pools and one native serum supplemented with TgAb for high analytical measuring interval (AMI) values) were tested in replicates of five per run, one run per day, over five days, resulting in 75 datapoints for each sample. The results are summarized in table below:

Sample	Mean (IU/mL)	N	Within-Run (Repeatability)		Between-Day		Between-Instrument		Reproducibility	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	2.6	75	0.1	4.7	0.1	1.9	0.1	2.8	0.2	5.8
2	184	75	4.1	2.2	2.9	1.6	4.8	2.6	6.9	3.8
3	744	75	19.2	2.6	12.1	1.6	2.5	0.3	22.8	3.1
4	1503	75	43.9	2.9	15.2	1.0	26.3	1.8	53.4	3.6
5	1966	75	68.2	3.5	102.2	5.2	23.9	1.2	125.1	6.4

c) *Lot-to-Lot Precision*

The lot-to-lot precision of Lumi-Phos PRO Substrate was assessed in K223921.

The reagent lot-to-lot precision was evaluated using three lots of the modified Access Thyroglobulin Antibody II (TgAb II) reagent and one calibrator lot on each of three DxI 9000 Access Immunoassay Analyzers. For each instrument, four native serum samples were run in five replicates per run, one run per day over 5 days, resulting in 75 datapoints per sample. Representative results from one instrument are summarized in table below:

Sample	Mean (IU/mL)	N	Within-Run (Repeatability)		Between-Day		Between-Reagent Lot		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	3.8	75	0.16	4.1	0.13	3.5	0.00	0.0	0.20	5.3
2	179	75	4.67	2.6	2.48	1.4	3.78	2.1	6.50	3.6
3	468	75	16.36	3.5	12.62	2.7	19.42	4.2	28.35	6.1
4	1590	75	71.92	4.5	56.66	3.6	107.35	6.8	141.09	8.9

2. Linearity:

The linearity of the modified Access Thyroglobulin Antibody II assay was assessed in accordance with the CLSI Guideline EP06, 2nd Ed. One individual native low sample, four low native pooled samples, and five high pooled native samples were used to prepare five overlapping dilution series, tiled across the AMI. For each series, the lowest sample was tested in replicates of eight, while all other samples were tested in replicates of four on one DxI 9000 Access Immunoassay Analyzer using one reagent lot and one calibrator lot. The data were analyzed by weighted least squares (WLS) regression by comparing observed results to expected concentrations for each linearity panel. Deviation from linearity predicted from WLS regression was calculated by determining the difference between observed and linear fit values for each dilution series, as well as a composite regress across all dilution series. The results are summarized in the table below:

Dilution Series		Slope (95% CI)	Intercept (95% CI)	R^2	%Deviation* (Deviation**)
1	0.04−29.60	0.954 (0.937−0.971)	-0.002 (-0.024−0.021)	0.996	-1% to 5% (-0.2 to 0.1 IU/mL)
2	11.83−264.77	1.017 (1.003−1.031)	-0.052 (-0.513−0.410)	0.998	-2% to 4% (-0.1 IU/mL)
3	258.80−608.34	1.050 (1.015−1.084)	-7.988 (-20.475−4.499)	0.992	-4% to 3%
4	607.89−1170.02	1.088 (1.029−1.148)	-35.279 (-82.419−11.861)	0.978	-5% to 3%
5	1095.44−2911.95	0.967 (0.917−1.017)	36.141 (-34.444−106.727)	0.987	-3% to 2%
All	0.04−2911.95	1.008 (1.001−1.015)	-0.020 (-0.047−0.007)	0.997	-6% to 7% (-0.7 to 0.02 IU/mL)

* % Deviation from Linearity for concentrations > 15 IU/mL
** Deviation (ng/mL) from Linearity for concentrations ≤ 15 IU/mL

The data support a linear interval from 0.04 to 2,911.95 IU/mL with the deviations from linearity within ± 10% for analyte concentration ≥15 IU/mL and ± 0.7 IU/mL for analyte concentration <15 IU/mL. The study results support the linearity of the claimed AMI: 1.5 – 2500 IU/mL.

3. Analytical Specificity/Interference and Cross-reactivity:

Refer to K213517.

4. Assay Reportable Range:

The reportable range is the same as the claimed analytical measuring interval: 1.5 IU/mL to 2500 IU/mL.

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

a) Traceability:

Traceability was established in K112933. The traceability of these modifications to the Access Thyroglobulin Antibody II assay is unchanged.

b) Stability:

The Access TgAb II Reagent kit and the Lumi-Phos PRO substrate are packaged separately. Access TgAb II Reagent kit stability was established in K213517. The proposed change introduces a new substrate (Lumi-Phos PRO). The shelf-life claims and on-board stability claims for Lumi-Phos PRO substrate were established in K221225.

6. Detection Capability:

CLSI guideline EP17-A2 was followed to determine the Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantitation (LoQ) for the modified Access TgAb II on DxI 9000 Access Immunoassay Analyzer.

a) LoB:

Five blank individual native serum samples were tested in five replicates per run, one run per day over three days using two modified Access TgAb II reagent lots (N=75 datapoints for each lot) on two DxI 9000 Access Immunoassay Analyzers. The LoB for each reagent lot was calculated using the 95% percentile of all datapoints for each of the two reagents. The claimed non-parametric LoB for the modified Access TgAb II on DxI 9000 Access Immunoassay Analyzer is 0.1 IU/mL.

b) LoD:

Eleven native serum samples containing low levels of TgAb II analyte were tested over five days, one run per day, and a minimum of eight replicates per run for each of two Access TgAb II reagent lots. Two DxI 9000 Access Immunoassay Analyzers were used for a minimum of N=492 datapoints for each reagent lot. The non-parametric method of LoD per CLSI EP17-A2 was used to determine the maximum observed LoD between the two lots. The claimed LoD for the modified Access TgAb II on the DxI 9000 Access Immunoassay Analyzer is 0.2 IU/mL.

c) LoQ:

Thirteen native serum samples or pools containing low levels of TgAb II analyte were tested in nine replicates per run, one run per day, for five days on each of two Access TgAb II reagent lots, on two DxI 9000 Access Immunoassay Analyzers. This resulted in a minimum of N=540 datapoints for each sample for each reagent lot. For LoQ determination, a precision model was used to estimate the within-laboratory %CV for each sample for each instrument and reagent lot combination. The precision profile was used to calculate an LoQ based on a 20% CV threshold. The claimed LoQ for the modified Access TgAb II on DxI 9000 Access Immunoassay Analyzer is 1.5 IU/mL.

7. Assay Cut-Off:

Not applicable

B Comparison Studies:

1. Method Comparison with Predicate Device:

   CLSI guideline EP09c, 3rd Edition was followed to compare the Access TgAb II assay on the DxI 9000 Access Immunoassay Analyzer to the predicate device, the Access TgAb II on the Access 2 Immunoassay System. A total of 114 de-identified patient serum samples within the AMI of the Access TgAb II assay were tested in singlicate with three Access TgAb II reagent lots and three calibrator lots, on three DxI 9000 Access Immunoassay Analyzers (candidate) as well as three Access 2 instruments (predicate). The comparison between measurement methods was analyzed using the Passing-Bablok regression method. Regression results are summarized in the following table:

N	Interval (IU/mL)	Slope (95% CI)	Intercept (95% CI)	R^2
114	2.3 − 2463	0.97 (0.95 − 0.99)	-0.37 (-0.99 − 0.047)	1.00

2. Matrix Comparison:

   The comparability of claimed matrices were previously reviewed in K213517.

C Clinical Studies:

Refer to K112933

D Clinical Cut-Off:

Refer to K112933

E Expected Values/Reference Range:

Refer to K213517

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.