510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K240469

B Applicant

Beckman Coulter, Inc

C Proprietary and Established Names

Access TPO Antibody

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:

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

B Measurand:

Thyroperoxidase antibody (TPO Ab)

C Type of Test:

Quantitative, Chemiluminescent Immunoassay

III Intended Use/Indications for Use:

A Intended Use(s):

The Access TPO Antibody assay is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of thyroperoxidase antibody (TPOAb) levels in human serum and plasma using the Access Immunoassay Systems.

The detection of TPOAb is an aid in the diagnosis of thyroid autoimmune disorders.

B Indication(s) for Use:

Same as Intended Use.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only
For In Vitro Diagnostic Use Only

D Special Instrument Requirements:

DxI 9000 Access Immunoassay Analyzer (K221225)

IV Device/System Characteristics:

A Device Description:

Each Access TPO Antibody reagent kit contains two reagent packs (50 tests/pack). Each pack contains the following:

- R1a (3.25 mL): Dynabeads paramagnetic particles coated with streptavidin and coupled to biotinylated human recombinant TPO in N-(2-acetamido)-2-aminoethanesulfonic acid (ACES) buffer with protein (bovine) and preservatives
- R1b (9.60 mL): Recombinant Protein A-alkaline phosphatase (bovine) conjugate in 2-Morpholinoethanesulphonic acid (MES) buffer with protein (bovine) and preservatives
- R1c (3.10 mL): TRIS buffer with protein (bovine) and preservatives

<u>Materials needed but not supplied:</u>

- Access TPO Antibody Calibrators: Six levels (0, 5, 20, 75, 300, and 1,000 IU/mL)
- Quality Control (QC) materials: commercial control material
- Substrate: Lumi-Phos PRO
- Unicel DxI Wash Buffer II
- Access Sample Diluent A (optional)

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

B Principle of Operation:

The modified Access TPO Antibody assay is a sequential two-step immunoenzymatic ("sandwich") assay. A sample is added to a reaction vessel with paramagnetic particles coated with human recombinant thyroperoxidase protein. The TPO antibody in serum or plasma binds to thyroperoxidase on the solid phase. After incubation in a reaction vessel, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. Then, the chemiluminescent substrate (Lumi-Phos PRO) 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 TPO antibody in the sample. The amount of analyte concentration is automatically determined from a stored calibration.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Access TPO Antibody

B Predicate 510(k) Number(s):

K061382

C Comparison with Predicate(s):

Device & Predicate Device(s):	**K240469 (Candidate)**	**K061382 (Predicate)**
Device Trade Name	Access TPO Antibody	Access TPO Antibody
General Device Characteristic Similarities		
Intended Use/ Indications for Use	The Access TPO Antibody assay is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of thyroperoxidase antibody (TPO Ab) levels in human serum and plasma using the Access Immunoassay Systems. The detection of TPO Ab is an aid in the diagnosis of thyroid autoimmune disorders.	Same

Analyte	TPO antibody	Same
Technology	Chemiluminescent	Same
Calibration	Multi-point calibration curve	Same
Sample Type	Serum and plasma (EDTA, Lithium Heparin)	Same
Measuring Range	0.25 – 1,000 IU/mL	Same
General Device Characteristic Differences		
Substrate	Lumi-Phos PRO Substrate	Access Substrate (Lumi-Phos 530)
Instrument	DxI 9000 Access Immunoassay Analyzer	Access 2 Immunoassay Analyzer

VI Standards/Guidance Documents Referenced:

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

- CLSI EP05-A3: Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – Third Edition
- CLSI EP06-2nd Edition-: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline
- CLSI EP09c 3rd Edition: Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Third Edition
- 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:

1. Precision/Reproducibility:

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

a) Within-Laboratory Precision:

The within-laboratory precision was evaluated using three reagent lots and three DxI 9000 Access Immunoassay Analyzers. Five levels of human serum samples in two replicates per run, two runs per day for 20 days, resulting in 80 datapoints for each sample per reagent lot per instrument. 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 percent coefficient of variation (%CV) were

calculated for each sample. The representative data of within-laboratory precision using one lot of reagents on one instrument are summarized in the table below.

Sample	Mean (IU/mL)	N	Within-Run (Repeatability)		Between-Run		Between-Day		Within-Laboratory	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	0.35	80	0.02	6.9	0.00	0.0	0.00	0.0	0.02	6.9
2	5.5	80	0.36	6.7	0.00	0.0	0.00	0.0	0.36	6.7
3	20	80	1.12	5.6	0.00	0.0	0.52	2.6	1.23	6.2
4	318	80	18.59	5.8	0.13	0.0	10.50	3.3	21.35	6.7
5	747	80	77.44	10.4	52.21	7.0	24.18	3.2	96.48	12.9

b) Lot-to-Lot Precision

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

The lot-to-lot precision of the modified Access TPO Antibody reagent was evaluated using three reagent lots on the DxI 9000 Access Immunoassay Analyzer. Five serum samples at different concentrations were tested in a minimum of five replicates per run, one run per day over five days, resulting a minimum of N=75 datapoints per sample on one instrument. The same study was also performed on two additional instruments. The data were 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)	N	Within-Run		Between-Day		Between-Lot		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	0.30	84	0.03	10.6	0.01	3.8	0.02	6.3	0.04	12.9
2	5.1	75	0.40	7.8	0.00	0.0	0.29	5.7	0.49	9.6
3	18	75	1.25	6.9	0.00	0.0	1.41	7.8	1.88	10.5
4	144	75	12.40	8.6	11.95	8.3	10.26	7.1	20.04	13.9
5	763	76	98.85	12.9	59.93	7.9	110.5	14.5	159.95	21.0

c) Instrument-to-Instrument Precision:

The study was performed by testing five serum samples at different concentrations on three DxI 9000 Access Immunoassay Analyzers. Each sample was tested in a minimum of five replicates per run, one run per day over five days, resulting in minimum N=75 datapoints using one lot of reagents. The same study was also performed on two additional reagent lots. The instrument-to-instrument reproducibility using one representative reagent lot are summarized in the table below.

Sample	Mean (IU/mL)	N	Within-Run		Between-Day		Between-Instrument		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	0.31	77	0.02	7.5	0.01	4.3	0.02	7.3	0.04	11.3
2	5.1	75	0.26	5.1	0.00	0.0	0.24	4.7	0.35	6.9
3	18	75	0.82	4.6	0.00	0.0	1.01	5.6	1.30	7.3
4	322	75	29.61	9.2	9.53	3.0	17.38	5.4	35.63	11.1
5	809	76	83.44	10.3	60.16	7.4	37.27	4.6	109.41	13.5

2. Linearity:

A linearity study of the modified Access TPO Antibody assay on the DxI 9000 Access Immunoassay Analyzer was performed in accordance with CLSI EP06-Ed2. Five linearity dilution series were prepared by mixing High and Low native serum samples. All dilution series included nine dilution samples covering the ranges shown in the table below. For all five series, the lowest samples were tested in replicates of eight, while all other samples were tested in replicates of four on one DxI 9000 Access Immunoassay Analyzer using one modified Access TPO Antibody reagent lot. For each level, the mean of the measured values, predicted value and the percent deviation from linearity were calculated. The data sets from the five series were also combined for a single linearity analysis. The results are summarized in the table below.

Range (IU/mL)	Slope (95% CI)	Intercept (95% CI)	R^2	Deviation*/ % Deviation**
0.24 − 55.45	0.986 (0.970, 1.002)	0.003 (-0.008, 0.015)	0.996	0.00003 IU/mL / -3% to 3%
42.53 − 317.08	0.957 (0.934, 0.981)	1.451 (-0.083, 2.985)	0.996	-5% to 4%
178.88 − 479.73	1.014 (0.979, 1.048)	-4.509 (-13.898, 4.880)	0.992	-3% to 1%
401.90 − 699.30	0.972 (0.862, 1.081)	21.607 (-34.173, 77.387)	0.893	-4% to 6%
646.57 – 1085.25	1.112 (0.939, 1.285)	-72.198 (-202.546, 58.150)	0.854	-4% to 8%
All Combined (0.24 − 1085.25)	0.997 (0.989, 1.004)	0.001 (-0.009, 0.011)	0.988	0.0002 IU/mL / -7% to 12%

* Deviation (IU/mL) from Linearity for concentrations ≤ 0.6 IU/mL
** % Deviation from Linearity for concentrations > 0.6 IU/mL

The data support the linearity interval from 0.24 to 1085.25 IU/mL with the %deviations from linearity within ±10% (Except one sample at mean value of 1018.33 IFU with 12% deviation from linearity). The study results support the linearity of the claimed analytical measuring interval (AMI): 0.25 – 1000 IU/mL.

3. Analytical Specificity/Interference:

Refer to K061382

4. Assay Reportable Range:

The assay reportable range for the Access TPO Antibody is the same as the claimed AMI: 0.25–1000 IU/mL.

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

a) Traceability:

The traceability was established in K061382. There is no change to the traceability of the modified Access TPO Antibody.

b) Stability:

The Access TPO Antibody reagent kit and the Lumi-Phos PRO substrate are packaged separately. Access TPO Antibody reagent kit stability was established in K061382. The proposed change is to replace the substrate (Lumi-Phos 530) with a new substrate (Lumi-Phos PRO) for the assay run on DxI Access Immunoassay Analyzer. The shelf-life claims and on-board stability claims of Lumi-Phos PRO substrate were established in K221225.

6. Detection Limit:

The Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantitation (LoQ) for the modified Access TPO Antibody on the DxI 9000 Access Immunoassay Analyzer were determined based on the CLSI guideline EP17-A2.

a) LoB:

The LoB was determined by testing five TPO antibody-depleted individual native serum samples using two modified Access TPO Antibody reagent lots on two DxI 9000 Access Immunoassay Analyzers. Samples were run in five replicates per run, one run per day, for three days on one DxI 9000 Access Immunoassay Analyzer, resulting in 75 replicates for one reagent lot on each instrument. LoB was defined as the value corresponding to the 95^{th} percentile of the rank position of the distribution of values. This resulted in the LoB values of 0.19 IU/mL and 0.14 IU/mL for two reagent lots. The claimed LoB for the modified Access TPO Antibody on the DxI 9000 Access Immunoassay Analyzer is 0.19 IU/mL.

b) LoD:

The LoD was determined by testing a minimum of five low level serum samples using three modified Access TPO Antibody reagent lots on three DxI Access 9000 Immunoassay Analyzers. Samples were run in nine replicates per run, one run per day, for five days for each reagent lot on each DxI 9000 Access Immunoassay Analyzer. The LoD was calculated for each reagent lot based on LoB + "SD was multiplied by the 95^{th} percentile of the standard normal distribution" per CLSI EP17-A2. This resulted in LoD values of 0.21, 0.21, and 0.23 IU/mL for three reagent lots. The claimed LoD for the

modified Access TPO Antibody assay on the DxI 9000 Access Immunoassay Analyzer is 0.23 IU/mL.

c) LoQ:

The LoQ was determined by testing a minimum of 13 low level serum samples using three modified Access TPO Antibody reagent lots on three DxI 9000 Access Immunoassay Analyzers. Samples were run a minimum of nine replicates per run, one run per day, for five days for each reagent lot on each DxI 9000 Access Immunoassay Analyzer. The estimated LoQ of the modified Access TPO antibody was set to be the TPO antibody concentration which met the within-laboratory imprecision of 20%CV. The claimed LoQ for the modified Access TPO Antibody assay on the DxI 9000 Access Immunoassay Analyzer is 0.25 IU/mL.

7. Assay Cut-Off:

An assay cut-off of 9 IU/mL was established in K061382.

B Comparison Studies:

1. Method Comparison with Predicate Device:

CLSI guideline EP09c, 3rd Edition was followed to compare the modified Access TPO Antibody assay on the DxI 9000 Access Immunoassay Analyzer to the predicate device, the Access TPO Antibody assay on the Access 2 Immunoassay Analyzer. Samples falling within the analytical measuring interval of both assays were evaluated. A total of 219 serum samples (192 were native individual serum samples, 27 samples were pools of individual native serum samples) were tested with six modified Access TPO Antibody reagent pack lots on six DxI 9000 Immunoassay Analyzers (candidate), and six Access TPO Antibody reagent pack lots on four Access 2 instruments (predicate). The comparison between paired measurements was analyzed using Passing-Bablok method by fitting the observed modified Access TPO Antibody on the DxI 9000 Access Immunoassay Analyzer (y) into a linear regression model, with the observed value from the predicate (x). The results are summarized in the following table:

N	Range of Observations (IU/mL)	Slope (95% CI)	Intercept (95% CI)	Correlation Coefficient (r)
219	0.35 – 980.9	1.06 (1.04 − 1.08)	-0.26 (-0.32 − -0.22)	0.978

2. Matrix Comparison:

Refer to K061382

C Clinical Studies:

Refer to K061382

D Clinical Cut-Off:

Refer to K061382

E Expected Values/Reference Range:

Refer to K061382

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.