510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:
k061382

B. Purpose for Submission:
New device

C. Measurand:
Anti-thyroid peroxidase antibodies

D. Type of Test:
Quantitative chemiluminescent immunoassay

E. Applicant:
Beckman Coulter, Inc.

F. Proprietary and Established Names:
Access TPO Antibody and Access TPO Antibody Calibrators

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
JZO System, Test, Thyroid Autoantibody	Class II	CFR 866.5870 Thyroid Autoantibody Immunological Test System	IM 82
JIT Calibrator, Secondary	Class II	CFR 862.1150 Calibrator	CH 75

H. Intended Use:

1. Intended use(s):
   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.
2. Indication(s) for use:
   The detection of TPO antibodies is an aid in the diagnosis of thyroid autoimmune disorders.
3. Special conditions for use statement(s):
   Prescription use only
4. Special instrument requirements:
   The Access TPO Antibody assay is intended for use with the Access Immunoassay Systems (Access, Access 2, Synchron LX® i725, UniCel DxI 800, and UniCel DxC 600i).

I. Device Description:

The Access TPO Antibody assay consists of reagent packs, calibrators and Sample Diluent A. The Access TPO Antibody assay, together with Access chemiluminescent substrate and wash buffer are designed for use with the Access family of analyzers. The reagent pack consists of three specific reagents: paramagnetic particles coated with streptavidin and coupled to biotinylated human recombinant TPO, suspended in buffer; Protein A-alkaline phosphatase conjugate in buffered protein solution; and

buffered protein solution. The calibrator kit includes calibrators at 6 levels: S0 is buffered protein solution; and calibrators S1-S5 consist of rabbit TPO antiserum in buffered protein solution. The calibrator levels are 0, 5, 20, 75, 300 and 1000 IU/mL.

J. Substantial Equivalence Information:

Similarities		
Item	Device	Predicate
	Beckman Coulter Access TPO Antibody/ TPO Calibrators	**[DPC] Immulite 2000 Anti-TPO Antibodies (k991096)**
Intended Use/Indications for Use	For the quantitative determination of thyroperoxidase antibody levels in human serum and plasma as an aid in the diagnosis of thyroid autoimmune disorders	For the quantitative measurement of anti-thyroid peroxidase antibodies in serum and EDTA plasma as an aid in the clinical diagnosis of thyroid diseases
Analyte	Autoantibodies to thyroid peroxidase	Same
Test principle	Chemiluminescence	Same
Assay principle	Sequential 2-step immunoenzymatic assay with a chemiluminescent substrate	Solid phase enzyme-labeled, chemiluminescent sequential immunometric assay

Differences		
Item	Device	Predicate
Instrument	Access Immunoassay Systems	IMMULITE 2000
Matrix	Serum and plasma (EDTA and lithium heparin)	Serum and EDTA plasma
Capture antigen	Recombinant human TPO	Highly purified human TPO
Calibration	6 levels (0, 5, 20, 75, 300 and 1000 IU/mL and contain rabbit TPO antiserum in a buffered protein solution; ready-to-use	2 levels (low and high) and contain TPO autoantibodies in a human serum/buffer matrix; lyophilized
Solid phase	Paramagnetic particles coated with streptavidin and coupled to biotinylated human recombinant TPO	Polystyrene bead coated with highly purified human TPO
Conjugate	Protein A-alkaline phosphatase (bovine)	Alkaline phosphatase-labeled anti-human IgG

Differences		
Item	Device	Predicate
	conjugate in buffered protein solution (bovine)	
Substrate	Lumi-Phos 530	Phosphate ester of adamantyl dioxetane in an AMP buffer

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

STANDARDS			
Title and Reference Number			
Interference Testing in Clinical Chemistry; Approved Guideline (EP 7-A)			
Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline (EP09-A2)			
Evaluation of Matrix Effects; Approved Guideline (EP14-A)			
Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline (EP5-A)			
Laboratory Support for the Diagnosis & Monitoring of Thyroid Disease, The National Academy of Clinical Biochemistry			
GUIDANCE			
Document Title	**Office**	**Division**	**Web Page**
Review Criteria for In Vitro Diagnostic Devices for the Assessment of Thyroid Autoantibodies using Indirect Immunofluorescence Assay (IFA), Indirect Hemagglutination Assay (IHA), Radioimmunoassay (RIA), and Enzyme Linked Immunosorbent Assay (ELISA)	**OIVD**	**DIHD**	**http://www.fda.gov/cdrh/ode/odecl051.html**

L. Test Principle:

The 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 thyroid peroxidase protein. The serum or plasma TPOAb binds to the thyroid peroxidase. After incubation in a reaction vessel, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. The thyroid peroxidase-alkaline phosphatase conjugate is added and binds to the TPOAb. After the second incubation, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. Then, the chemiluminescent substrate Lumi-Phos 530 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 TPOAb in the sample. The amount of analyte in the sample is determined from a stored, multi-point calibration curve. This is a well-recognized assay methodology that presents no new technical issues.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Assay precision was verified using a method based on CLSI/NCCLS EP05-A, *Evaluation of Precision Performance of Clinical Chemistry Devices*. The method consisted of assaying six serum samples for a minimum of 19 runs, minimum of 4 replicates per assay over 30 days completing one run per day on the Access, Access 2 and UniCel DxI 800 platforms. Three lots of reagents and one lot of calibrators were tested in this study. The concentrations for this study were chosen to represent the typical distribution of values to be found in patient samples. The mean of the replicates, standard deviation, and the percent CV for within run, between run and total precision were determined by analysis of variance (ANOVA) per EP05-A.

The Access TPO Antibody assay exhibited total imprecision of <12% at concentrations ≥ 0.6 IU/mL. All 3 lots of reagents tested met this total imprecision claim. Design specifications for total imprecision were met. Results from one of the lots of reagents tested are provided in the tables below.

Table 1 Precision Summary-Access Instrument

Sample	n	Mean (IU/mL)	Within Run SD	Within Run %CV	Between Run SD	Between Run %CV	Total Run SD	Total Run %CV
1	105	0.6	0.02	3.5	0.01	2.2	0.02	4.1
2	110	0.7	0.02	3.2	0.03	3.6	0.04	4.8
3	110	4.9	0.15	3.2	0.10	2.0	0.18	3.7
4	100	18.5	0.66	3.6	0.48	2.6	0.82	4.4
5	110	137	5.4	3.9	3.1	2.3	6.2	4.5
6	110	787	45.8	5.8	38.6	4.9	61.4	7.6

b. Linearity/assay reportable range:

Dilution Recovery (Linearity)

Dilution recovery studies for the Access TPO Antibody assay were completed using the UniCel DxI 800 platform. Six dilutions (1:2, 1:5, 1:10, 1:25, 1:50 and 1:100) were prepared from each of six serum samples or pools using Sample Diluent A and tested in replicates of four. All samples were tested on a UniCel DxI 800 instrument. For each dilution, an observed value was calculated by computing the mean of the replicates. The percent recovery was then calculated as follows: (Observed value ÷ Expected value) x 100%. In addition, the observed values were plotted vs. the expected values for each sample and a linear regression analysis was performed.

The Access TPO Antibody assay exhibited acceptable recovery upon sample dilution with slopes ranging from 0.920 to 1.057 and the intercepts ranging from -4.8 to -0.1 IU/mL. The study results shown in the tables below met the design specifications. The expected and observed values are expressed in IU/mL. In antibody assays, dilution recovery results may be affected by the antibody affinity, so an appropriate statement was added to the Access TPO Antibody insert: "Due to varying antigen specificity, affinity and avidity of thyroid peroxidase antibodies in their epitope reactions, some samples may not dilute linearly".

The assay reportable range is 0 to 1000 IU/mL.

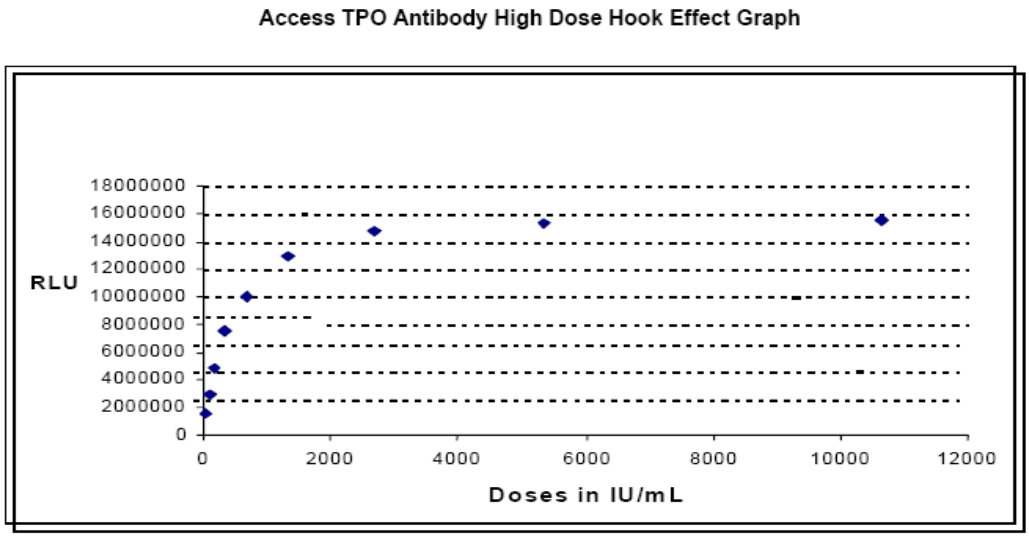
Table 1: Access TPO Antibody Dilution Recovery Summary – (IU/mL)				
Sample	**Dilution**	**Expected**	**Observed**	**% Recovery**
1	0	720.17	720.17	-
	1/2	360.09	377.16	104
	1/5	144.04	146.38	102
	1/10	72.02	65.29	91
	1/25	28.81	25.64	89
	1/50	14.41	12.77	89
	1/100	7.2	5.90	82
			Mean % Recovery	**95**
Sample	**Dilution**	**Expected**	**Observed**	**% Recovery**
2	0	46.83	46.83	-
	1/2	23.42	24.01	103
	1/5	9.37	8.51	91
	1/10	4.69	4.64	99
	1/25	1.88	1.60	85
	1/50	0.94	0.83	88
	1/100	0.47	0.40	85
			Mean % Recovery	**93**
Sample	**Dilution**	**Expected**	**Observed**	**% Recovery**
3	0	20.13	20.13	-
	1/2	10.07	9.22	92
	1/5	4.03	3.60	89
	1/10	2.02	1.81	90
	1/25	0.81	0.64	79
	1/50	0.41	0.33	82
	1/100	0.20	0.16	79
			Mean % Recovery	**86**
Sample	**Dilution**	**Expected**	**Observed**	**% Recovery**
4	0	89.15	89.15	-
	1/2	44.58	44.20	99
	1/5	17.83	17.13	96
	1/10	8.92	7.35	82
	1/25	3.57	3.10	87
	1/50	1.78	1.60	90
	1/100	0.89	0.73	81
			Mean % Recovery	**91**
Sample	**Dilution**	**Expected**	**Observed**	**% Recovery**
5	0	129.10	129.10	-
	1/2	64.55	61.83	96
	1/5	25.82	24.60	95
	1/10	12.91	11.05	86
	1/25	5.16	4.40	85
	1/50	2.58	2.10	81
	1/100	1.29	1.03	79
			Mean % Recovery	**89**
Sample	**Dilution**	**Expected**	**Observed**	**% Recovery**
6	0	843.78	843.78	-
	1/2	421.89	401.70	95
	1/5	168.76	151.18	90
	1/10	84.38	75.35	89
	1/25	33.75	27.95	83
	1/50	16.88	13.25	79
	1/100	8.44	6.85	81
			Mean % Recovery	**87**

High-Dose Hook Effect

High dose hook or prozone effect can occur in 2-site simultaneous immunoassays when at high doses, the concentration of analyte exceeds the

capacity of the capture antibody to bind it. Free analyte is sequestered by labeled second antibody and the resultant value "hooks" back and reads on the standard curve, giving a falsely depressed value. A naturally occurring high TPOAb patient serum sample with a value >10,000 IU/mL was diluted serially 1:2, 1:4, 1:8, 1:16, 1:32, 1:64, 1:128, and 1:256 in Sample Diluent A. All dilutions were assayed in duplicate on an Access 2 instrument. The results were plotted graphically (dose vs. RLU) and the graph and data were visually evaluated for the presence of a high dose hook. Although the RLUs tended to plateau at doses higher than the standard curve S5 value of 1000 IU/mL, there was no indication of a hook effect as high as the highest assayed value of 10,654 IU/mL. The RLUs at 10,654 IU/mL did not fall below the S5 RLU. Therefore there was no hook effect up to 10,000 IU/mL and the assay met the design specification. Results are summarized in the table and graph below.

Access TPO Antibody High Dose Hook Effect Test Data			
Sample 1	Theoretical Dose	Mean Sample RLU	S5 RLU
Neat	10,654	15,492,850	12,206,600
1:2	6,327	15,336,450	12,206,600
1:4	2,664	14,682,900	12,206,600
1:8	1,332	12,949,250	12,206,600
1:16	666	10,042,735	12,206,600
1:32	333	7,490,685	12,206,600
1:64	166	4,882,225	12,206,600
1:128	83	2,897,320	12,206,600
1:256	42	1,537,200	12,206,600



c. *Traceability, Stability, Expected values (controls, calibrators, or methods):* The TPO antibodies in calibrators S1-S5 are traceable to international standard WHO 66/387. The traceability process was based on EN ISO 17511.

Calibrator Stability

Open vial - To verify the open vial stability for the calibrators at the recommended storage conditions of 2-10°C, three quality control samples were assayed at five time points (0, 1, 2, 3 and 6 months). The mean value for each control level at each time period was compared to the expected range. All results for all time periods were within range. The manufacturer recommends an open vial stability of 120 days.

Calibration curve - To verify the 56 day stability for the stored calibration curve, three quality control samples were assayed in replicates of two, and five patient samples were assayed in replicates of five at multiple time points between day 0 and day 63 after the establishment of a new six point calibration curve. The mean value for each control level at each time period was compared to the target value of that control on day zero and compared to the expected range. All points were within range and support a recommended calibration curve stability of 56 days.

Shelf-life - To verify the stability for the calibrators at the recommended storage conditions of 2-10°C, two quality control samples and five patient samples were assayed at various time points, including time 0, 3, 6, 9, 12, 13, and 15 months. The mean value for each control level at each time period is compared to the target value of that control on day zero and compared to the expected range. All points were within range and support a calibrator shelf-life of 12 months at 2-10°C.

d. Detection limit/analytical sensitivity:

The analytical sensitivity or theoretical lower limit of detection is defined as the lowest detectable level of TPO Ab that, with 95% confidence, can be distinguished from the S0 calibrator. A six-point calibration curve, controls and ten replicates of the zero calibrator were run in multiple assays on each platform. The mean SD and %CV were calculated for each set of ten replicates and the analytical sensitivity value was calculated from the curve at the point that was two standard deviations from the mean fitted S0 calibrator signal (RLUs). Ten studies were conducted in which a six-point calibration curve, controls and ten replicates of the TPO Antibody calibrator S0 were run in multiple assays. The experiments incorporated two lots of reagent, one lot of calibrators and the Access, Access 2, and UniCel DxI 800 platforms. The mean, SD and %CV were calculated for each set of ten replicates.

The lowest detectable level of TPO Ab distinguishable from zero (Access TPO Antibody S0 Calibrator) with 95% confidence was 0.0034 IU/mL on the Access platform, 0.0036 IU/mL on the UniCel DxI platform, and 0.0049 IU/mL on the Access 2 platform. The results of these studies demonstrated that the Access TPO Antibody assay met the design specification. In order to assure claims are consistently met, the following information is provided in the Access TPO Antibody directional insert: "The lowest detectable level of thyroid peroxidase antibodies distinguishable from zero (Access TPO Antibody Calibrator S0) with 95% confidence is 0.25 IU/mL."

e. Analytical specificity:

The Access TPO Antibody assay was tested for analytical specificity, as described in CLSI/NCCLS EP07-A, *Interference Testing in Clinical Chemistry*. Interference from normal human blood constituents (hemoglobin, triglycerides, bilirubin and human serum albumin), heterophile antibodies, and commonly encountered medications were evaluated in the Access TPO Antibody assay.

Interference from Heterophile Antibodies

Immunoenzymetric assay technology may demonstrate interferences from heterophile antibodies, including human anti-mouse antibodies (HAMA). While the assay has been formulated to minimize the effects of these antibodies, results must be carefully evaluated. To address this issue, a cautionary note, regarding samples containing such antibodies, is included in the labeling:

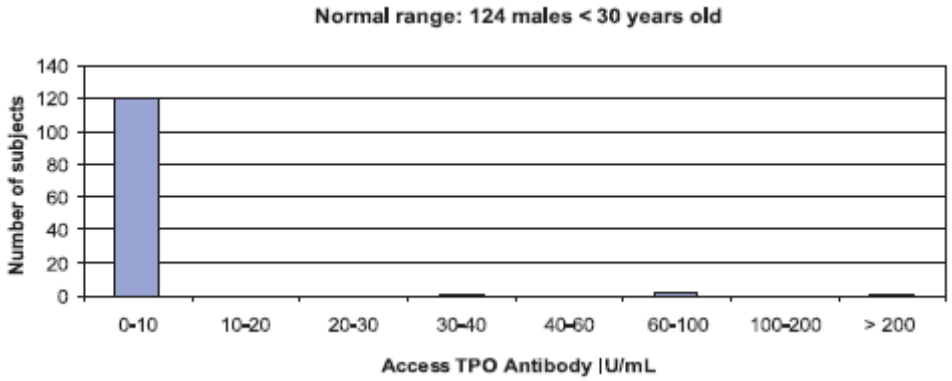
Interfering Substances

To evaluate potential interference, the substances listed in the table below were spiked individually into normal human serum. Samples were measured using the Access TPO Antibody assay and the dose of each spiked sample was compared to the dose of the neat sample. For each substance analyzed, an observed value was calculated by computing the mean of fifteen replicate measurements of the spiked sample. The expected value was equal to the mean of the replicates of the neat sample prior to addition of the substance. The interference was calculated as follows: [mean observed value - mean expected value / mean expected value] X 100 = Mean % Interference. The Access TPO Antibody assay exhibited no significant interference when samples were spiked with the substances listed in the table below. The results of the studies met design specifications.

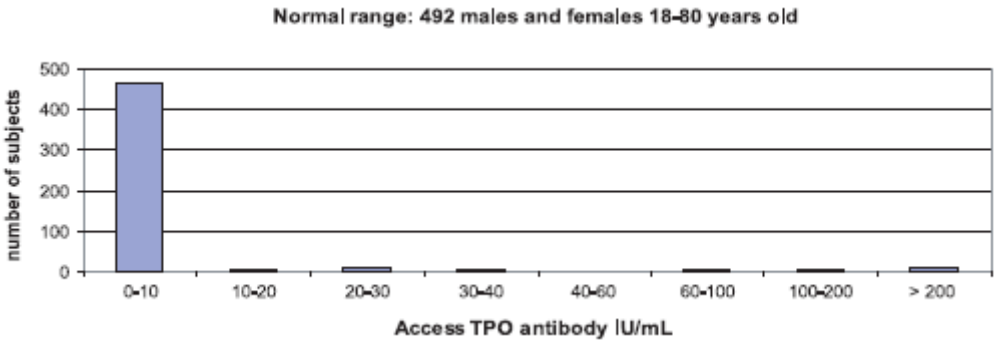
Interfering Substances				
Substance added	Concentration added	Expected (IU/mL)	Observed (IU/mL)	Mean % interference
Bilirubin (conjugated)	40 mg/dL	21.3	20.2	-5.2
Hemoglobin	500 mg/dL	16.9	17.7	5.0
Triglycerides	3000 mg/dL	20.1	20.3	1.1
Human serum albumin	6000 mg/dL	20.5	19.0	-7.1
Heparin	8000 mg/dL	20.1	19.5	-3.0
Acetaminophen	20 mg/dL	20.5	20.2	-1.6
Acetylsalicylic acid	50 mg/dL	20.5	20.9	1.8
Ibuprofen	40 mg/dL	20.5	21.2	3.3
Multi vitamins	1:20 dilution	20.3	19.4	-4.6

f. Assay cut-off:

Sera samples were obtained in the United States from 166 males, 30 years of age following the criteria outlined by the National Academy of Clinical Biochemists (NACB) for establishing a normal reference range for thyroid antibody tests. The screening criteria included: serum TSH levels between 0.5 and 2.0 mIU/L; no goiter; no personal or family history of thyroid disease; and absence of non-thyroid autoimmune disease. After completing the screen, 124 samples were tested generating a 95% non-parametric upper reference limit below 9 IU/mL.



Additionally, 679 normal samples were collected in the United States from both males and females ranging in age from 18–80 years old. The screening criteria included the same criteria as listed above. After completing the screen, 492 samples were tested and 93% of these samples fell below 9 IU/mL.

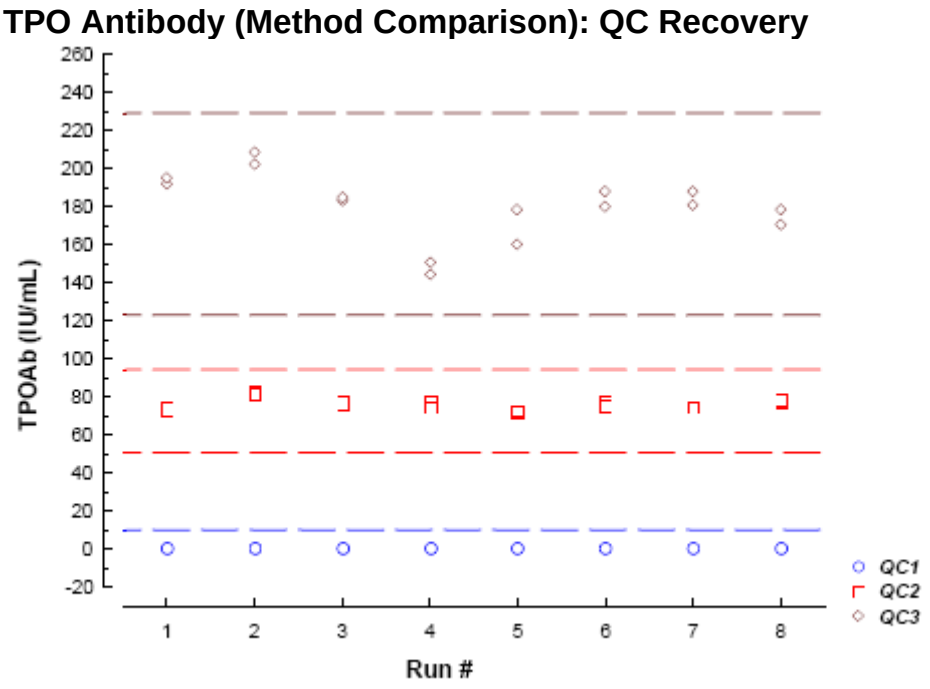


2. Comparison studies:

a. Method comparison with predicate device:

The correlation between results obtained using the Access Immunoassay System TPO Antibody assay and the DPC Immulite 2000 Anti-TPO Ab assay was evaluated by linear regression and concordance analyses. The DPC Immulite 2000 Anti-TPO Ab assay was chosen as the predicate device as it is a well established assay on an automated platform. The studies described below followed applicable ICH (International Conference of Harmonization) and GCP (Good Clinical Practice) requirements. IEC (Internal Ethics Committee) oversight and approval was received prior to study initiation. A

total of 320 residual de-linked serum samples were enrolled and tested on Access 2 and Immulite 2000 automated immunoassay analyzers at an external laboratory. All specimens were originally submitted to the laboratory for thyroid marker (including thyroid peroxidase antibody) testing; they were enrolled in the study based on the result of the TPOAb assay used by the site for diagnostic testing. Residual specimens from males and females 18 years of age and greater were included. Only one sample from any given subject was enrolled. All 320 results were included in the concordance analysis. The graph below illustrates the outcomes of quality control sample testing over the course of the study. The upper and lower limits of acceptance for each control level are indicated by dashed lines. All controls fell within the established boundaries.

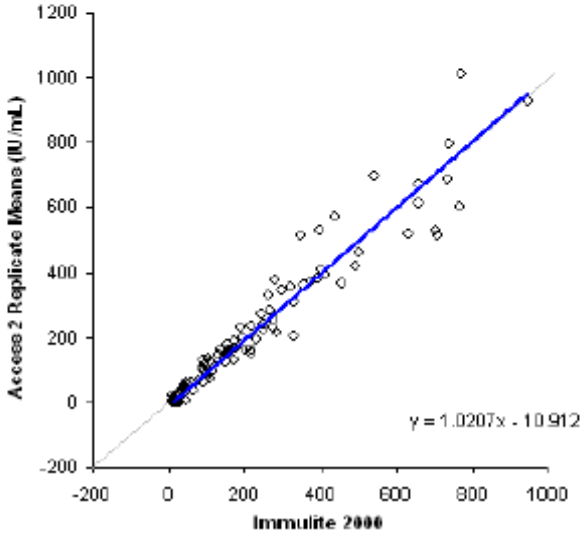


Results from the comparison (mean of duplicates for the Access TPO Antibody assay and singlicate results for the Immulite 2000 Anti-TPO Ab assay) were analyzed using Deming regression to determine the correlation between the two assays.

n	119		

	Coefficient	SE	95% CI
Intercept	-10.9123	6.9327	-24.6421 to 2.8175
Slope	1.0207	0.0245	0.9722 to 1.0693

r statistic	0.97	
95% CI	0.95	to 0.98
2-tailed p	<0.0001	(t approximation)



Using Deming regression analysis, results from the Methods Comparison across the 0-1000 IU/mL concentration range demonstrated acceptable agreement between the Access and DPC Immulite assays. The correlation coefficient (r) was 0.97 and the slope of the regression line was 1.0207 with a 95% confidence interval of 0.9722 to 1.0693. The y-intercept was -10.9123 with a 95% confidence interval of -24.6421 to 2.8175. The results of the study indicate that the slope and intercept and were not significantly different from one and zero.

Concordance was evaluated using specimens that provided a total of 97 final determinations classified as positive by the Immulite 2000 Anti-TPOAb method and 223 final determinations classified as negative by the Immulite 2000 Anti-TPOAb method. The Immulite 2000 Anti-TPOAb cut-off is 35 IU/mL and the Access TPO Antibody assay upper reference limit was determined to be < 9 IU/mL. The table below shows the concordance between the Access TPO Antibody assay and the Immulite 2000 Anti-TPOAb method. Results from the concordance analysis met design specifications.

	Immulite 2000 Anti-TPO Ab					
Access TPO Antibody Assay		+	-	Total		95% Confidence intervals
	+	96	15	111	Positive percent agreement = 99.0%	94.4 – 100%
	-	1	208	209	Negative percent agreement = 93.3%	89.1 – 96.2%
	Total	97	223	320	Overall agreement = 95.0%	

Method Comparison: Access Systems Cross-Platform Studies

To verify the equivalence of the Access platform family members with respect to the Access TPO Antibody assay, a method comparison study was performed. The study provided the following paired platform comparisons:

- Access 2 vs. Access
- UniCel DxI 800 vs. Access
- UniCel DxI 800 vs. Access 2

The LXi Synchron 725 and UniCel DxC 600i incorporate an Access 2 system and were represented by the Access 2 in this correlation study. Additional information on the equivalence of the LXi Synchron 725 and the UniCel DxC 600 I to the other members of the Access instrumentation family can be found in 510(k) notifications k060256 and k023049.

Ten patient samples with TPOAb concentrations distributed from 0.5 to 770 IU/mL were tested in duplicate, in two runs per day, for a period of five days, on each of the Access platforms. A new calibration curve was run on each of the five days in order to simulate the variability observed across multiple instruments. Controls were run each day to monitor performance of the Access TPO Antibody assay system. Following CLSI/NCCLS recommendations in EP9-A2 *Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline, 2nd Ed*. a linear regression model was used to evaluate cross platform equivalence. An evaluation of the slopes observed in this study showed analytical differences between the platforms of less than or equal to 4%, when compared to each other and to a theoretical slope of 1.0. The slope differences, although statistically significant ($p<0.5$) for the Access vs. DxI comparison, met the design specification of ≤10% difference between the platforms. The intercepts were not statistically different from zero in any of the comparisons. The linear regression data is summarized in the table below.

Platform Verification Method Comparison			
	Access (x) vs. Access 2 (y)	Access (x) vs. Dxl (y)	Access 2 (x) vs. Dxl (y)
Slope (95% confidence interval)	0.9741 (0.947, 1.001)	0.9661 (0.938, 0.994)	0.9901 (0.959, 1.021)
Intercept (95% confidence interval)	0.5625 (-7.836, 8.961)	-1.2342 (-9.811, 7.342)	-1.5200 (-10.861, 7.821)

b. Matrix comparison:

A comparison study was performed using 37 matched serum and plasma (EDTA and lithium heparin) samples that span the assay range. Samples were run as duplicates on an Access, Access 2 or UniCel DxI 800 system. Twenty-seven (27) samples were tested on the Access and UniCel DxI 800 systems. Ten (10) samples were tested on the Access 2 system. For the serum versus EDTA plasma study, n=64. This number represents the 27 samples tested both on the Access and UniCel DxI 800 systems and the 10 samples tested on the Access 2 system (27+27+10 =64). For the serum versus lithium heparin study, n=61. This number represents the 27 samples tested on both the Access and UniCel DxI 800 systems and the 10 tested on the Access 2 system, minus 3 samples that were removed from the analysis due to either insufficient testing volume or instrument error (27+27+10-3= 61).

Following CLSI/NCCLS recommendations in EP14-A2, *Evaluation of Matrix Effects, 2nd Ed*., a linear regression model was used to evaluate the correlation between the sample types. The slope and intercept were determined using a Deming regression; the correlation coefficient was determined by linear regression. Acceptable correlation was demonstrated between plasma (EDTA, heparin) and serum sample types. The slope differences, although statistically significant ($p<0.05$), were less than 7% and met design specifications.

Serum versus lithium heparin plasma			
N	Slope (95% confidence interval)	Intercept (IU/mL) (95% confidence interval)	Correlation coefficient (r)
61	1.0459 (1.0221, 1.0696)	-2.4262 (-7.2245, 2.3721)	0.9911

Serum versus EDTA plasma			
N	Slope (95% confidence interval)	Intercept (IU/mL) (95% confidence interval)	Correlation coefficient (r)
64	1.0339 (1.0150, 1.0528)	-0.8313 (-4.5925, 2.3900)	0.9927

3. Clinical studies:
   a. Clinical Sensitivity:
   Methodology: The Access TPO Antibody assay was evaluated using sera obtained from 54 patients diagnosed with Hashimoto's Thyroiditis and 40 patients diagnosed with Graves' disease. These pathological samples were acquired from independent laboratories with an established diagnosis. The presence of TPO antibodies was not a criterion for disease diagnosis. Duplicates of each sample were tested for TPO Ab using a UniCel DxI 800 instrument. Statistical Analysis: The mean TPO Antibody result was obtained and compared against the upper reference limit for normal samples of 9 IU/mL. Results are summarized in the table below.

Disease state	Number of patients	Percent positive
Hashimoto's thyroiditis	54	100%
Grave's disease	40	77.5%

   The Access TPO Antibody assay results provided above are consistent with the literature which reports that for patients with autoimmune thyroid disease, TPO Ab is almost invariably positive in Hashimoto's Thyroiditis and is often positive in Graves' disease. (Feldt-Rasmussen, U. Clin Chem 1996; 42: 160-163, Analytical and clinical performance goals for testing autoantibodies to thyroid peroxidase, thyroglobulin, and thyrotropin receptor).

   b. Clinical specificity:
   In normal population studies, 492 samples were tested and 93% of these samples fell below the established cut-off.
   c. Other clinical supportive data (when a. and b. are not applicable):
   Not applicable.
4. Clinical cut-off:
   See assay cut-off.
5. Expected values/Reference range:
   Up to 5% of the normal healthy blood donor population may have thyroid autoantibodies even with no prior history of thyroid or other autoimmune disease. Moderately increased levels of TPO antibodies may be found in patients with non-thyroid autoimmune disease such as pernicious anemia, Type I diabetes mellitus, or other disorders which activate the immune system.

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.