510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

I Background Information:

A 510(k) Number

K242022

B Applicant

Beckman Coulter Inc.

C Proprietary and Established Names

Access Toxo IgG

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
LGD	Class II	21 CFR 866.3780 - Toxoplasma Gondii Serological Reagents	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:

Modification of a previously cleared device - Clearance of Access Toxo IgG assay to add the DxI 9000 Access Immunoassay Analyzer

B Measurand:

IgG antibodies to *Toxoplasma gondii*

C Type of Test:

Chemiluminescent Immunoassay

III Intended Use/Indications for Use:

A Intended Use(s):
See Indications for Use below.

B Indication(s) for Use:
The Access Toxo IgG assay is a paramagnetic-particle, chemiluminescent immunoassay for the qualitative and quantitative determination of IgG antibodies to *Toxoplasma gondii* in human serum using the Access Immunoassay Systems. The Access Toxo IgG assay aids in the diagnosis of *Toxoplasma gondii* infection and may be used to assess the immune status of pregnant women.

This product is not FDA cleared/approved for the screening of blood or plasma donors. Assay performance characteristics have not been established for immunocompromised or immunosuppressed patients, cord blood, neonatal specimens or infants.

C Special Conditions for Use Statement(s):
Rx - For Prescription Use Only

D Special Instrument Requirements:
DxI 9000 Access Immunoassay Analyzer

IV Device/System Characteristics:

A Device Description:

The Access Toxo IgG assay is a paramagnetic-particle chemiluminescent immunoassay for the qualitative and quantitative detection of *Toxoplasma gondii*-specific IgG antibody in adult human serum using the Access Immunoassay Systems.

The Access Toxo IgG assay consists of the reagent pack, calibrators, and quality controls (QCs), packaged separately. Other items needed to run the assay include substrate and wash buffer.

B Principle of Operation:

The Access Toxo IgG assay is an enzyme immunoassay using an indirect technique. A sample is added to a reaction vessel with paramagnetic particles coated with *Toxoplasma gondii* membrane antigen. Specific antibodies present in the sample bind to the antigen. After incubation in a reaction vessel, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. Alkaline phosphatase-conjugated monoclonal anti-human IgG antibody is then added and attaches to the IgG antibodies captured on the particles. A second separation and wash steps remove unbound conjugate. 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 Toxo IgG antibody in the sample. The amount of analyte in the sample is determined from a stored, multi-point calibration curve.

The Access Toxo IgG assay results interpretation is as follows:

Results	Results Interpretation	Comment
< 7.5 IU/mL	Non-reactive	Samples are considered non-reactive for the presence of *Toxoplasma gondii IgG* antibodies. A non-reactive result may indicate that an individual has not been infected with *Toxoplasma gondii* and is thus susceptible to infection. A non-reactive result, however, does not rule out an acute infection. If exposure to the pathogen is suspected despite an initial non-reactive result, a second sample should be collected and tested at least two to three weeks later.
≥ 7.5 IU/mL to < 10.5 IU/mL	Equivocal	Samples are considered equivocal for the presence of *Toxoplasma gondii* IgG antibodies. Specimens that are equivocal may contain low levels of anti-Toxo IgG. As any cutoff is a statistically determined value, it is recommended that results close to the cutoff are interpreted cautiously and further investigated. If exposure to the pathogen is suspected despite an initial equivocal result, a second sample should be collected and tested at least two to three weeks later.
≥ 10.5 IU/mL	Reactive	Samples are considered reactive for the presence of *Toxoplasma gondii* IgG antibodies. A reactive result is generally indicative of recent or past exposure to the pathogen.

V Substantial Equivalence Information:

A Predicate Device Name(s):
Access Toxo Igg, Access Toxo Igg Calibrators And Access Toxo Igg Qc

B Predicate 510(k) Number(s):
K080869

C Comparison with Predicate(s):

Candidate & Predicate Devices:	Candidate K242022	Predicate K080869
Device Trade Name	Same	Access Toxo IgG
General Device Characteristic Similarities		
Intended Use/Indications For Use	Same	The Access Toxo IgG assay is a paramagnetic-particle, chemiluminescent immunoassay for the qualitative and quantitative determination of IgG antibodies to *Toxoplasma gondii* in human serum using the Access Immunoassay Systems. The Access Toxo IgG assay aids in the diagnosis of

Candidate & Predicate Devices:	Candidate K242022	Predicate K080869
		Toxoplasma gondii infection and may be used to assess the immune status of pregnant women. This product is not FDA cleared/approved for the screening of blood or plasma donors. Assay performance characteristics have not been established for immunocompromised or immunosuppressed patients, cord blood, neonatal specimens or infants.
Analyte	Same	IgG antibody to *T. gondii*
Technology	Same	Two-step immunoenzymatic assay
Format	Same	Chemiluminescent
Method	Same	Automated
Calibration	Same	Utilizes a stored calibration curve
Calibration Frequency	Same	28 days
Sample Type	Same	Serum
Analytical Measuring Interval	3.2 – 450 IU/mL	0 – 450 IU/mL
Results Interpretation	Same	<7.5 IU/mL: Non-Reactive ≥7.5 - <10.5 IU/mL: Equivocal ≥10.5 IU/mL: Reactive
Capture Reagent	Same	Paramagnetic particles coated with T. gondii (strain RH) solubilized membrane antigen
Detection Antibody	Same	Mouse monoclonal anti-human IgG antibody- alkaline phosphatase (bovine) conjugate
Open Kit Stability	Same	28 days after opening, 2-10°C
General Device Characteristic Differences		
Substrate	Lumi-Phos PRO substrate	Access Substrate
Instrument	DxI 9000 Access Immunoassay Analyzer	Access 2 Immunoassay 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

- CLSI EP06-Ed 2: Evaluation of the Linearity of Quantitative Measurement Procedures
- CLSI EP09c-Ed 3: Measurement Procedure Comparison and Bias Estimation Using Patient Samples
- CLSI EP12-Ed3, Evaluation of Qualitative, Binary Output Examination Performance, Third Edition

VII Performance Characteristics (if/when applicable):

A. Analytical Performance:

1. Precision/Reproducibility:

a) *Within-Laboratory Precision:* A 20-day within-laboratory precision study was conducted using 3 lots of the Access Toxo IgG reagents, 3 lots of the Access Toxo IgG calibrators and 3 DxI 9000 Access Immunoassay Analyzer systems. Six human serum samples were tested in 2 replicates at 2 runs per day over 20 days using 3 reagent lot/calibrator lot combinations, where a unique reagent lot and calibrator lot are paired. The data were analyzed for repeatability (within-run), between-run, between-day, and within-laboratory precision. Within-laboratory precision data summary is shown in **Table 1**.

Table 1: Access Toxo IgG 20-day Within-Laboratory Precision

Sample	N	Mean (IU/mL)	Within-Run (Repeatability)		Between-Run		Between-Day		Between Lot and Instrument[a]		Overall Precision[b]	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Sample 1	240	2.7	0.15	5.3	0.16	5.8	0.10	3.6	0.29	10.8	0.38	13.9
Sample 2	240	8.3	0.36	4.3	0.24	2.9	0.43	5.2	0.61	7.3	0.86	10.4
Sample 3	240	13.1	0.56	4.3	0.54	4.2	0.35	2.7	1.34	10.2	1.59	12.1
Sample 4	240	69.3	3.03	4.4	3.17	4.6	2.17	3.1	6.56	9.5	8.18	11.8
Sample 5	240	174.2	7.29	4.2	6.80	3.9	6.28	3.6	14.01	8.0	18.30	10.5
Sample 6	240	361.0	20.45	5.7	12.55	3.5	20.38	5.6	14.07	3.9	34.48	9.6

[a] Access Toxo IgG reagent lot, Access Toxo IgG calibrator lot and DxI 9000 instruments are confounded, and the confounding effect is represented by between-lot and instrument.

[b] Overall within-laboratory variability includes within-run, between-run, between-day, and between-lot variance components.

b) *Reproducibility (between-Instrument Precision):* An additional precision study was conducted over 5-day by testing six serum samples on 3 DxI 9000 Access Immunoassay Analyzers in an internal site. The samples were tested with 3 lots of Access Toxo IgG reagents, and 1 lot of Access Toxo IgG calibrator on each instrument with 5 replicates per run and 1 run per day over 5 days. Between-instrument reproducibility data is shown in **Table 2**.

Table 2: Access Toxo IgG Assay Reproducibility (Between-Instrument Precision)

Sample	N	Mean (IU/mL)	Within-Run (Repeatability)		Between-Day/Runs[a]		Between Reagent Lot		Between-Instruments		Reproducibility[b]	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Sample 1	225	2.5	0.16	6.4	0.17	7.0	0.11	4.5	0.14	5.6	0.29	11.9
Sample 2	225	7.9	0.40	5.0	0.42	5.3	0.25	3.1	0.35	4.5	0.72	9.1
Sample 3	225	12.4	0.57	4.6	0.51	4.1	0.58	4.7	0.55	4.4	1.11	8.9
Sample 4	225	67.4	3.17	4.7	2.96	4.4	3.66	5.4	2.90	4.3	6.37	9.4
Sample 5	225	169.7	7.83	4.6	9.04	5.3	9.64	5.7	6.24	3.7	16.58	9.8
Sample 6	225	377.5	25.58	6.8	30.77	8.2	22.70	6.0	21.45	5.7	50.76	13.4

[a] Days and runs are confounded.

[b] Reproducibility includes within-run, between-run, between-day, and between-lot variance components.

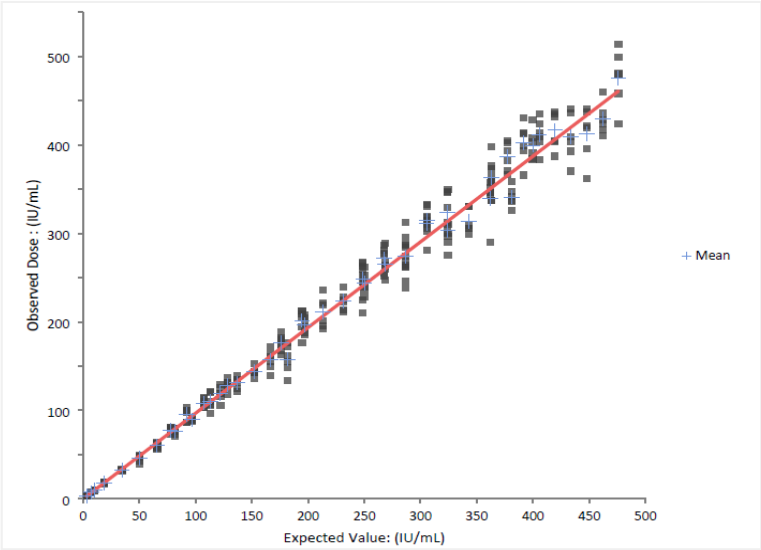
c) *Reproducibility (between-site precision):* Refer to K080869.

2. Linearity:

Linearity of the Access Toxo IgG on the DxI 9000 Access Immunoassay Analyzer was evaluated following CLSI Guideline EP06, 2nd Edition "*Evaluation of Linearity of Quantitative Measurement Procedures"*. A tiled approach was used to evaluate the linearity of five segments of the measuring range. Five sample panels were generated by diluting unique pairs of high and low Toxo IgG antibody positive serum samples in various ratios. Each panel consisted of 7 – 9 dilutions in addition to high and low concentration samples. The table below indicates the number of dilutions and concentration ranges covered by each sample panel.

Panel	Concentration Range (IU/mL)	Number of Samples per Panel
1	3.08 – 128.59	11
2	77.44 – 196.66	9
3	176.17 – 323.84	9
4	248.91 – 399.72	9
5	363.24 – 475.99	9

This study was run on one DxI 9000 Access Immunoassay Analyzer, using one reagent lot and one calibrator lot. Low sample was run in replicates of eight, and all other samples were run in replicates of six. Two quality controls were run in replicates of two. The linearity of the Access Toxo IgG assay was considered acceptable if the data set was determined to be linear and if the deviation from linearity within or equal to ± 10% for samples with concentrations ≥ 3.2 IU/mL. This assay is linear across the analytical measuring interval of 3.2 to 450.0 IU/mL.



Regression equation: y = 0.9685x - 0.02095

3. Analytical Specificity: Interference and Cross-Reactivity:

Refer to K080869.

4. Assay Reportable Range:

3.2 IU/mL – 450.0 IU/mL. See linearity above.

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

Refer to K080869. The Access Toxo IgG Calibrators are referenced to the Third International Standard Preparation for Anti-Toxoplasma Serum (NIBSC code: TOXM).

6. Detection Limit:

The Limit of Blank (LoB), Limit of Detection (LoD) and Lower Limit of Quantitation (LLoQ) for the Access Toxo IgG assay on DxI 9000 Access Immunoassay Analyzer were established following CLSI guideline EP17-A2 (Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition). In order to obtain at least 60 replicates of each sample level, the LoB was established with 5 zero-analyte samples tested in replicates of 5 over 3 days; the LoD with 6 low-analyte samples tested in replicates of 9 over 5 days; and the LLoQ with 11 low-analyte samples tested in replicates of 9 over 5 days. Detection Limit for the Access Toxo IgG assay on the Dxl 9000 Access Immunoassay Analyzer are:

LoB = 0.8 IU/mL.
LoD = 1.5 IU/mL.
LLoQ = 3.2 IU/mL.

7. Assay Cut-Off:

Refer to K080869.

8. Carry-Over:

Not applicable.

B. Comparison Studies:

a. Comparison of Access Toxo IgG assay on the Access 2 Immunoassay Analyzer to the DxI 9000 Access Immunoassay Analyzer:

A method comparison study was conducted to compare the performance of the Access Toxo IgG Assay on DxI 9000 Access Immunoassay Analyzer to the Access Toxo IgG Assay on the Access 2 Immunoassay System. A total of 140 native serum samples were tested. Positive percent agreement (PPA) and negative percent agreement (NPA) between the DxI 9000 Access Immunoassay Analyzer and the Access 2 Immunoassay system was calculated for the Access Toxo IgG assay and shown in Table 3.

Table 3: Performance Agreement of Access Toxo IgG assay on the Access 2 Immunoassay Analyzer and the DxI 9000 Access Immunoassay Analyzer (n=140)

Access Toxo IgG		**Access 2 Immunoassay Analyzer**			
		Reactive	**Equivocal**	**Non-reactive**	**Total**
DxI 9000 Access Immunoassay Analyzer	Reactive	40	0	0	40
	Equivocal	0	1	0	1
	Non-Reactive	0	0	99	99
	Total	40	1	99	140
	PPA[a]	100.00% (40/40)	95% CI = 91.24% to 100.00%		
	NPA[b]	100.00% (99/99)	95% CI = 96.26% to 100.00%		

[a, b] 95% CI for PPA and NPA were estimated using the Wilson score method.

b. Matrix Comparison:

Not applicable.

C Clinical Studies:

1. Clinical Sensitivity:

   Not applicable.

2. Clinical Specificity:

   Not applicable.

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

   For clinical agreement study, refer to K080869.

D Clinical Cut-Off:

Not applicable.

E Expected Values/Reference Range:

Refer to K080869.

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.