510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K221114

B Applicant

Beckman Coulter Laboratory Systems (Suzhou) Co., Ltd.

C Proprietary and Established Names

Immunoglobulin G (IgG)

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
CFN	Class II	21 CFR 866.5510 - Immunoglobulins A, G, M, D, And E Immunological Test System	IM - Immunology
JJE	Class I	21 CFR 862.2160 - Discrete Photometric Chemistry Analyzer For Clinical Use	CH - Chemistry

II Submission/Device Overview:

A Purpose for Submission:

Addition of the DxC 500 AU analyzer for the previously cleared device

B Measurand:

Immunoglobulin G (IgG)

C Type of Test:

Quantitative immunoturbidimetric assay

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

System reagent for the quantitative determination of IgG immunoglobulins in human serum, plasma and cerebrospinal fluid on Beckman Coulter AU/DxC AU analyzers. The measurement of IgG aids in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

Beckman Coulter AU/DxC AU analyzers: AU480, AU680, AU5800, DxC 700 AU (K162208), and DxC 500 AU (K220977)

IV Device/System Characteristics:

A Device Description:

The device consists of two reagents: R1 buffer (Tris buffer pH 7.2, polyethylene glycol 6000) and R2 (goat anti-IgG antiserum). The reagents contain sodium azide as preservative.

Reagent (for Serum/Plasma Application)

- Tris buffer pH 7.2 — 48 mmol/L
- Polyethylene glycol 6000 — 3.1%
- Goat anti-IgG antiserum — Dependent on titer

Reagent (for Cerebrospinal Fluid Application)

- Tris buffer pH 7.2 — 63 mmol/L
- Polyethylene glycol 6000 — 4.9%

Goat anti-IgG antiserum — Dependent on titer

Serum Protein Multi-Calibrator is needed but not supplied with reagent kit.

B Principle of Operation:

The IgG assay is a reagent for the quantitative determination of IgG immunoglobulins in human serum, plasma and cerebrospinal fluid (CSF) on Beckman Coulter AU/DxC AU analyzers.

The device consists of two reagents: R1 buffer (Tris buffer pH 7.2, polyethylene glycol 6000) and R2 (goat anti-IgG antiserum). When a sample is mixed with R1 buffer and R2 antiserum solution, human IgG reacts specifically with anti-human IgG antibodies to yield insoluble aggregates. Immune complexes formed in solution scatter light in proportion to their size, shape,

and concentration. Turbidimeters then measure the reduction of incident light due to reflection, absorption, or scatter of the colloidal suspension. The decrease in intensity of light transmitted (i.e., increase in absorbance) through particles suspended in solution is a result of complexes formed by antigen-antibody reactions.

V Substantial Equivalence Information:

A Predicate Device Name(s):

DxC 700 AU Clinical Chemistry Analyzer, IgG Reagent

B Predicate 510(k) Number(s):

K162208

C Comparison with Predicate(s):

Device & Predicate Device(s):	K221114 (Device)	K162208 (Predicate)
Device Trade Name	IgG, DxC 500 AU Clinical Chemistry Analyzer	IgG, DxC 700 AU Clinical Chemistry Analyzer
General Device Characteristic Similarities		
Intended Use/ Indications For Use	System reagent for the quantitative determination of IgG immunoglobulins in human serum, plasma, and cerebrospinal fluid on Beckman Coulter AU/DxC AU analyzers. The measurement of IgG aids in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents.	System reagent for the quantitative determination of IgG immunoglobulins in human serum, plasma, and cerebrospinal fluid on Beckman Coulter AU analyzers. The measurement of IgG aids in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents.
Measurement	Quantitative	Same
Methodology	Immunoturbidimetric	Same
Antibody	Goat anti-IgG	Same
Specimen Type	Serum, EDTA or lithium heparin plasma, and cerebrospinal fluid	Same
Calibrator	Serum Protein Multi-Calibrator	Same
On-board Stability	90 Days	Same
Calibration Stability	Serum/Plasma: 90 days CSF: 2 days	Same
Analytical Measuring Interval	Serum/Plasma: 75–3000 mg/dL CSF: 2–50 mg/dL	Same
Limit of Quantitation (LoQ)	Serum/Plasma: 75 mg/dL CSF: 2 mg/dL	Same

Traceability	Preparation CRM 470	Same
General Device Characteristic Differences		
Instrument Required	Beckman Coulter Analyzer: AU480, AU680, AU5800, DxC 500 AU and DxC 700 AU	Beckman Coulter Analyzer: AU400/400e/480, AU640/640e /680, AU2700/5400/AU5800 and DxC 700 AU

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 the Linearity of Quantitative Measurement Procedures
- CLSI EP07-A3, Interference Testing in Clinical Chemistry – 3rd 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 EP28-A3c, Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline – Third Edition
- CLSI EP25-A, Evaluation of Stability of *In Vitro* Diagnostic Reagents; Approved Guideline

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

The precision of the IgG assay was designed in accordance with the CLSI EP05-A3 guideline and evaluated by testing five human sera and three CSF samples on one DxC 500 AU analyzer using one reagent lot and one calibrator lot. Each sample was tested with two replicates per run, two runs per day for 20 days (N=80). The results are summarized in the table below:

Sample	Mean (mg/dL)	Repeatability (Within-run)		Between-Run		Between-Day		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
Serum (mg/dL)									
1	88.31	1.6	1.8	1.2	1.3	3.8	4.3	4.3	4.9
2	503.99	5.8	1.2	0.0	0.0	2.3	0.5	6.3	1.2
3	835.56	7.2	0.9	2.0	0.2	12.8	1.5	14.8	1.8
4	1797.53	43.1	2.4	0.0	0.0	3.1	0.2	43.2	2.4
5	2576.22	86.9	3.4	38.2	1.5	0.0	0.0	94.9	3.7
CSF (mg/dL)									
1	4.14	0.2	4.7	0.13	3.1	0.03	0.7	0.2	5.6
2	11.20	0.2	2.1	0.2	1.7	0.2	1.7	0.4	3.1
3	36.32	0.6	1.6	0.0	0.0	0.7	2.0	0.9	2.6

The instrument-to-instrument precision of the IgG assay was evaluated by testing three human sera and three CSF samples pools using one reagent lot and one calibrator lot. Each sample was tested in five replicates per run, one run per day for five days on three DxC 500 AU analyzers (N=75). The results are summarized in the table below.

Sample Pool	Mean (mg/dL)	Repeatability (Within-run)		Between-Day		Between-Instrument		Reproducibility	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
Serum (mg/dL)									
1	481.20	3.7	0.8	2.8	0.6	0.0	0.0	4.6	1.0
2	1669.57	24.5	1.5	15.7	0.9	1.3	0.1	29.1	1.7
3	2404.48	66.7	2.8	54.4	2.3	0.0	0.0	86.1	3.6
CSF (mg/dL)									
1	3.53	0.1	1.7	0.1	4.1	0.1	1.5	0.2	4.7
2	11.31	0.1	0.9	0.2	1.7	0.0	0.0	0.2	1.9
3	37.18	0.3	0.9	0.4	1.0	0.0	0.0	0.5	1.4

2. Linearity:

Linearity of the serum IgG assay was evaluated per CLSI EP-06 2nd Edition guideline. A high concentration native IgG sample pool was mixed with gamma-globulin depleted native serum sample pool to create a 11-dilution level test series covering the analytical measuring interval (75–3000 mg/dL). Sample dilutions were assayed in quadruplicate using one lot of IgG reagent on one DxC 500 AU analyzer. Linearity of the CSF IgG assay was also evaluated using the same study design. The linearity of the IgG with serum and CSF application tested on the DxC 500 AU is summarized in the table below:

Sample Type	Dilution Range (mg/dL)	Slope (95% CI)	Intercept (95% CI)	R^2	% Bias
Serum	73.3–3261.9	1.00 (0.97–1.03)	0.00 (-7.43–7.43)	0.998	-5.0% – 7.3%
CSF	1.9–53.0	1.00 (0.99–1.01)	0.03 (-0.12–0.17)	1.000	-8.8% – 1.7%

The results support the linearity of the claimed measuring range of the IgG assay: 75–3000 mg/dL for serum sample, and 2–50 mg/dL for CSF sample.

Prozone/Hook Effect:

The potential for a prozone effect of the IgG assay on the DxC 500 AU was evaluated using three reagent lots and one calibrator lot. Testing 15 inter-dilutions of one high serum pool did not indicate a prozone effect with serum IgG concentrations up to 36,785 mg/dL. Testing 18 inter-dilutions of the high CSF pool did not indicate a prozone effect with CSF IgG concentrations up to 7,419 mg/dL.

Automatic Dilution:

The automatic dilution study was performed to evaluate the accuracy of the analyzer's auto-dilution function to obtain IgG results for samples with analyte concentrations above the

primary measuring range. Three serum sample pools were used for the study ranging from 3831–5347 mg/dL. Each sample was diluted at 1:10 manually as well as automatically by the instrument and measured in 20 replicates. The results are summarized below:

Sample	Manual Dilution			Auto-Dilution			%Bias (Manual vs Auto-Dilution)
	Mean* (mg/dL)	SD	%CV	Mean* (mg/dL)	SD	%CV	
1	3831	40.4	1.1%	3934	118.2	3.0%	-3%
2	4750	24.8	0.5%	4722	130.2	2.8%	1%
3	5186	35.7	0.7%	5347	96.7	1.8%	-3%

* Results account for dilution factor of 10×

3. Analytical Specificity/Interference:

For the IgG assay, the effect of the presence of endogenous interferents in samples was evaluated by testing two serum samples (IgG concentration at 1000 and 2000 mg/dL) and two CSF samples (IgG concentration at 5 and 20 mg/dL) with a range of concentrations of the interferent substances listed below. Each sample was tested at four concentrations of each interferent in duplicate using one reagent lot and one calibrator lot on one DxC 500 AU analyzer. Samples without interferent were used as control for each interferent substance. No interference was observed up to the following concentration of each tested substance:

Substance	Concentration Tested Without Interference	
	Serum	CSF
Unconjugated Bilirubin	40 mg/dL	36 mg/dL
Intralipid	1000 mg/dL	Not tested
Hemolysate	500 mg/dL	500 mg/dL
RF	1200 IU/mL	Not tested

4. Assay Reportable Range:

- Serum IgG: The claimed measuring range is from 75 mg/dL to 3000 mg/dL
- CSF IgG: The claimed measuring range is from 2 mg/dL to 50 mg/dL

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

Traceability:

Refer to K162208

Stability:

Shelf-life: The claimed reagent shelf-life is 24 months. Refer to K073490

On-board stability: Study was performed to support the stability of reagent and calibration when stored on-board the instrument, DxC 500 AU analyzer. Four serum samples (with concentration level at 502.8, 1779.2, 978.4, and 2197.3 mg/dL) and five CSF samples (with concentration level at: 4.15, 6.61, 10.98, 978.4, and 2197.3 mg/dL) were used. The testing was performed using one lot and one calibrator lot on one DxC 500 AU analyzer at testing time points of 0, 34, 66, and 98 days for serum IgG and 0, 97, 98, and 100 days for CSF IgG. The results support the following on-board stability for the IgG reagent stored in the refrigerated compartment of the analyzer and calibration stability when the assay run on the DxC 500 AU analyzer:

Sample Type	On-board IgG Reagent Stability	IgG Calibration Stability
Serum	90 days	90 days
CSF	90 days	2 days

6. Detection Limit:

The detection limit of the IgG assay on the DxC 500 AU analyzer was performed according to CLSI EP17-A2.

The limit of blank (LoB) for the IgG assay was determined by testing four analyte-depleted blank serum samples tested in six replicates per day for three days on the DxC 500 AU using two reagent lots generating a total of 72 datapoints per reagent lot. All measurements yielded values below 5.6 mg/dL for serum and below 0.11 mg/dL for CSF.

The limit of detection (LoD) and limit of quantitation (LoQ) for the IgG assay was determined by testing 10 low-level native samples 10 replicates per day for five days on the DxC 500 AU using two reagent lots generating a total of 500 datapoints per reagent lot for each serum and CSF application. LoD is defined as the lowest concentration of analyte that can be consistently detected and LoQ is the lowest amount of a measurand that can be quantitatively determined with stated precision. The LoD and LoQ for serum sample are: 8.6 mg/dL and 18.5 mg/dL (with precision of 10% CV), respectively. The LoD and LoQ for CSF sample are 0.31 and 0.63 (with precision of 20% CV), respectively.

The results support the claimed the LoQ for the IgG assay as 75 mg/dL for serum application and 2 mg/dL for CSF application when tested on the DxC 500 AU.

7. Assay Cut-Off:

See Reference Range.

8. Carry-over

The carry-over of the instrument DxC 500 AU was evaluated under K220977.

B Comparison Studies:

1. Method Comparison with Predicate Device:

The method comparison of the IgG assay on DxC 500 AU analyzer (candidate device) and on DxC 700 AU analyzer (predicate) was evaluated by testing a total of 147 remnant serum samples collected from a hospital laboratory and 114 commercially sourced CSF samples. Samples covered the analytical measuring intervals, i.e., 75–3000 mg/dL for serum and 2–50 mg/dL for CSF. Each sample was tested in duplicates. Deming regression analysis was performed using only the first replicate result. The results are summarized in the table below:

	IgG (Serum)	**IgG (CSF)**
N	147	114
Sample Range (DxC 700 AU)	80.15–2877.06 mg/dL	2.03–47.87 mg/dL
Sample Range (DxC 500 AU)	82.78–2880.36 mg/dL	2.50–48.36 mg/dL
Slope (95% CI)	1.015 (1.005–1.025)	0.998 (0.992–1.004)
Intercept (95% CI)	-25.422 (39.761–11.084)	0.114 (0.0232–0.2050)
R	0.9981	0.9995

2. Matrix Comparison:

Refer to K162208

C Clinical Studies:

1. Clinical Sensitivity/ Specificity:

Not applicable

2. Other Clinical Supportive Data:

Not applicable

D Clinical Cut-Off:

Not applicable

E Expected Values/Reference Range:

The reference range was verified to be the same as in the predicate device (refer to K162208) as shown below:

Application	**Reference Range (mg/dL)**
Serum (Adult)	635 – 1741 mg/dL
CSF	15–20 years: 3.5 mg/dL ± 2.0 mg/dL 21–40 years: 4.2 mg/dL ± 1.4 mg/dL 41–60 years: 4.7 mg/dL ± 1.0 mg/dL

The device's labeling includes the following statement: "Expected values may vary with age, sex, diet, and geographical location. Each laboratory should determine its own expected values as dictated by good laboratory practice."

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.