510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE

A. 510(k) Number:

k112412

B. Purpose for Submission:

New Clinical Chemistry Analyzer

The sponsor selected three representative analytes (Glucose, Magnesium and Potassium) to show that these previously cleared reagents have the same performance characteristics on the new AU5800 analyzer as compared to the previously marketed AU series of chemistry analyzers.

C. Measurand:

Glucose, Magnesium, Potassium

D. Type of Test:

Quantitative, photometric and ion selective electrodes

E. Applicant:

Beckman Coulter, Inc.

F. Proprietary and Established Names:

AU5800 Clinical Chemistry Analyzer

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
CEM	Class II	21 CFR 862.1600 Potassium test system	Clinical Chemistry (75)
CFR	Class II	21 CFR 862.1345 Glucose test system	Clinical Chemistry (75)
JGJ	Class I, reserved	21 CFR 862.1495 Magnesium test system	Clinical Chemistry (75)
JJE	Class I	21 CFR 862.2160 Discrete photometric	Clinical Chemistry (75)

		chemistry analyzer for clinical use	

H. Intended Use:

1. Intended use(s):

   Refer to indications for use below.

2. Indication(s) for use:

   The Beckman Coulter AU5800 Clinical Chemistry Analyzer is an automated chemistry analyzer that measures analytes such as Glucose, Magnesium, and Potassium in samples, in combination with appropriate reagents, calibrators, quality control (QC) material and other accessories. This system is for in vitro diagnostic use only. Applications include colorimetric, turbidimetric, latex agglutination, homogeneous enzyme immunoassay, and ion selective electrode.

   The Glucose test system is for the quantitative measurement of glucose in human serum, plasma, urine and cerebrospinal fluid on Beckman Coulter AU analyzers. Glucose measurements are used in the diagnosis and treatment of carbohydrate metabolism disorders including diabetes mellitus, neonatal hypoglycemia, and idiopathic hypoglycemia, and of pancreatic islet cell carcinoma.

   The Potassium test system is for the quantitative measurement of potassium in serum, plasma, and urine. Measurements obtained by this device are used to monitor electrolyte balance in the diagnosis and treatment of diseases conditions characterized by low or high blood potassium levels.

   The Magnesium test system is for the quantitative measurement of Magnesium in human serum, plasma and urine on Beckman Coulter AU analyzers. Magnesium measurements are used in the diagnosis and treatment of hypomagnesemia (abnormally low plasma levels of magnesium) and hypermagnesemia (abnormally high plasma levels of magnesium).

3. Special conditions for use statement(s):

   For *in vitro* diagnostic use only.

   For prescription use.

4. Special instrument requirements:

   AU5800 Clinical Chemistry Analyzer

I. Device Description:

The Beckman Coulter AU5800 Clinical Chemistry Analyzer carries out automated analysis of serum, plasma, urine samples and other body fluids and automatically generates results. The device is an automated chemistry analyzer that measures analytes in samples, in combination with appropriate reagents, calibrators, quality control (QC) material and other accessories. This system is for in vitro diagnostic use only. Applications include colorimetric, turbidimetric, latex agglutination, homogeneous enzyme immunoassay, and ion selective electrode. Electrolyte measurement is performed using a single or double cell Ion Selective Electrode (ISE) which is also common among the other members of the AU family.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Beckman Coulter, AU2700 Clinical Chemistry System

2. Predicate 510(k) number(s):

   k003721

3. Comparison with predicate:

Feature	Proposed Device: AU5800 Clinical Chemistry Analyzer	Predicate Device: AU2700 Clinical Chemistry System
Intended Use:	The Beckman Coulter AU5800 Clinical Chemistry Analyzer is an automated chemistry analyzer that measures analytes in samples, in combination with appropriate reagents, calibrators, quality control (QC) material and other accessories. This system is for in vitro diagnostic use only. Applications include colorimetric, turbidimetric, latex agglutination, homogeneous enzyme immunoassay, and ion selective electrode.	Same
Sample Types:	Blood serum, urine, CSF, or Plasma	Same
Assay Type:	End Point, Kinetic, Ions Selective Electrode (ISE) Optional. Applications: Colorimetric, Turbidimetric, Latex Agglutination, Homogenous EIA.	Same
Reactant Volume:	80µl to 287µl	120µl to 430µl
Sample Volume	1.0 to 17.0 uL	1.6uL to 25.0 uL
Prevention of Sample Carry Over	Same as AU2700 New function: extra optional DI wash sequence	Deionized Water Wash with Contamination Avoidance Parameters and enhanced washing sequence

Feature	Proposed Device: AU5800 Clinical Chemistry Analyzer	Predicate Device: AU2700 Clinical Chemistry System
Recognition of Sample	Read from the barcode	Same
Reagent On-board chemistries	Reagent 1 – 54 bottle capacity Reagent 2 – 54 bottle capacity	Reagent 1 – 48 bottle capacity Reagent 2 – 48 bottle capacity
Reagent Bottle	Reagent bottles with a capacity of 15mL, 30 mL, 60 mL,120mL, 180mL	Same
Reagent Volume Normal Pipette Diluent Volume	10 to 170 µL (can be set by 1uL) 0,10 to 160 uL (can be set by 1uL) Max (reagent+diluent) less than 170uL	15 to 250 µL (can be set by 1uL) 0,10 to 235 uL (can be set by 1uL) Max (reagent+diluent) less than 250uL
Wave length (nm)	Halogen Lamp 340 to 800 nm 13 wavelengths: 340, 380, 410, 450, 480, 520, 540, 570, 600, 660, 700, 750 and 800 nm	Same
Cuvette	Square, glass cuvette 4 x 5 mm (Inside) Capacity: 500 uL Light Path: 5mm	Square, glass cuvette 6x5 mm (Inside) Capacity: 750 uL Light Path: 6mm
Cycle time of photometry measuring point	28 points in 8.5 minutes (±.5 min)	Same

The AU5800 analyzer utilizes the same cleared reagents as the predicate analyzer. Potassium reagent was cleared in k921718; Magnesium reagent was cleared in k944407; Glucose reagent was cleared in k944406/k924601.

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

1. CLSI EP5-A2. Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline.

2. CLSI EP07-A2. Interference Testing in Clinical Chemistry

3. CLSI EP9-A2. Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline.

4. CLSI EP17-A. Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline.

5. IEC 61010-1. Safety Requirements for Electrical Equipment for Measurement, Control, and Laboratory Use

6. IEC 61326. Electrical equipment for measurement, control and laboratory use-EMC requirement 2005.

L. Test Principle:

Glucose:

Glucose is phosphorylated by hexokinase (HK) in the presence of adenosine triphosphate (ATP) and magnesium ions to produce glucose-6-phosphate (G-6-P) and adenosine diphosphate (ADP). Glucose-6-phosphate dehydrogenase (G6P-DH) specifically oxidizes G-6-P to 6-phosphogluconate with the concurrent reduction of nicotinamide adenine dinucleotide (NAD+) to nicotinamide adenine dinucleotide, reduced (NADH). The change in absorbance at 340/380 nm is proportional to the amount of glucose present in the sample.

Magnesium:

The Magnesium procedure utilizes a direct method in which magnesium forms a colored complex with xylidyl blue in a strongly basic solution, where calcium interference is eliminated by glycoletherdiamine-N,N,N`,N`-tetraacetic acid (GEDTA).3,4,5 The color produced is measured bichromatically at 520/800 nm and is proportional to the magnesium concentration.

Potassium:

The ISE module for K^+ employs crown ether membrane electrodes that are specific for K^+ ion in the sample. An electrical potential is developed according to the Nernst Equation. When compared to the Internal Reference Solution, this electrical potential is translated into voltage and then into the K^+ ion concentration of the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

The purpose of the performance studies was to validate that these previously cleared reagents have the same performance characteristics on the proposed new analyzer (AU5800) as compared to the previously marketed AU family of chemistry analyzers. The sponsor has chosen three representative analytes, Potassium, Magnesium, and Glucose using serum as the representative sample matrix.

a. Precision/Reproducibility:

Validation of precision on AU5800 were carried out using 2 or 3 levels of serum control pools, each sample was measured in duplicate in each run, two runs per day over a period of 20 days. The mean, standard deviation (SD), and coefficients of variation (CV) were determined for each control level and for each assay. The results are summarized in the below tables:

Validation of precision performance for Potassium across several cells on AU5800.

Analyzer Cell	Units*	Mean	Within Run		Total	
			SD	CV %	SD	CV %
Cell 1	mEq/L	6.124	0.038	0.6	0.048	0.8
		3.089	0.026	0.9	0.033	1.1
Cell 2	mEq/L	6.155	0.048	0.8	0.060	1.0
		3.075	0.020	0.7	0.024	0.8

* Meq/L is equivalent to mmol/L for Potassium

Validation of precision performance for Glucose and Magnesium on AU5800.

Measurand	Units	Mean	Within Run		Total	
			SD	CV %	SD	CV %
Glucose	mg/dL	54.5	0.3	0.5	0.5	1.0
		117.2	0.5	0.4	0.6	0.5
		297.7	1.2	0.4	2.1	0.7
Magnesium	mg/dL	2.26	0.02	1.0	0.03	1.4
		2.67	0.03	1.0	0.04	1.6
		7.62	0.12	1.6	0.16	2.1

b. Linearity/assay reportable range:

Linearity studies were carried out following an internal protocol. Samples were prepared by diluting a high serum pool with a low sample pool to obtain 11 concentrations across the measuring range. Linear regression analyses results and claimed reportable ranges are shown below. Results of the study support the sponsor's measuring range claims as established in the predicates (Potassium, k921718; Magnesium, k944407; Glucose, k944406/k924601).

Measurand	Slope	Intercept	Sample Range	Claimed Range
Potassium (cell 1)	1.000	0.007	0.18-10.9 mEq/L	1.0-10.0 mEq/L
Potassium (cell 2)	0.995	0.005	0.13-10.8 mEq/L	
Magnesium	0.986	0.002	0.003-9.2 mg/dL	0.5-8.0 mg/dL
Glucose	1.009	-1.832	7-878 mg/dL	10-800 mg/dL

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

Please refer to k043460.

d. *Detection limit:*

Limits of Blank (LoB), Limits of Detection (LoD), and Limit of Quantitation were evaluated following CLSI EP17-A guideline.

For LoB determination, saline supplemented with 5% Bovine Serum Albumin was measured in triplicate using 2 lots of reagents on 2 analyzers over 5 days (N=60). The LoB is defined as $LoB=Mean_B+1.645\ SD_B$

For LoD/LoQ determination, five low serum samples were prepared using low patient serum samples diluted with the blank (Saline+5% BSA). Each sample is measured in duplicate using 2 lots of reagents on 2 analyzers over 5 days (N=40). The LoD is defined as LoD = LoB + (1.645 * STDEV of Low samples). LoQ is defined as the lowest concentration at which 95% CI of the CV is less or equal to the CAP goal of Total Error.

The results are summarized in the below Table:

Analyte	LoB	LoD	LoQ	CAP TE goal
Magnesium (mg/dL)	0.0	0.1	0.2	25%
Glucose (mg/dL)	0.6	1.3	4.9	12%

See linearity study in section M.1.b of this 510(k) decision summary for ISE methods.

e. *Analytical specificity:*

To validate the analytical specificity of the reagents on AU5800, the sponsor determined the level of interference from the substances normally present in serum. Each of the substances was spiked at different concentrations into pooled patient serum samples with low and high analyte concentrations. The pooled serum samples are altered when necessary to give rise to the desired analyte concentration.

The sponsor defines no significant interference as <10% difference between the spiked and the control samples. The interference substances examined and their concentrations tested are listed in the following table:

Reagent & Application	Measurand Levels	Interferent	Interferent level	Specification
Glucose OSR6x21	73 mg/dL 117 mg/dL	Lipemia*	700 mg/dL	<10%
	83 mg/dL 112 mg/dL	Bilirubin	40 mg/dL	<10%
	74 mg/dL 115 mg/dL	Hemolysis	500 mg/dL	<10%
Magnesium OSR6x89	4.02 mg/dL 6.46 mg/dL	Lipemia*	500 mg/dL	<10%
	4.11 mg/dL 6.53 mg/dL	Bilirubin	36 mg/dL	<10%
	4.08 mg/dL 6.50 mg/dL	Hemolysis	150 mg/dL	<10%
	5.97 mg/dL 3.63 mg/dL	Calcium	30 mg/dL	<10%

* Claim based on Intralipid: a 20% IV fat emulsion used to emulate extremely turbid samples.

For Potassium there are no specific interference claims. The sponsor declares in the labeling that "Separate serum from blood cells as soon as possible. Avoid hemolysis since it can lead to falsely elevated K+ values." "Certain anticoagulants, preservatives, drugs, and organophilic compounds may affect electrolyte determinations. For further information on interfering substances, refer to Young for a compilation of reported interferences with this test. Visually turbid urine specimens should be centrifuged prior to analysis. Grossly lipemic samples may show an inappropriate decrease in, potassium, and results due to volume displacement. Such samples should be ultracentrifuged and the analysis performed on the infranatant (middle clear layer)."

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

Unscreened patient serum samples were used in the method comparison studies. When necessary, samples were spiked or diluted to cover the entire measuring range. For Magnesium, 109 patient samples were studied with 3.7% of the samples altered. For Glucose, 173 patient samples were studied with 18% of the

samples altered. For Potassium, 200 patient samples were studied with 26% of the samples altered.

The summary of method comparison data for Potassium (AU5800 vs. AU680 analyzers), Glucose (AU5800 vs. AU2700), and Magnesium (AU5800 vs. AU2700) are presented in the below table.

Reagent & Sample type	Units	Sample Range	N	R	Slope	Intercept
Potassium	mEq/L*	1.99 to 9.93	199	0.9995	0.990	0.075
Glucose	mg/dL	22.3 to 784.6	173	0.9998	0.993	-1.6
Magnesium	mg/dL	0.5 to 7.2	109	0.9985	1.034	0.0

* Meq/L is equivalent to mmol/L for Potassium

b. Matrix comparison:

Serum is the only matrix tested in this submission.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

The sponsor performed studies to verify the reference ranges (listed below) of the following analytes following CLSI C28-A3 guidelines. 20 serum samples were collected from apparently healthy volunteers and tested. The sponsor's acceptance criteria were that no more than 2 (10%) of the test results should fall outside the ranges referenced. The sponsor's test results passed the acceptance criteria.

Serum K^+, 3.5 - 5.1 mEq/L
Tietz, N.W., editor, Fundamentals of Clinical Chemistry, 3rd Edition, W.B.Saunders 1987.

Serum Glucose, 70 – 105 mg/dL
Bondar, R.J.L. and Mead, D.C., Clin Chem, 20: 586, 1974.

Serum Magnesium, 1.9 - 2.7 mg/dL
Beckman Coulter Inc. data on samples collected from 200 blood donors in North Texas.

Beckman recommend in the labeling that "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."

N. Instrument Name:

Beckman Coulter AU5800 Clinical Chemistry Analyzer

O. System Descriptions:

1. Modes of Operation:

   Fully automated, random access, routine and STAT modes.

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes ____x____ or No _____

3. Specimen Identification:

   Bar code

4. Specimen Sampling and Handling:

   Instruction on sample handling is provided in the reagent labeling.

5. Calibration:

   Calibration stability for each measurand is indicated in the reagent labeling.

6. Quality Control:

   Beckman Coulter recommends that during operation of the AU analyzer, at least two

levels of an appropriate quality control material should be tested a minimum of once a day. In addition, controls should be performed after calibration, with each new lot of reagent, and after specific maintenance or troubleshooting steps described in the appropriate User's Guide. Quality control testing should be performed in accordance with regulatory requirements and each laboratory's standard procedure.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

None

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.