510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

k131546

B. Purpose for Submission:

New Device

C. Measurand:

Carbon Dioxide

D. Type of Test:

Quantitative, enzymatic, photometric method

E. Applicant:

Beckman Coulter, Inc.

F. Proprietary and Established Names:

AU Bicarbonate Reagent

G. Regulatory Information:

1. Regulation section:

   21 CFR § 862.1160

2. Classification:

   Class II

3. Product code:

   KHS

4. Panel:

   Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See indications for use below.

2. Indication(s) for use:

   AU Bicarbonate reagent is intended for the quantitative determination of Bicarbonate in human serum and plasma on Beckman Coulter AU analyzers. Bicarbonate measurements are used in the diagnosis and treatment of numerous potentially serious disorders associated with changes in body acid-base balance. For In Vitro Diagnostic Use

3. Special conditions for use statement(s):

   Prescription use only

4. Special instrument requirements:

   Beckman Coulter AU5800

I. Device Description:

The AU Bicarbonate reagent kit is a liquid, ready to use and consists of four R1 reagent vials in various fill volumes.

Reagent Components	Concentration/Amount
Microbial Malate dehydrogenase (MD)	2000 U/L
Microbial Phosphonenol pyruvate carboxylase (PEPC)	572 U/L
Magnesium	2.8 mmol/L
Phosphoenol pyruvate (PEP)	8.2 mmol/L
Nicotinamide adenine dinucleotide (NADH)	1.6 mmol/L
Sodium azide	< 0.1%

The calibrator used for this test is a lyophilized chemistry calibrator which has been previously cleared in k043460 and is sold separately.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Trace America, Carbon Dioxide - DST

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

k960035

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Intended for the quantitative determination of Bicarbonate in human serum.	Same
Measurement	Same	Quantitative
Assay methodology/operating principle	Same	Enzymatic photometric
Linearity range	2.0 – 45.0 mEq/L	3 – 50 mEq/L
Expected values	Same	23.0 – 29.0 mEq/L

Differences		
Item	Device	Predicate
Instrumentation	Beckman Coulter AU 5800 analyzers	Automated and manual systems
Specimen Type	Serum, Lithium Heparin, and Sodium Heparin Plasma	Serum
Reagent On Board Stability	Opened reagents are stable for seven days when stored in the refrigerated compartment of the analyzer	Not specified

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

CLSI Guideline EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures

CLSI Guideline EP09-A2 IR: Method Comparison and Bias Estimation Using Patient Samples

CLSI Guideline EP07-A2: Interference Testing in Clinical Chemistry

CLSI Guideline EP06-A: Evaluation of the Linearity of Quantitative Measurement Procedures

CLSI Guideline EP05-A2: Evaluation of Precision Performance of Quantitative

Measurement Methods

CLSI Guideline C28-A3c: Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory

L. Test Principle:

The AU Bicarbonate reagent is an enzymatic method utilizing Bicarbonate (HCO3-) and phosphoenolpyruvate (PEP), which are converted to oxaloacetate to malate with the concomitant oxidation of reduced nicotinamide adenine dinucleotide (NADH). This oxidation of NADH results in a decrease in absorbance of the reaction mixture measured bichromatically at 380/410 nm proportional to the Bicarbonate content of the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Precision studies were conducted in-house following the CLSI guidance document EP05-A2. Within-run and total precision were evaluated by testing samples at three levels, (low, mid and high) of a commercially available, multi-analyte standard. Samples were analyzed in duplicate on the Beckman Coulter AU 5800 analyzer for 20 days, 4 runs per day (N=80). Results are summarized below:

Sample	Mean (mEq/L)	Within-Run		Total	
		%CV	SD	%CV	SD
Low	12.3	2.5	0.30	7.5	0.92
Medium	31.0	1.1	0.35	4.0	1.23
High	40.3	0.8	0.34	3.6	1.47

An additional within-run and total precision study were evaluated by testing two levels, (low and mid) of a commercially available, serum based control. Samples were analyzed in triplicate on the Beckman Coulter AU 5800 analyzer for 5 days, 1 run per day (N=15). Results are summarized below.

Sample	Mean (mEq/L)	Within-Run		Total	
		%CV	SD	%CV	SD
Low	11.3	2.3	0.27	4.3	0.49
Medium	28.9	2.3	0.67	2.6	0.75

b. Linearity/assay reportable range:

A commercially available multi-analyte standard was diluted with saline to achieve 11 linearity concentration levels from 0.420 to 49.845 mEq/L and the linearity determined using the Beckman AU 5800analyzer. Each dilution level was tested in quadruplicate.

The mean observed results were plotted against the relative analytical concentration. The linear regression correlation between the expected values and the measured values for the CO_2 is summarized below:

Analyte Tested	Linear Regression	r^2
CO_2 (mEq/L)	y = 1.002x – 0.112	0.99979

The claimed measuring range of the device is 2 - 45 mEq/L.

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

Traceability: The CO_2 assay is traceable to NIST SRM 351

Calibrator materials were previously cleared under k043460

The sponsor recommends the use of a commercially available control for use with this assay.

d. Detection limit:

The Limit of blank (LoB), limit of detection (LoD), and limit of quantitation (LoQ) were determined according to CLSI EP17-A2 using the Beckman AU5800 analyzer. For the LoB and LoD studies, 4 blank samples and 5 low samples were tested in multiple replicates over three days using 2 lots of reagents on one AU5800 analyzer. A total of 60 blank replicated and 60 low sample replicates per reagent lot were generated. LoQ studies were performed using 4 low samples with 3 replicates per sample measured over 3 days using 2 lots of reagents (N=36). LoQ is determined based on inter-assay precision of <20%CV. The results are determined as follows:

Analyte	LoB	LoD	LoQ
CO_2 (mEq/L)	1.20	1.95	1.95

e. Analytical specificity:

Interference studies were performed to determine the effects from potential interferents on the AU5800. The interfering substances were analyzed at two levels of Bicarbonate; 20 mEq/L and 35 mEq/L. High serum pools were spiked with Bicarbonate concentrate and low serum pools were diluted with 0.9% saline. The various concentration of interferent was spiked into two serum pools. All samples were tested in quadruplicate. Ten interferent levels and the control were tested for each interferent. Interference is defined as a result that is different from the control by ±10%. The tested ranges and analyte concentrations are presented in the product labeling.

Interferent	Highest Concentration with No Significant Interference (mg/dL)
Lipid	1000
Hemolysis	500
Unconjugated Bilirubin	40
Conjugated Bilirubin	20
Ascorbic acid	20

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

An in-house method comparison study to the predicate device (Trace CO_2 assay) was performed with 129 serum patient samples (2 spiked and 7 diluted) on the Beckman Coulter AU5800 analyzer. Samples were spiked or diluted to cover the low and high end of the assay range. The results are presented in the table below:

Analyte	N	Regression Equation	r^2	Sample range (mEq/L)
CO_2	129	Y = 0.924x - 1.086	0.9910	4.69 – 41.85

b. Matrix comparison:

Matrix comparison studies were completed following the CLSI guidance document, EP9-A2 IR. Samples were tested on the Beckman AU5800 Analyzer. 41 measurements were made in singlicate for paired serum/lithium heparin plasma and serum/sodium heparin plasma samples drawn from the same individuals. Of these samples, 15% were altered (3 spiked and 3 diluted) allowing for testing across the assay range.

The following charts summarize the matrix comparison studies:

Anti-Coagulant	N	Range (mEq/L)	Deming regression	r
Lithium Heparin	41	6.930 – 44.375	Y = 0.985x – 0.03	0.9951
Sodium Heparin	41	7.145 – 45.120	Y = 1.006x + 0.1788	0.9957

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. Clinical studies are not typically submitted for this device type.

5. Expected values/Reference range:

   The following expected values are provided in the product insert based on the literature[1]. The sponsor stated that each laboratory should determine the expected values as dictated by good laboratory practices.

   CO_2: 23-29 mEq/L

   [1]Tietz Textbook of Clinical Chemistry and Molecular Diagnostic. 5''' Edition, 2012.

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.