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

A. 510(k) Number:

k060295

B. Purpose for Submission:

New device

C. Measurand:

Carbon Dioxide

D. Type of Test:

Quantitative enzymatic assay

E. Applicant:

Abbott Laboratories

F. Proprietary and Established Names:

Carbon Dioxide Reagent

G. Regulatory Information:

1. Regulation section

   21 CFR §862.1160, Bicarbonate/carbon dioxide test

2. Classification:

   Class II

3. Product code:

   KHS

4. Panel:

   75 (Chemistry)

H. Intended Use:

1. Intended use(s):

   See Indications for use.

2. Indication(s) for use:

   Bicarbonate/ carbon dioxide measurements are used in the diagnosis and treatment of numerous potentially serious disorders associated with changes in body acid-base balance.

3. Special conditions for use statement(s):

   For Prescription use only.

4. Special instrument requirements:

   Abbott AEROSET® and Abbott ARCHITECT® c8000®

I. Device Description:

The carbon dioxide reagent is supplied as a liquid, ready-to-use, single reagent kit in three sizes which contain:

10 x 23 mL – estimated tests per kit: 3,000
10 x 50 mL – estimated tests per kit: 7,500
10 x 77 mL – estimated tests per kit: 12,000

Reactive Ingredients	Concentration
Phospho (enol) pyruvate	63 mmol/L
NADH analog	3.0 mmol/L
Phospho (enol) pyruvate Carboxylase (Microbial)	>2,000 U/L
Malate Dehydrogenase (Mammalian)	>20,000 U/L

The calibrators for use with this assay were previously cleared under k981706.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Carbon Dioxide (CO2L) on the Hitachi 717 Analyzer

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

   k032377

3. Comparison with predicate:

Assay Characteristics	**New Device - Carbon Dioxide (k060295)**	**Carbon Dioxide (CO2L) on Hitachi 717 Analyzer (k032377)**
Analyte Measured	Carbon Dioxide	Carbon Dioxide
Intended Use	The Carbon Dioxide assay is used for the quantitation of carbon dioxide (CO_2) in human serum or plasma.	The Carbon Dioxide assay is used for the quantitation of carbon dioxide (CO_2) in human serum or plasma.
Assay Principle	Carbon Dioxide, as bicarbonate (HCO_3^-), and phospho(enol)pyruvate (PEP) are converted to oxalacetate and phosphate in the reaction catalyzed by phosphor(enol)pyruvate Carboxylase (PEPC). Malate dehydrogenase (MDH) catalyzes the reduction of oxalacetate to malate with the concomitant oxidation of reduced nicotinamide adenine dinucleotide (NADH) analog. The resulting decrease in absorbance at 404 nm is proportional to the CO_2 content in the sample.	Carbon Dioxide, as bicarbonate (HCO_3^-), and phospho(enol)pyruvate (PEP) are converted to oxalacetate and phosphate in the reaction catalyzed by phosphor(enol)pyruvate Carboxylase (PEPC). Malate dehydrogenase (MDH) catalyzes the reduction of oxalacetate to malate with the concomitant oxidation of reduced nicotinamide adenine dinucleotide (NADH) analog. The resulting decrease in absorbance at 415 nm is proportional to the CO_2 content in the sample.
Detection of Analyte	Endpoint	2-point rate
Samples	Serum and plasma	Serum and plasma
Assay Range	5 to 50 mEq/L	1.5 to 50 mEq/L
Analysis Medium	Aqueous solution	Aqueous solution
Use of Calibrators	Yes	Yes
Use of Controls	Yes	Yes

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

CLSI (formerly NCCLS) Document EP5-A.
CLSI (formerly NCCLS) Document EP6-A.
CLSI (formerly NCCLS) Document EP 17-A.
CLSI (formerly NCCLS) Document EP9-A2

L. Test Principle:

According to the sponsor the Abbott Carbon Dioxide Reagent is a quantitative enzymatic assay based on the PEP Carboxylase methodology. Carbon Dioxide, as bicarbonate (HCO_3^-), and phospho (enol) pyruvate (PEP) are converted to oxalacetate and phosphate in the reaction catalyzed by phosphor (enol) pyruvate Carboxylase (PEPC). Malate dehydrogenase (MDH) catalyzes the reduction of oxalacetate to malate with the concomitant oxidation of reduced nicotinamide adenine dinucleotide (NADH) analog. The resulting decrease in absorbance at 404 nm is proportional to the CO_2 content in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

To determine the within-run, between-run, between-day, and total precision of the Carbon Dioxide assay on the AEROSET and ARCHITECT *c*8000 Systems, the total precision as well as the precision for each component of variation (between-day, between-run, and within-run) was estimated in accordance with CLSI EP5-A. The sponsor indicated that two control levels (Level 1 and Level 2) at normal and abnormal analyte concentrations were tested. These controls were evaluated over 20 days, two runs per day, and two replicates per run. The sponsor determined that precision was considered acceptable if the total SD is $\leq$ 1 mEq/L or total %CV is $\leq$ 5.5%, whichever is greater. Precision was reported as the total percent CV. The precision results are summarized in the below tables.

AEROSET Precision

Control		**Level 1**	**Level 2**
N		80	80
Mean (mEq/L)		38.04	19.69
Within Run	SD	0.25	0.17
	%CV	0.66	0.88
Between Run	SD	0.68	0.32
	%CV	1.80	1.60
Between Day	SD	0.24	0.30
	%CV	0.63	1.52
Total	SD	0.77	0.47
	%CV	2.01	2.38

ARCHITECT Precision

Control		Level 1	Level 2
N		80	80
Mean (mEq/L)		37.8	19.6
Within Run	SD	0.37	0.25
	%CV	1.0	1.3
Between Run	SD	0.41	0.28
	%CV	1.1	1.4
Between Day	SD	0.54	0.32
	%CV	1.4	1.6
Total	SD	0.78	0.49
	%CV	2.1	2.5

b. Linearity/assay reportable range:

The sponsor indicated that the linear range of analyte concentrations of the Carbon Dioxide assay on the AEROSET and ARCHITECT *c*8000 Systems linearity was evaluated in accordance with a modified protocol based on CLSI EP6-A. Ten (10) samples at various concentrations spanning the desired linear range of the assay were run in four replicates. At least one level was included which exceeded the desired linear range. The percent recovery for each sample was determined by dividing the mean observed result by the predicted value. Results are presented below.

AEROSET Linearity

Level	N	Mean Conc. (mEq/L)	SD	Predicted Results (mEq/L)	Difference (mEq/L)	%Difference
1	4	2.888	0.075	3.007	-0.119	-3.973
2	4	5.430	0.041	5.720	-0.290	-5.068
3	4	8.425	0.131	8.433	-0.008	-0.093
4	4	13.825	0.042	13.859	-0.034	-0.243
5	4	30.113	0.198	30.136	-0.024	-0.079
6	4	36.725	0.199	35.562	1.163	3.270
7	4	46.290	0.494	46.414	-0.124	-0.266
8	4	51.828	0.221	51.840	-0.012	-0.023
9	4	54.580	0.435	54.552	0.028	0.051
10	4	56.685	1.370	57.265	-0.580	-1.013

ARCHITECT Linearity

Level	N	Mean Conc. (mEq/L)	SD	Predicted Results (mEq/L)	Difference (mEq/L)	%Difference
1	4	3.165	0.018	3.240	-0.075	-2.319
2	4	5.753	0.123	5.942	-0.188	-3.165
3	4	8.616	0.164	8.643	-0.027	-0.308
4	4	14.095	0.255	14.045	0.050	0.355
5	4	30.297	0.288	30.263	0.033	0.111
6	4	36.412	0.248	35.666	0.746	2.092
7	4	46.434	0.283	46.471	-0.038	-0.081
8	4	51.369	0.645	51.874	-0.505	-0.973
9	4	54.189	1.122	54.575	-0.386	-0.707
10	4	57.665	0.347	57.276	0.388	0.678

The data generated above indicate the Carbon Dioxide assay is linear from 5 to 50 mEq/L (mmol/L), with recovery within $\pm$ 4.3% or ± 1 mEq/L of the predicted value with 95% confidence.

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

The reagent calibration stability was determined by the recovery method on multiple lots of Carbon Dioxide reagent. Fresh reagent was calibrated with fresh calibrators on Day 0. Control material (normal and abnormal) and a prepared test sample near the linear high were analyzed on Day 0, 2, 7, 14, 15, and 17. The sponsor's acceptance criteria for recovery on each day are the Mean value of the samples $\leq$ 4.3% or $\leq$ 1 mEq/L, whichever is greater, of the Day 0 results. All test points up to and including Day 17 met the target for recovery. The resulting calibration stability claim is 14 days.

The reagent open onboard stability was also determined by the recovery method on multiple lots of Carbon Dioxide reagent. Fresh reagent was calibrated with fresh calibrators on Day 0. Control material (normal and abnormal) and a prepared test sample near the linear high were analyzed on Day 0, 2, 7, 14, 15, and 17 without recalibration. Day 17 testing was repeated after re-calibration with both the onboard and fresh reagent.
All test points up to and including Day 17 met the target for recovery. The resulting open on-board stability claim is 14 days. The sponsor claims a product shelf-life/expiration of 12 months. Protocols and acceptance criteria were reviewed.

d. Detection limit:

The sponsor determined the Limit of Quantitation (LOQ) on the AEROSET and the ACHITECT c8000 Systems. The LOQ is the analytical concentration at which the CV = 20%. An internal verification study by the sponsor produced a CV of 10.5% at a CO_2 concentration of 3.7 mEq/L (3.7 mmol/L).

The Limit of Detection (LOD) testing for Carbon Dioxide was performed using a study design based on CLSI EP17-A. An internal verification study by the sponsor produced an LOD for Carbon Dioxide of 1.5 mEq/L (1.5 mmol/L). The proportions of false positives (α) and false negatives (β) were less than 5% and the limit of blank (LOB) was 1.3 mEq/L (1.3 mmol/L).
The sponsors claim an LOQ of 4 mEq/L and an LOD of 2 mEq/L for the Carbon Dioxide assay.

e. Analytical specificity:

The sponsor conducted studies to evaluate interferences in the Carbon Dioxide assay caused by bilirubin, hemoglobin, and intralipid on the AEROSET and ARCHITECT *c*8000 Systems. Interference effects were assessed at medical decision levels of the analyte. Human serum samples (reference) at two Carbon Dioxide concentrations (Lower Decision Level and Upper Decision Level) were spiked with various levels of interferents.

According to the sponsor, four replicates of each interferent level and four replicates of reference sample were run. The percent recovery was determined by dividing the mean result of replicates for each interferent level by the mean result of the replicates of the reference sample. The sponsor's acceptance criteria were the level of interference was considered acceptable if there was no more than ± 4.3% or ± 1 mEq/L, whichever greater, difference between the interferent result and the reference result.

Testing was performed using the AEROSET System. The tables below summarize the results for serum samples at each level, indicating the highest interferent concentration at which the degree of interference was within ± 4.3% or ± 1 mEq/L.

Interfering Substances – Lower Decision Level

Interfering Substance	Interfering Substance Concentration	Target (mEq/L)	Observed	
			(mEq/L)	(%Target)
Bilirubin	30 mg/dL	20.5	20.4	100
	60 mg/dL	20.5	20.2	99
Hemoglobin	1,000 mg/dL	20.1	19.9	99
	2,000 mg/dL	20.1	19.1	95

Interfering Substance	Interfering Substance Concentration	Target (mEq/L)	Observed	
			(mEq/L)	(%Target)
Intralipid	1,000 mg/dL	20.0	20.0	100
	2,000 mg/dL	20.0	20.3	102

Interfering Substances – Upper Decision Level

Interfering Substance	Interfering Substance Concentration	Target (mEq/L)	Observed	
			(mEq/L)	(%Target)
Bilirubin	30 mg/dL	36.9	37.1	101
	60 mg/dL	36.9	36.9	100
Hemoglobin	1,000 mg/dL	34.9	35.5	102
	2,000 mg/dL	34.9	35.3	101
Intralipid	1,000 mg/dL	36.8	36.4	99
	2,000 mg/dL	36.8	36.2	98

The percent interference was within ± 4.3% difference or ± 1 mEq/L, whichever was greater, for serum samples containing 60 mg/dL bilirubin; 2,000 mg/dL hemoglobin; and 2,000 mg/dL Intralipid, for both Lower and Upper Decision Levels.

f. Assay cut-off:

Not applicable for this type of device.

2. Comparison studies:

a. Method comparison with predicate device:

The sponsor performed comparative studies using the AEROSET® and ARCHITECT® *c*8000® Systems compared to the Roche Carbon Dioxide (CO2L) assay on the Hitachi 717 Analyzer. The AEROSET System showed a correlation coefficient of 0.994, slope of 0.99, and Y-intercept of – 0.20 mEq/L when compared to the Hitachi 717 Analyzer. The ARCHITECT *c*8000 System showed a correlation coefficient of 0.9893, slope of 0.98, and Y-intercept of – 0.75 mEq/L when compared to the Hitachi 717 Analyzer.

The sponsor performed method comparison correlations between the AEROSET System and ARCHITECT *c*8000 System using the Carbon Dioxide assay. The ARCHITECT c8000 System showed a correlation coefficient of 0.995, slope of 0.98 and Y-intercept of –0.55 mEq/L when compared to the AEROSET System.

b. Matrix comparison:

Twenty-six (26) subjects were tested using each of the collection tubes to be evaluated. The serum tube used for the baseline was the only glass tube; all other specimen tubes were plastic. Data were analyzed for statistical differences between different tube types. The sponsor's acceptance criteria were acceptability of each anticoagulant is based on a difference of less than ± 4.3% or ± 1 mEq/L, whichever is greater, between the mean values of all samples / replicates for each tube type in question and the plain glass serum tube.

Testing was performed using the AEROSET System. The table below summarizes the results of the specimen tube study.

Specimen Tube – Data Summary

		Differences (mEq/L)			**% Differences**			**% Recoveries**		
Substance	**N**	**Mean**	**Min**	**Max**	**Mean**	**Min**	**Max**	**Mean**	**Min**	**Max**
Lithium Hep Plasma	26	-0.084	-2.058	0.853	-0.329	-8.824	3.221	99.671	91.176	103.22
Lithium Hep PST	26	-0.417	-2.333	0.453	-1.580	-10.00	1.610	98.420	89.997	101.61
Na Hep Plasma	26	-0.147	-2.863	0.843	-0.598	-12.28	3.026	99.402	87.724	103.03
SST Serum	26	0.076	-1.050	1.115	0.311	-4.503	4.770	100.31	95.497	104.77

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):

4. Clinical cut-off**:**

   Not applicable**.**

5. Expected values/Reference range:

   The sponsor claims reference ranges published in the literature (Burtis CA, Ashwood ER, editors. Tietz Textbook of Clinical Chemistry, 3rd ed. Philadelphia, PA: WB Saunders; 1999:1066):

Serum/Plasma

	Range (mEq/L)
Cord	14 to 22
Newborn	13 to 22
Premature, 1 week	14 to 27
Infant	20 to 28
Child	20 to 28
Adult	22 to 29
> 60 years	23 to 31

For Carbon Dioxide, results expressed in mEq/L are equivalent to mmol/L.

The sponsor recommends that each laboratory determine its own reference range based upon its particular locale and population characteristics.

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.