

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE ONLY TEMPLATE**

A. 510(k) Number:

k042362

B. Purpose for Submission:

Add plasma as an acceptable sample matrix

C. Analyte:

Carbon Dioxide

D. Type of Test:

Quantitative

E. Applicant:

Diagnostic Chemicals Limited

F. Proprietary and Established Names:

Carbon Dioxide-L3K Assay

G. Regulatory Information:

1. Regulation section:

21 CFR §862.1160 Bicarbonate/carbon dioxide test system,
(Enzymatic, Carbon Dioxide)

2. Classification:

Class II

3. Product Code:

KHS

4. Panel:

75 - Chemistry

H. Intended Use:

1. Intended use(s):

See Indications for Use below.

2. Indication(s) for use:

Carbon Dioxide – L3K Assay is indicated for the quantitative determination of carbon dioxide in serum and plasma. For *in vitro* diagnostic use. Elevated blood CO₂ is almost synonymous with respiratory acidosis. The later is restricted to clinical conditions with a primary increase in carbon dioxide in the inspired air or increased metabolic production of carbon dioxide.

Decreased blood CO₂ is almost synonymous with respiratory alkalosis. The later is restricted to clinical conditions with primary decrease in carbon dioxide which can result from increased pulmonary ventilation due to mechanical ventilation or stimulation of the respiratory center.

Classic techniques for the measurement of carbon dioxide (CO₂) involve the addition of acid to liberate the carbon dioxide and the measurement of carbon dioxide thus released by either manometric, volumetric, or titrimetric

techniques. These procedures are both time consuming and cumbersome. The DCL Carbon Dioxide-L3K assay is an enzymatic procedure, employing phosphoenolpyruvate (PEPC) and a stabilized NAD analog, which is easy to use and applicable to routine laboratory instrumentation.

3. Special condition for use statement(s):
For in vitro diagnostic use only
4. Special instrument Requirements:
Any instrument with temperature control of $\pm 0.5^{\circ}\text{C}$ that is capable of reading absorbance with a sensitivity of 0.001 at 405 or 415 nm.

I. Device Description:

Carbon Dioxide reagent is a solution containing buffer (pH 7.6 at 25°C), 12.5 mmol/L PEP, > 400 U/L PEPC (microbial), > 4100 U/L malate dehydrogenase (mammalian), 0.6 mmol/L NADH analog, activators, stabilizers, a surfactant, and a preservative.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Carbon Dioxide-L3K Assay
2. Predicate K number(s):
k990754
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Same	Same
Test Type	Enzymatic	Enzymatic
Reagents	Liquid reagents	Liquid reagents
Differences		
Item	Device	Predicate
Sample type	Serum & Plasma	Serum

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

NCCLS EP6-P – Evaluation of the Linearity of Quantitative Analytical Methods
NCCLS EP9-A – Method Comparison and Bias Estimation Using Patient Samples

L. Test Principle:

Carbon Dioxide – L3K Assay is based on enzymatic reactions. The specimen is first alkalized to convert CO_2 and carbonic acid to HCO_3^- . By catalysis of phosphoenolpyruvate carboxylase (PEPC), the reaction of bicarbonate and phosphoenolpyruvate (PEP) produces oxalacetate and phosphate. Malate dehydrogenase catalyzes the reduction of oxalacetate to malate with the simultaneous oxidation of reduced nicotinamide adenine dinucleotide (NADH) to NAD^+ . Decrease

in absorbance of NADH at 415 nm is proportional to the total CO₂ content in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Within run precision was established by assaying two control sera twenty times each.

Carbon Dioxide	Mean Mmol/L(mEq/L)	Standard Deviation Mmol/L(mEq/L)	Coefficient of Variation %
Serum 1	13.5	0.18	1.3
Serum 2	24.0	0.40	1.7

Run to run precision was established by assaying two control sera in triplicate in each of 5 runs.

Carbon Dioxide	Mean Mmol/L(mEq/L)	Standard Deviation Mmol/L(mEq/L)	Coefficient of Variation %
Serum 1	14.1	0.24	1.7
Serum 2	24.8	0.27	1.1

b. *Linearity/assay reportable range:*

Linearity studies were designed using NCCLS EP6-P, Evaluation of the Linearity of Quantitative Analytical Methods. The linearity of the procedure described is 50 mmol/L (mEq/L). The lower limit of detection of the procedure described is 2.9 mmol/L (mEq/L). These data result in a reportable range of 2.9-50 mmol/L (2.9-50 mEq/L).

c. *Traceability (controls, calibrators, or method):*

No traceability was provided.

A carbon dioxide standard is not included with the reagents, however one should be used as directed to calibrate the procedure.

d. *Detection limit:*

Lower Limit of Detection (LLD) is defined as the concentration that can be differentiated from zero using a predetermined confidence interval. Ten samples of saline were analyzed and results were calculated using $LLD = \text{Mean} + 3 \text{ SD}$ with $LLD = 0.767 \text{ mmol/L}$.

e. *Analytical specificity:*

Interferences from icterus, lipemia, and hemolysis were evaluated for this carbon dioxide method on a Hitachi 717 analyzer using a significance criterion of >10% variance from the control. No significant lipemia interference was found at

Intralipid levels from 0-1000 mg/dL (0-3000 mg/dL triglycerides) in a 24.6 mmol/L (mEq/L) carbon dioxide sample. No significant icteric interference was found at bilirubin levels from 0-40 mg/dL (0-684 mg/dL triglycerides) in a 27.1 mmol/L (mEq/L) carbon dioxide sample.

Hemoglobin levels of 0-155 mmol/L (0-1000 mg/dL) were studied with acceptable results to a level of 93 umol/L (600 mg/dL). At a hemoglobin level of 93 umol/L (600 mg/dL), a 10.3% positive interference was displayed in a 26.3 mmol/L (mEq/L) carbon dioxide sample. A summary of the influence of drugs on clinical tests is referenced within the package insert

f. Assay cut-off:
Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Accuracy was evaluated based on NCCLS Protocol EP9-A2. The performance of this method (y) on a Hitachi was compared with performance of a similar carbon dioxide method (x) on a Cobas Mira. Forty-five serum samples ranging from 15.4-43.7 mmol/L (mEq/L) gave a correlation coefficient of 0.9861. Linear regression analysis gave the following equation:
This method = 1.00 (reference method) – 0.42 mmol/L (mEq/L).

b. Matrix comparison:

Recovery Study for CO₂ in Serum and Plasma:

This study was conducted to provide supporting evidence for the acceptability of using plasma samples with the DCL CO₂ L3K assay. The data presented below demonstrate an equivalent performance when sodium bicarbonate is spiked into serum and plasma samples.

Serum Recovery:

Control Sample -	0.5 mL serum from patient A + 0.025 mL saline
Test Sample I -	0.5 mL serum from patient A + 0.025 mL 100 mmol/L CO ₂ standard
Test Sample II -	0.5 mL serum from patient A + 0.025 mL 300 mmol/L CO ₂ standard

Sample	Concentration Measured (mmol/L)	Concentration Added (mmol/L)	Concentration Recovered (mmol/L)	Recovery (%)
Control	23.7			
Test I	28.3	4.8	4.7	97.9
Test II	37.7	14.3	14.0	97.9
Average Recovery in Serum				97.9%

Plasma Recovery:

Control Sample - 0.5 mL plasma from patient A + 0.025 mL saline
 Test Sample I - 0.5 mL plasma from patient A + 0.025 mL 100mmol/L CO₂ standard
 Test Sample II - 0.5 mL plasma from patient A + 0.025 mL 300 mmol/L CO₂ standard

Sample	Concentration Measured (mmol/L)	Concentration Added (mmol/L)	Concentration Recovered (mmol/L)	Recovery (%)
Control	25.0			
Test I	29.7	4.8	4.7	97.9
Test II	38.7	14.3	13.7	95.8
Average Recovery in Serum				96.9%

The acceptable criteria for the recovery studies was set to Recovery = 95 – 105%. Therefore all recovery data are acceptable and plasma is considered to be equivalent to serum.

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)*
None

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Values of 22-29 mmol/L (mEq/L) are reported in Tietz, NW. (Editor), Textbook of Clinical Chemistry, W.B. Saunders Co., Philadelphia (1986). These values are suggested guidelines. The applicant recommends that each laboratory establish the reference range for the area in which it is located.

N. Conclusion:

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