

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

A. 510(k) Number:

k070251

B. Purpose for Submission:

New device

C. Measurand:

Carbon Dioxide

D. Type of Test:

Quantitative enzymatic assay

E. Applicant:

Pointe Scientific, Inc.

F. Proprietary and Established Names:

Carbon Dioxide Liquid Stable Reagent

G. Regulatory Information:

1. Regulation section:

21 CFR § 862.1160, Bicarbonate/carbon dioxide test system

2. Classification:

Class II

3. Product code:

KHS - enzymatic, carbon-dioxide

4. Panel:

75 (Clinical Chemistry)

H. Intended Use:

1. Intended use(s):

See Indications for use.

2. Indication(s) for use:

This product is to be used for the quantitative determination of carbon dioxide in human serum by spectrophotometric analysis. The determination of the level of carbon dioxide in serum is commonly performed as an indicator of acid-base balance disturbances.

3. Special conditions for use statement(s):

For Prescription use only

4. Special instrument requirements:

Assay performance was demonstrated on the Hitachi 917 chemistry analyzer.

I. Device Description:

The carbon dioxide reagent is supplied as a liquid, ready-to-use, single reagent kit. It contains Phosphoenolpyruvate 8.0 mM, Magnesium Ions (20 mM), NADH analog 0.5 mM, Phosphoenolpyruvate carboxylase (PEPC) (Microbial) >200 U/L, Malate Dehydrogenase (Porcine) >1200 U/L, and Buffer, pH 7.5 ± 0.1 non-reactive stabilizers with surfactants and preservative. The reagent is supplied in three sizes: 120 mL, 500 mL, and 1000 mL volumes.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Carbon Dioxide - L3k Assay (Diagnostic Chemicals Ltd)
2. Predicate 510(k) number(s):
k990754
3. Comparison with predicate:

Characteristics	Carbon Dioxide Liquid Stable Reagent (Proposed Device)	Diagnostic Chemicals Limited (DCL) (Predicate Device)
Intended Use	This product is to be used for the quantitative determination of carbon dioxide in human serum by spectrophotometric analysis. For <i>in vitro</i> diagnostic use only.	For the quantitative determination of carbon dioxide in serum. For IN VITRO diagnostic use.
Reagent	PEP 8.0mM, Magnesium Ions 20mM, NADH analog, MDH (porcine) ≥ 1200U/L, PEPC (microbial) ≥ 200U/L, Buffer, pH 7.5 ± 0.1 non-reactive stabilizers with surfactants and preservative.	PEP 12.5 mmol/L, NADH analog, MDH (mammalian) > 4100 U/L, PEPC (microbial) > 400 U/L, Buffer, pH 7.5 at 25°C, activators, stabilizers, surfactant and a preservative.
Format	Reagent provided as a ready to use liquid.	Reagent is provided in a ready to use format.
Stability	<ul style="list-style-type: none">● Reagent is stable until expiration date indicated on vial label when stored tightly capped at 2-8°C.● Shelf life is 15 months when stored tightly capped at 2-8°C.	Reagent is stable until the expiration date stated on the label at 2-8°C. Specific Shelf life not indicated.
Linearity / Assay range	2.0 – 40.0 mmol/L	2.9 – 50.0 mmol/L
Limit of Detection	2.0 mmol/L	2.9 mmol/L
Interference	No interference was observed by bilirubin up to 20.0 mg/dL, hemoglobin up to 400 mg/dL and	No significant (> 10.0%) lipemic interference found at Intralipid levels from 1-1000

	lipemia (intralipid) up to 1000 mg/dl. (using a criteria of >10% variance from control)	mg/dl (0-3000 mg/dl Triglyceride). No significant (> 10.0%) icteric interference at Bilirubin levels of 0-40 mg/dl. Hemoglobin levels of 600 mg/dl gave a positive bias of 10.3% in a 26.3 mmol/L carbon Dioxide sample.
--	---	--

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

CLSI EP5-A: Evaluation of Precision Performance of Clinical Chemistry Devices

L. Test Principle:

Carbon Dioxide Reagent is a quantitative enzymatic assay based on the PEP Carboxylase methodology. Carbon Dioxide (in the form of bicarbonate ions) reacts with phosphoenolpyruvate (PEP), in the presence of phosphoenolpyruvate carboxylase (PEPC) to form oxaloacetate. Malate dehydrogenase (MDH) catalyzes the reduction of oxalacetate to malate with the concomitant oxidation of reduced nicotinamide adenine dinucleotide (NADH) analog. Spectrophotometric determination of the decrease in absorbance monitored between 405 and 415 nm is proportional to the amount of CO₂ in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

The precision was evaluated using Pointe Scientific chemistry controls containing low and normal levels of CO₂ on the Hitachi 917 chemistry analyzer. Within-day precision was evaluated by running the two specimens in replicates of 20 on the same day. Day-to-day precision was evaluated by performing one run per day in duplicate over 20 days using the same control material. The results are tabulated below.

Within-day Precision

Description	Control 1	Control 2
Number of data points	40	40
Mean (mmol/L)	16.5	27.4
SD (mmol/L)	0.5	0.6
CV	3.1%	2.2%

Day-to-day Precision

Description	Control 1	Control 2
Number of data points	40	40
Mean (mmol/L)	18.2	27.1
SD (mmol/L)	0.5	0.9
CV	2.9%	3.1%

b. Linearity/assay reportable range:

To determine the linearity range, the sponsor prepared eleven CO₂ test samples through serial dilution of a 100 mmol/L CO₂ standard. The samples ranged in concentration from 0.67 to 95.3 mmol/L. All eleven CO₂ levels were run in triplicate on the Hitachi 917 analyzer. The reagent showed the assay is linear up to 47.7 mmol/L. Up to this level, the linear regression analysis demonstrated a linear regression equation, $Y=0.999X-0.3$. The assay range claimed by the sponsor is 2.0 to 40 mmol/L.

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

No information was provided for traceability. The device does not include calibrators and controls. The sponsor recommends using an aqueous CO₂ standard (30 mmol/L) or an appropriate serum calibrator. To monitor the reliability of results, the sponsor also recommends two levels of control sera with known CO₂ values to be run along with patient samples.

Accelerated stability of the CO₂ reagent was determined based on Arrhenius equations from J. Pharmaceutical Sciences, 53:7, 8158-8180, 1964.

Accelerated stability of reagent for 12, 18, and 24 month duration was tested using New England Reagent Laboratory (NERL) standards (0, 10, 20, 30, and 40 mmol/L) and two Pointe Scientific controls (14-26 mmol/L and 22-42 mmol/L). Based on this study, accelerated stability of the CO₂ reagent was demonstrated to be at least 18 months. The sponsor has established a 15-month shelf life for the CO₂ reagent when tightly capped and stored at 2-8°C.

d. Detection limit:

To demonstrate the limit of detection, a known NERL standard of CO₂ (10 mmol/L) and a blank sample (0 mmol/L) were tested in five replicates. The sponsor defined the limit of zero-concentration (blank) sample as $\pm 2SD$, which was demonstrated to be 0.5 mmol/L. Based on these results, the sponsor claimed LOD of 2.0 mmol/L.

e. Analytical specificity:

The sponsor evaluated the effect of bilirubin (0-20 mg/dL), hemoglobin (0-500 mg/dL), and lipemia (intralipid) (0-1000 mg/dL) on a sample at CO₂ concentration of 19 mmol/L. Based on the sponsor-defined interference limit of $\pm 10\%$ of control, results indicated that there was no interference up to the concentrations tested above for any of the substances.

f. Assay cut-off:
Not Applicable.

2. Comparison studies:

a. Method comparison with predicate device:

Performance of the Carbon Dioxide Liquid Stable Reagent was compared with performance of the predicate device, Carbon Dioxide - L3k Assay (Diagnostic Chemicals Ltd) (k990754). The study was performed on Hitachi 917 chemistry analyzer using 136 samples ranging from 14 to 40 mmol/L of CO₂. Comparison of the data based on 2 methods gave a correlation coefficient of 0.986. Linear regression analysis resulted in the equation, $y = 0.965x + 1.2$.

b. Matrix comparison:

Carbon Dioxide Liquid Stable Reagent is to be used with serum only.

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 expected values for CO₂ were based on published literature, Henry, R.J., Clinical Chemistry: Principles and Technics, Harper & Row, Publishers, New York, N.Y., 1974. They are stated as 23-34 mmol/L . In the labeling, the sponsor recommends that each laboratory determine its own reference range.

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.