Symbols

CE
This product fulfills the requirements of the European Directive for *In Vitro* Diagnostic Medical Devices.

Manufacturer

Use by date
YYYY-MM-DD or YYYY-MM

Temperature limit

Health hazard

IVD
In vitro diagnostic medical device

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LOT
Batch Code

Consult instructions for use

REF
Catalog number

EC REP
Authorized representative
In the European Community

℞ ONLY
For use by or on the order of a physician only
(applicable to USA classification only)

SEKISUI DIAGNOSTICS

sekisuidiagnostics.com

SEKURE® CHEMISTRY

CARBON DIOXIDE L3K®-C ASSAY

CATALOGUE NUMBER: 288-36 **SIZE**: 3 x 60 mL
288-80 1 x 1000 mL

Note: Changes are highlighted.

INTENDED USE

For the *in vitro* quantitative measurement of carbon dioxide in human serum and plasma.

TEST SUMMARY

Diagnostic determination of serum or plasma carbon dioxide (CO_2) is used in conjunction with other clinical and laboratory testing for the evaluation of acid-based balance. Blood pH is buffered by the presence of the weak carbonic acid (H_2CO_3) and conjugate base bicarbonate (HCO_3^-). As CO_2 concentration in blood increases, so does hydrogen ion (H^+) concentration. Respiration rate, which is controlled by CO_2 concentration in the blood, compensates by increasing or decreasing in an attempt to maintain equilibrium by promoting CO_2 elimination or retention respectively.

$$CO_2 + H_2O \rightleftarrows H_2CO_3 \rightleftarrows HCO_3^- + H^+$$

High CO_2 content is often indicative of respiratory acidosis or metabolic alkalosis. Low CO_2 content is often indicative of respiratory alkalosis or metabolic acidosis. Further laboratory testing is necessary to differentiate between metabolic and respiratory conditions.[1]

Classic techniques for the measurement of carbon dioxide (CO_2) 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 SEKISUI Diagnostics' Carbon Dioxide L3K®-C assay is an enzymatic procedure, employing phosphoenolpyruvate carboxylase (PEPC)[2] and a stabilized NADH analog,[3] which is easy to use and applicable to routine laboratory instrumentation.

TEST PRINCIPLE

$$\text{Phosphoenolpyruvate} + HCO_3^- \xrightarrow[\text{MDH}]{\text{PEPC} + Mg^{++}} \text{oxaloacetate} + H_2PO_4^-$$

$$\text{Oxaloacetate} + \text{reduced cofactor} + H^+ \longrightarrow \text{malate} + \text{cofactor}$$

PEPC catalyses the first reaction which produces oxaloacetate. In the presence of MDH, the reduced cofactor is oxidized by oxaloacetate. The decrease in concentration of the reduced cofactor is monitored between 405 and 415 nm and is proportional to the total carbon dioxide concentration in the sample.
PEPC is specific for the bicarbonate ion (HCO_3^-) and its action disturbs the following equilibrium which results in conversion of the CO_2 to HCO_3^-.

$$CO_2 + H_2O \rightleftarrows H_2CO_3 \rightleftarrows H^+ + HCO_3^-$$

REAGENTS

Carbon Dioxide Reagent: A solution containing buffer (pH 7.5 at 25°C), 63 mmol/L PEP, > 2000 U/L PEPC (microbial), >20 KU/L malate dehydrogenase (mammalian), 3.0 mmol/L NADH analog, activators, stabilizers, a surfactant, and a preservative.

WARNINGS & PRECAUTIONS FOR USE

IVD
For *in vitro* diagnostic use

℞ ONLY

Carbon Dioxide L3K®-C Reagent

Warning
Contains: ethanediol, ethylene glycol (CAS No) 107-21-1
Hazard statements
H373 - May cause damage to organs through prolonged or repeated exposure

Precautionary statements
P260 - Do not breathe dust/fume/gas/mist/vapors/spray. P314 - Get medical advice/attention if you feel unwell. P501 - Dispose of contents/container to hazardous or special waste collection point, in accordance with local, regional, national and/or international regulation.

May cause damage to organs (kidney) through prolonged or repeated exposure.

Obtain special instructions before use. Do not handle until all safety precautions have been read and understood. Wear protective gloves/protective clothing/eye protection/ face protection.

Avoid contact with skin and eyes. See Safety Data Sheet for additional information.

REAGENT PREPARATION, STORAGE AND STABILITY

Reagents are ready for use. Supplied reagent stable at 2-8°C until expiry date. Stability claims are based on real time studies.

REAGENT DETERIORATION

The reagent solution should be clear. Turbidity would indicate deterioration.

DISPOSAL

Reagents must be disposed of in accordance with all Federal, Provincial, State, and local regulations.

SPECIMEN

Freshly drawn serum or plasma are the specimens of choice. Serum or plasma should be separated from cells immediately and stored at 2-8°C. Exposure of samples to air should be minimized. Samples should be stored tightly sealed to prevent loss of carbon dioxide and assayed as soon as possible after collection. For plasma samples, the anticoagulant, lithium heparin, has been tested and may be used with this assay. [5]

SAMPLE STORAGE

Samples should be stored at 2-8°C.[7]

ANALYTICAL SPECIFICITY (CLSI EP7)[6]

Cross contamination studies have not been performed on automated instruments. Certain reagent / instrument combinations used in sequence with this assay may interfere with reagent performance and test results. The existence of, or effects of, any potential cross contamination issues are unknown.

Interferences from icterus, lipemia, hemolysis, and ascorbic acid were evaluated for this carbon dioxide method on a Hitachi® 717 analyzer using a significance criterion of >10% variance from control. Data for plasma is similar to that present for serum.

Concentration of Analyte		Substance Tested	Concentration of Interferent Where Interference is Insignificant	
Conventional Units	S1 Units			
30.8 mmol/L	30.8 mEq/L	Hemoglobin	1000 mg/dL	155 µmol/L
32.8 mmol/L	32.8 mEq/L	Ascorbic Acid	3000 µg/dL	170 µmol/L
32.9 mmol/L	32.9 mEq/L	Bilirubin	40 mg/dL	684 µmol/L
30.4 mmol/L	30.4 mEq/L	Intralipid	1000 mg/dL	3000 mg/dL (33.9 mmol/L) Simulated Triglycerides

Samples containing elevated levels of Immunoglobulin M (IgM) or samples from patients with Waldenstrom's Macroglobulinemia may produce unreliable results.

The information presented above is based on results from SEKISUI Diagnostics studies and is current at the date of publication.
A summary of the influence of drugs on clinical laboratory tests may be found by consulting Young, D.S.[4]

ANALYTICAL PROCEDURE

MATERIALS PROVIDED

SEKISUI Diagnostics' Carbon Dioxide L3K®-C Reagent.

MATERIALS REQUIRED (BUT NOT PROVIDED)

1) Automated analyzer capable of adding a system diluent and capable of accurately measuring absorbance at appropriate wavelengths as per instrument application.
2) Calibration material.
3) Quality Control materials.

TEST CONDITION

For the data presented in this insert, studies using this reagent were performed on an automated analyzer using an endpoint test mode, with a sample to reagent ratio of 1:100, and a wavelength reading of 405 nm or 415 nm. For assistance with applications on automated analyzers within Canada and the U.S., please contact SEKISUI Diagnostics Technical Services at (800)565-0265. Outside Canada and the U.S., please contact your local distributor.

CALIBRATION

Calibration material should be used to calibrate the procedure. The frequency of calibration using an automated system is dependent on the system and the parameters used.

QUALITY CONTROL

A normal and abnormal concentration control should be analyzed as required in accordance with local, state and federal guidelines. The results should fall within the acceptable range as established by the laboratory.

CALCULATIONS

The analyzer automatically calculates the carbon dioxide concentration of each sample.

TEST LIMITATIONS

A sample with a carbon dioxide concentration exceeding the linearity limit should be diluted with 0.9% saline and reassayed incorporating the dilution factor in the calculation of the value.

REFERENCE INTERVALS

22-29 mmol/L (22-29 mEq/L)[5]

These values are suggested guidelines. It is recommended that each laboratory establish its own expected range.

PERFORMANCE CHARACTERISTICS

Data presented was collected on Hitachi® 717 analyzer unless otherwise stated.

RESULTS

Carbon Dioxide concentration is reported as mmol/L (mEq/L).

REPORTABLE RANGE (CLSI EP6)[6]

The linearity of the procedure described is 50.0 mmol/L (mEq/L). The lower limit of detection of the procedure described is 1.0 mmol/L (mEq/L). This data results in a reportable range of 1.0-50.0 mmol/L (1.0-50.0 mEq/L).

PRECISION STUDIES (CLSI EP5)[6]

Precision estimates for serum were obtained using two concentrations of control sera. Plasma based precision materials were prepared in-house and spiked to appropriate levels.

Total precision was collected on two concentrations of control samples in 40 runs conducted over 20 days.

Carbon Dioxide	Concentration mmol/L (mEq/L)	Total SD	Total CV%
Serum 1	13.3	0.6	4.4
Serum 2	24.9	1.2	4.6

Within run precision data was collected on two concentrations of control samples, each run 20 times in a single assay.

Carbon Dioxide	Concentration mmol/L (mEq/L)	Within Run SD	Within Run CV%
Serum 1	13.3	0.2	1.2
Serum 2	24.9	0.3	1.3
Plasma 1	14.1	0.2	1.3
Plasma 2	22.5	0.4	1.9

ACCURACY (CLSI EP9)[6]

The performance of this method (y) was compared with the performance of another carbon dioxide method (x) on a Hitachi® 717 analyzer.

Forty-five serum samples ranging from 9.4 to 48.3 mmol/L (mEq/L) were tested and gave a correlation coefficient of 0.9944. Linear regression analysis gave the following equation:

This method = 1.014(reference method) + 0.50 mmol/L (mEq/L).

Fifty plasma samples ranging from 9.6 to 46.8 mmol/L (mEq/L) gave correlation coefficient of 0.9907. Linear regression analysis gave the following equation:

This method = 0.973(reference method) + 0.89 mmol/L (mEq/L).

REFERENCES

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5. Burtis, C.A., Ashwood, E.R.T. (Editors), *Tietz Textbook of Clinical Chemistry*, 3rd Edition, W.B. Saunders Company, Philadelphia (1999).
6. *CLSI Guidelines and Standards*, Clinical and Laboratory Standards Institute, Wayne, PA.
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