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

A. 510(k) Number:

k170200

B. Purpose for Submission:

New device

C. Measurand:

Carbon dioxide

D. Type of Test:

Quantitative enzymatic assay

E. Applicant:

Teco Diagnostics, Inc.

F. Proprietary and Established Names:

Carbon Dioxide Reagent Set

G. Regulatory Information:

1. Regulation section:

   21 CFR § 862.1160, Bicarbonate/carbon dioxide test system

2. Classification:

   Class II

3. Product code:

   KHS

4. Panel:

   Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See Indications for Use below.

2. Indication(s) for use:

   Teco Carbon Dioxide Reagent Set intended for the quantitative determination of carbon dioxide level in human serum, in vitro use only. Test results may provide information regarding the status in the assessment of acid-base balance of metabolic alkalosis or respiratory acidosis.

3. Special conditions for use statement(s):

   For Prescription use only

4. Special instrument requirements:

   Assay performance was demonstrated on the TC-Matrix Clinical Chemistry Analyzer

I. Device Description:

Teco Carbon Dioxide Reagent Set is supplied as a liquid, ready-to-use, single reagent kit. It contains phosphoenolpyruvate 8.0 mM, magnesium ions (20 mM), NADH analog 0.6 mM, phosphoenolpyruvate carboxylase (PEPC) >200 U/L, malate dehydrogenase >1200 U/L, buffer, pH 7.5 ± 0.1 and non-reactive stabilizers with surfactants and preservative.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Carbon Dioxide Liquid Stable Reagent

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

   k070251

3. Comparison with predicate:

Similarities		
Item	Candidate Device: Carbon Dioxide Reagent Set (k170200)	Predicate Device: Carbon Dioxide Liquid Stable Reagent (k070251)
Intended Use	For the quantitative determination of carbon dioxide in human serum.	Same

Similarities		
Item	Candidate Device: Carbon Dioxide Reagent Set (k170200)	Predicate Device: Carbon Dioxide Liquid Stable Reagent (k070251)
Sample type	Serum	Same
Test Methodology	Enzymatic; malate dehydrogenase and phosphoenolpyruvate carboxylase	Same
Instrument Mode	Automatic Instrument	Same
Detection Wavelength	405 nm	Same
Storage temperature	2 - 8ºC	Same

Differences		
Item	Candidate Device: Carbon Dioxide Reagent Set (k170200)	Predicate Device: Carbon Dioxide Liquid Stable Reagent (k070251)
Reportable Range	8.7 to 40.0 mmol/L	2.0 to 40.0 mmol/L
Detection Limit (LoQ)	1.77 mmol/L	2.0 mmol/L

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

CLSI EP5-A3 *Evaluation of Precision of Quantitative Measurement Procedures*
CLSI EP6-A: *Evaluation of the Linearity of Quantitative Measurements Procedures*
CLSI EP7-A2: *Interference Testing in Clinical Chemistry*
CLSI EP9-A3 *Measurement Procedure Comparison and Bias Estimation Using Patient Samples*
CLSI EP17-A2: *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures*
CLSI EP25-A: *Evaluation of Stability of In Vitro Diagnostic Reagents*

L. Test Principle:

The carbon dioxide in the sample reacts with phosphoenolpyruvate (PEP) in the presence of phosphoenolpyruvate carboxylase (PEPC) and magnesium to yield oxaloacetic acid (OAA) and phosphate. In the second reaction, in the presence of malate dehydrogenase (MDH), the reduced NADH cofactor is oxidized by OAA. The reduced cofactor absorbs strongly at 405 nm, whereas its oxidized form does not. Spectrophotometric determination of the decrease in absorbance monitored at 405 nm/415 nm, is directly proportional to the total carbon dioxide concentration in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

The precision study was conducted in accordance with the CLSI EP5-A2 guideline. The precision study was performed utilizing 2 reagent lots, using serum based control material and human serum samples that were spiked with carbon dioxide concentrations. Two replicates of each of the control and serum samples were tested on two separate runs per day over 20 days, leading to the generation of 80 data points per sample. The mean, SD, and %CV calculated for within-run and total imprecision for each lot yielded similar results. The results from one representative lot are shown below.

Sample	Mean (mmol/L)	Repeatability		Within-Laboratory	
		SD	%CV	SD	%CV
QC Level 1	30.6	0.1782	0.582	1.62	5.31
QC Level 2	20.5	0.7065	3.426	187	9.07
Serum Level 1	12.0	0.1275	1.065	0.69	5.75
Serum Level 2	26.6	0.1521	0.571	0.85	3.21
Serum Level 3	37.4	0.1949	0.521	0.59	1.58

b. Linearity/assay reportable range:

The linearity studies were performed in accordance with the CLSI EP6-A guideline. Samples were prepared by mixing a high spiked serum sample (64 mmol/L CO_2) with a low diluted serum sample (2.0 mmol/L CO_2) to obtain 11 concentrations. Each sample was assayed in replicates of three using two different Carbon Dioxide Reagent lots. The results of the linear regression analyses for one representative lot are summarized below:

$y = 1.0192x + 0.0351$, $R^2 = 0.9993$

The sponsor claims a linearity range from 8.70 to 40.0 mmol/L.

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

Traceability:

The Carbon Dioxide Reagent Set is traceable to NIST SRM 351. The CO_2 assay is calibrated by comparing the change in absorbance of the unknown sample to the change in absorbance of the 30 mEq/L CO_2 standard. The CO_2 standard was previously cleared under k936245.

Stability:

Accelerated shelf-life stability, real-time open-vial stability and on-board stability studies for the Carbon Dioxide Reagent were performed. The protocols and acceptance criteria for stability were reviewed and are found to be acceptable. The studies support a shelf life stability claim of 21 months from the date of manufacture for reagent when stored at 2 to 8°C, an open-vial stability claim for the Carbon Dioxide Reagent of 28 days when stored at 2 to 8°C, and a reagent on-board stability claim of 13 days. The real-time shelf-life stability testing is on-going.

d. *Detection limit:*

Detection limit studies have been carried out in accordance with CLSI EP17-A2 guideline. Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantification (LoQ) studies were performed on two lots of reagents tested on one TC-MATRIX analyzer. For the LoB studies, four (4) blank samples were tested in five replicates over three days. For LoD studies four low CO_2 level samples with target concentrations ranging from 0.92 to 3.68 mmol/L were tested in five replicates using two lots over three days. For LoQ study, five different samples with target concentrations ranging from 0.7 to 4.08 mmol/L were tested in replicates of three using two lots over a three days period.

LoB, LoD and LoQ results are summarized in the following table:

Analyte	LoB	LoD	LoQ
CO_2 (mmol/L)	0.92	1.5	1.77

e. *Analytical specificity:*

Interference studies have been carried out in accordance with CLSI EP7-A2 guideline. Human serum samples with two (2) different concentrations of carbon dioxide (20 mmol/L and 35 mmol/L) were used to evaluate interference testing using two reagent lots. Serum samples with added potential interferents were tested in replicates of ten (10) and compared to a sample without interferent. The sponsor defined no significant interference as <10 % difference from the control sample.

Interferent	Concentration at which no significant interference was observed
Hemoglobin	1,000 mg/dL
Total Bilirubin	60 mg/dL
Conjugate Bilirubin	30 mg/dL
Triglycerides	2,000 mg/dL
Intralipid	2,000 mg/dL
Ascorbic Acid	6 mg/dL

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

Method comparison studies were carried out in accordance with CLSI guideline EP9-A2. One hundred and seventy-six (176) patient serum samples spanning a range from 8.7 to 37.2 mmol/L were tested in singlicate using the Pointe Scientific Inc. Carbon Dioxide Reagent (predicate) and Teco Carbon Dioxide Reagent Set (candidate device). Eight samples were contrived (4.5%). The linear regression analysis yielded the following results:

$y = 0.9785x + 0.2636$, $R^2 = 0.9925$

b. Matrix comparison:

Not applicable.

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.

5. Expected values/Reference range:

The following expected values are provided in the product insert based on the literature[1]:

Normal range for carbon dioxide (Serum): 23 – 33 mmol/L

[1]Tietz NW. Clinical Guide to Laboratory Tests, 3rd ed. Philadelphia, PA: WB Saunders Company; 1995:110-111.

The reference interval for Carbon Dioxide was verified by testing human serum from 23 apparently healthy donors in singlicate using two reagent lots. Results of the study indicate that all values measured are within the expected values of the cited literature, therefore the reference interval has been verified for the Carbon Dioxide Reagent Set.

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.