

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

A. 510(k) Number:

k091153

B. Purpose for Submission:

New device

C. Measurand:

Carbon Dioxide (CO₂)

D. Type of Test:

Quantitative enzymatic assay

E. Applicant:

Beckman Coulter, Inc.

F. Proprietary and Established Names:

SYNCHRON Systems Enzymatic CO₂ (CO₂E) 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:

Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

See indications for use below

2. Indication(s) for use:

CO₂E reagent, when used in conjunction with UniCel® DxC 800 System and SYNCHRON® Systems AQUA CAL 1 and 3, is intended for the quantitative determination of Carbon Dioxide in human serum or plasma. 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:

UniCel® DxC 800 System

I. Device Description:

The SYNCHRON Enzymatic CO₂ (CO₂E) Reagent contains two 300-test cartridges that are packaged separately from the associated calibrator. The reagent cartridge contains the following ingredients: Tris-buffer (pH 7.6), phosphoenolpyruvate (PEP), phosphoenolpyruvate carboxylase (PEPC), malate dehydrogenase, NADH analog, activators, stabilizers, a surfactant and a preservative.

The SYNCHRON® Systems AQUA CAL 1 and 3 are aqueous solutions which were cleared in k965240. AQUA CAL 3 is spiked with bicarbonate to achieve a CO₂ concentration of 30.0 mmol/L, while AQUA CAL 1 contains 0.0 mmol/L of CO₂.

J. Substantial Equivalence Information:

1. Predicate device name(s):

UniCel DxC 600/800 SYNCHRON Clinical Systems CO₂ rate pH

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

k042291

3. Comparison with predicate:

Similarities and Differences		
Item	Candidate device	Predicate device (k042291)
Intended Use	CO2E reagent, when used in conjunction with UniCel® DxC 800 System and SYNCHRON® Systems AQUA CAL 1 and 3, is intended for the quantitative determination of Carbon Dioxide in human serum or plasma.	ISE Electrolyte Buffer reagent, ISE Electrolyte Reference reagent, CO2 Alkaline Buffer and CO2 Acid reagent, when used in conjunction with SYNCHRON LX® Systems, UniCel® DxC 600/800 Systems and SYNCHRON® Systems AQUA CAL 1 and 3, are intended for quantitative determination of Carbon Dioxide concentration in human serum or plasma
Sample Types	Serum or Plasma	Same
Limit of Detection	5.0 mmol/L	Same
Analytical Range	5.0 - 45.0 mmol/L	5.0 - 50.0 mmol/L
Sample Volume	6 µl	40 µl
Methodology	Enzymatic method	pH rate change method
Instrument Platforms	UniCel DxC 800 System	SYNCHRON LX and UniCel DxC 600/800 Systems
Calibration Frequency	Every 72 hours	Every 24 hours

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

Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – Second Edition (CLSI EP5-A2)

Evaluation of the Linearity of Quantitative Measuring Procedures: A Statistical Approach; Approved Guideline (CLSI EP6-A)

Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition (CLSI E7-A2)

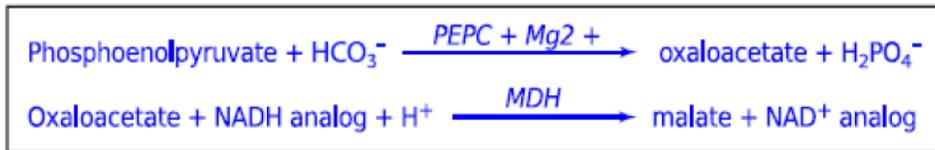
Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline (CLSI EP17-A)

Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Second Edition (CLSI EP9-A2)

L. Test Principle:

The SYNCHRON Systems CO₂E assay is an enzymatic method utilizing phosphoenolpyruvate carboxylase (PEPC) and a stabilized NADH analog in two coupled enzymatic reactions. In the first reaction, PEPC catalyzes the reaction between the phosphoenolpyruvate (PEP) and HCO₃⁻ to yield oxaloacetate and inorganic phosphate. In the second step, oxaloacetate is reduced by a stable NADH analog to malate in the presence of malate dehydrogenase (MDH). The resulting decrease in absorbance at 410 nm is spectrophotometrically measured and is directly proportional to the CO₂ concentration in the test sample via measurement of bicarbonate ions (HCO₃⁻).

The chemical reaction scheme follows:



M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

The sponsor performed precision studies in accordance with the CLSI EP5-A2 guideline. One serum pool and three serum controls were used to evaluate the within-run and total imprecision. Samples were analyzed in duplicate, twice a day, for 20 days. Results are summarized below:

UniCel Dx C 800 SYNCHRON Clinical System

Sample	Mean (mmol/L)	S.D. (mmol/L)	%C.V.	N
Within-Run Imprecision				
SYNCHRON Control Level 1	11.50	0.39	3.4	80
SYNCHRON Control Level 2	19.55	0.45	2.3	80
SYNCHRON Control Level 3	27.50	0.52	1.9	80
Serum Pool	21.60	0.61	2.8	80
Total Imprecision				
SYNCHRON Control Level 1	11.50	0.53	4.6	80
SYNCHRON Control Level 2	19.55	0.55	2.8	80
SYNCHRON Control Level 3	27.50	0.68	2.5	80
Serum Pool	21.60	0.74	3.4	80

b. Linearity/assay reportable range:

The sponsor performed linearity studies in accordance with the CLSI EP6-A guideline. The study protocol utilized inter-dilutions of a patient serum specimen with a zero-level (saline) sample. A high CO₂ level was prepared by spiking with bicarbonate solution. Seven different levels of CO₂ concentrations (ranging 5 to 47 mmol/L) were tested in triplicate on the DxC 800 analyzer. The recovered CO₂ values were plotted against the expected values and an appropriate line fitted by standard linear regression resulting in: $y = 0.9979x + 1.121$; $R^2 = 0.9967$.

The claimed measuring range of this device is 5.0 to 45.0 mmol/L.

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

The enzymatic CO₂ assay is traceable to NIST SRM 351.

AQUA CAL 1 and 3 calibrators were previously cleared under k965240.

The sponsor states that the unopened CO₂E reagent is stable until the expiration date when stored at 2 to 8°C, and for 14 days at 2 to 8°C once opened. The calibrators are stable unopened until the expiration date when stored at 2 to 8°C, and for 30 days at room temperature after opening unless the expiration date is exceeded.

d. Detection limit:

The sponsor determined the limit of detection (LoD) according to the CLSI EP-17-A guideline. LoD is defined as the actual concentration at which an observed test result is very likely to exceed the limit of blank (LoB) and may therefore be declared as “detected”.

The limit of the blank (LoB) was determined by analyzing a blank sample (deionized water) 20 times on a DxC 800 analyzer. To determine the LoD an aqueous CO₂ standard at 5 mmol/L was used as the 100% sample, while 80% and 60% samples were prepared by diluting the standard with deionized water. These 3 low concentration standards were analyzed 20 times each. The results demonstrated that the LoD is 5.0 mmol/L.

The claimed measuring range of this assay is 5.0 to 45.0 mmol/L.

e. Analytical specificity:

The sponsor performed interference studies according to the EP7-A2 guideline. Patient sample pools representing low (~20 mmol/L), mid (22 to 28 mmol/L) and high (35 mmol/L) analytes levels were used. Five levels of each interferent were

tested in replicates of four on a DxC 800 analyzer. The level of interference was considered not significant if there was no more than 2 mmol/L or 6% difference between the interferent result and the reference result.

No significant interferences were found for bilirubin (unconjugated) up to 40 mg/dL, hemoglobin up to 500 mg/dL, acetoacetic acid up to 250 mg/dL, lipemia up to 500 mg/dL of Intralipid or up to a serum index of 6.

f. Assay cut-off:

Not Applicable

2. Comparison studies:

a. Method comparison with predicate device:

Method comparisons to the predicate device were performed in accordance with the CLSI EP9-A2 guideline using the DxC 800 analyzer. A total of 99 serum samples were used, some samples were spiked and diluted to fully span the claimed measuring range. The range of the samples tested was 5 to 44 mmol/L. The CO₂E recovery results (Y) were compared to the corresponding CO₂ ISE recovery results (X) and Deming regression analysis was performed resulting in: $y = 0.978x + 0.35$; $r = 0.996$.

b. Matrix comparison:

The sponsor performed matrix comparisons using 59 apparently health subjects. Serum samples and plasma samples (lithium heparin, sodium heparin, and potassium oxalate/sodium fluoride) were drawn from the same donor. CO₂ samples ranging from 25 to 32 mmol/L were analyzed on the DxC 800. The plasma results (Y) were compared to the corresponding serum results (X) for the same donor and Deming regression analysis was performed. The sponsor claimed that lithium heparin, sodium heparin, and potassium oxalate/sodium fluoride are acceptable anticoagulants to be used. Results are summarized below.

Anticoagulant Study Summary

Anticoagulant	Level Tested for In Vitro Interference	Deming Regression Analysis
Lithium Heparin	14 units/mL	$Y = 1.052X - 1.129$; $r = 0.826$
Sodium Heparin	14 units/mL	$Y = 1.000X - 0.221$; $r = 0.910$
Potassium Oxalate / Sodium Fluoride	2.0 / 2.5 mg/dL	$Y = 1.014X - 0.553$; $r = 0.922$

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 reference range is 23-29 mmol/L based on the following literature:

Wu, A., ed., *Tietz Clinical guide to Laboratory Tests* 4th Edition, Saunder Elsevier, St. Louis, MO (2006).

The sponsor recommends that each laboratory establish its own reference intervals based on upon its patient population.

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.