

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

A. 510(k) Number:

k071340

B. Purpose for Submission:

New device

C. Measurand:

Carbon Dioxide

D. Type of Test:

Quantitative enzymatic assay

E. Applicant:

Thermo Fisher Scientific

F. Proprietary and Established Names:

Carbon Dioxide (CO2)

sCal, code 981831

Nortrol, code 981043

Abtrol, code 981044

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
Enzymatic, Carbon Dioxide (KHS)	Class II	21 CFR 862.1160 Bicarbonate/carbon dioxide test system	75 Clinical Chemistry(CH)
Product Code	Classification	Regulation Section	Panel
Calibrator, Multi- Analyte Mixture (JIX)	Class II	21 CFR 862.1150 Calibrator	75 Clinical Chemistry(CH)
Product Code	Classification	Regulation Section	Panel
Control (JJY)	Class I reserved	21 CFR§ 862.1660 Quality control material (assayed and unassayed)	75 Clinical Chemistry(CH)

H. Intended Use:

1. Intended use(s):

See Indications for use below.

2. Indication(s) for use:

Carbon dioxide (CO₂)

Carbon dioxide (CO₂) reagent is intended for the quantitative determination of total carbon dioxide in human serum and plasma (Li-heparin) on T60 analyzer. Bicarbonate measurements, in conjunction with tests such as glucose, urea, sodium, potassium, and chloride, are used in the assessment of disturbances of acid base balance resulting from metabolic or respiratory causes.

sCal

For in vitro diagnostic use on T60 analyzer. sCal is used as a multicalibrator for quantitative measurements using methods defined by Thermo Fisher Scientific Oy.

Nortrol

For in vitro diagnostic use for quantitative testing on T60 analyzer. Nortrol is a control serum to monitor trueness and precision of the analytes listed in the separate Nortrol value sheet. The given values are valid for T60 Clinical Chemistry Analyzers using methods defined by Thermo Fisher Scientific Oy.

Abtrol

For in vitro diagnostic use for quantitative testing on T60 analyzer. Abtrol is a control serum to monitor trueness and precision of the analytes listed in the separate Abtrol value sheet. The given values are valid for T60 Clinical Chemistry Analyzers using methods defined by Thermo Fisher Scientific Oy.

3. Special conditions for use statement(s):

For Prescription use only

4. Special instrument requirements:

To be used with T60 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/L, NADH 1.6 mM/L, Phosphoenolpyruvate carboxylase (PEPC) (Microbial) >1000 U/L, Malate Dehydrogenase (microbial) > 200U/L, Buffer (66 mmol/L), NaN₃, pH 8.05 at 20°C, and stabilizers.

All human materials included in the calibrators and controls were tested by FDA approved methods and found to be negative for the presence of antibodies to HIV-1, HIV-2, HBsAg, and HCV.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Roche Diagnostics/Hitachi Bicarbonate Liquid

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

k032377

3. Comparison with predicate:

Characteristics	Carbon Dioxide (CO ₂)	Roche Diagnostics/Hitachi Bicarbonate Liquid
Indications for Use	Carbon dioxide (CO ₂) reagent is intended for the quantitative determination of total carbon dioxide in human serum. Bicarbonate measurements, in conjunction with tests such as glucose, urea, sodium, potassium, and chloride, are used in the assessment of disturbances of acid base balance resulting from metabolic or respiratory causes.	In vitro test for the quantitative determination of bicarbonate in human serum and plasma on Roche automated clinical chemistry analyzers.
Assay protocol	Enzymatic rate	Enzymatic rate
Sample type	Serum, plasma (Li-heparin)	Serum, plasma (Li-heparin)
Reagent	PEP 8.0 mM, NADH (1.6 mmol/L), MDH (microbial) > 200U/L, PEPC (microbial) ≥ 1000U/L, Buffer (66 mmol/L), NaN ₃ , pH 8.05 at 20°C, stabilizers.	PEP > 60 mmol/L, NADH analog (3 mmol/L), MDH (porcine) > 20000 U/L, PEPC (microbial) > 2000 U/L, buffer, stabilizer, preservative.
Format	Reagent provided as a ready to use liquid.	Reagent is provided in a ready to use format.
Storage/Stability	Reagent in unopened vial is stable at 2-8°C until expiration date indicated on vial label.	Shelf life at 2-8°C until the expiration date on the label.
Expected Values	22 – 29 mmol/L	22 – 29 mmol/L
Linearity / Assay range	5.0 – 40.0 mmol/L	1.5 – 50.0 mmol/L

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

CLSI EP5-A: Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline. Vol. 19 No.2. February 1999.

CLSI EP9-A: Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline. Vol. 15 No. 17. December 1995.

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) to NAD⁺. Spectrophotometric determination of the decrease in absorbance monitored at 380 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 three lots of reagents and three levels of quality control serum containing normal and abnormal levels of CO₂ on the T60 analyzer. Studies were carried out in duplicate in two runs per day over 20 days (40 runs). The results are tabulated below.

Within-day Precision

Description	Control Level 1	Control Level 2	Control Level 3
Lot No. 1			
Number of data points			
Mean (mmol/L)	15.6	25.3	34.6
SD (mmol/L)	0.3	0.5	0.5
CV (%)	2.0	1.9	1.4
Lot No. 2			
Number of data points	80	80	80
Mean (mmol/L)	15.7	25.2	34.3
SD (mmol/L)	0.3	0.4	0.4
CV (%)	1.9	1.6	1.3
Lot No. 3			
Number of data points	80	80	80
Mean (mmol/L)	15.5	25.1	34.1
SD (mmol/L)	0.2	0.3	0.4
CV (%)	1.3	1.0	1.2

Between Run Precision

Description	Control Level 1	Control Level 2	Control Level 3
Lot No. 1			
Number of data points	-	-	-
Mean (mmol/L)	15.6	25.3	34.6
SD (mmol/L)	0.7	1.1	1.3
CV (%)	4.4	4.3	3.6

Lot No. 2			
Number of data points	80	80	80
Mean (mmol/L)	15.7	25.2	34.3
SD (mmol/L)	0.8	1.0	1.5
CV (%)	5.3	3.9	4.5
Lot No. 3			
Number of data points	80	80	80
Mean (mmol/L)	15.5	25.1	34.1
SD (mmol/L)	0.7	1.0	1.7
CV (%)	4.2	4.0	5.0

b. *Linearity/assay reportable range:*

To determine the linearity range, the sponsor prepared ten CO₂ test samples through serial dilution of a 60 mmol/L bicarbonate standard made by dissolving 0.252g of Sodium Bicarbonate in 50 mL deionized water. Test samples concentrations ranged from 4.67 - 44 mmol/L. All ten CO₂ levels were run in duplicate on T60 analyzer. The sponsor's acceptance criteria are based on measurement values between 15-50 mmol/L with % recovery being within 95 – 105% of the assigned values, and below 15 mmol/L, ± 2 mmol/L from the assigned value. For the range tested, the linear regression analysis demonstrated a linear regression equation, $Y = 1.029X - 0.564$. The assay range claimed by the sponsor is 5.0 - 40 mmol/L. The sponsor also conducted studies to show the linearity of the reagent maintained through out the claimed shelf life of one year using a reagent lot at the completion of one year storage at 2-8°C. The linear regression analysis demonstrated equation, $Y = 1.025X - 0.127$. Using the same acceptance criteria, the sponsor claimed the linear range of 5 – 40 mmol/L.

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

The sponsor's protocols indicate that each calibrator (sCal), and control (Nortrol and Abtrol) lot is traceable to the manufacturer's primary reference material. The values are assigned based on multi determinations performed using T60 instruments. The assigned value is the median of all the values generated for each calibrator and control. Additionally, control range is calculated as the target value ± 2 standard deviations. The value assignment sheet lists the lot-specific values.

In the labeling the sponsor recommends calibrating the test at least every three days and every time a new reagent bottle is used. The sponsor also recommends using quality control samples at least once a day, after each calibration and when a new bottle is used. However, the sponsor also suggests the control intervals must be adapted to the individual laboratory requirement.

The sponsor claims that all open on-board reagents are stable for 5 days. Based on the stability studies conducted, the sponsor claimed open vial

stability at 2 - 8°C is 7 days and shelf life (unopened) stability at 2 - 8°C is 4 years for calibrators and 3 years for controls.

d. *Limit of Blank (LOB):*

To demonstrate the limit of the blank, a serum matrix equivalent solution, Serasub, containing no CO₂ (blank sample) was tested in eleven replicates. The sponsor defined the limit of zero-concentration (LOB) sample as $\pm 3SD$, which was demonstrated to be 0.7467 mmol/L and 0.5022 mmol/L for Serasub aged 2 months and 12 months, respectively. Along with the results from linearity studies and LOB determined here, the sponsor established the assay range of 5.0 – 40 mmol/L.

e. *Analytical specificity:*

The sponsor evaluated the effect of some known endogenous and exogenous interferences by spiking those substances in an aliquot of normal sera and comparing with an unspiked aliquot of the same sample. The interferences and the test range included hemoglobin (0 – 1000 mg/dL), lipemia (0 – 2000 mg/dL), unconjugated bilirubin (0 – 60 mg/dL), and conjugated bilirubin (0-60 mg/dL). Based on the sponsor's defined acceptance criteria on interference limit of $\pm 10\%$ of control, the results indicate that there are no interferences up to the concentrations tested for any of the substances. The sponsor also conducted CO₂ reagent assay interference by sample hemolysate (0 – 1040 mg/dL) and based on the same acceptance criteria confirmed that there is no interference up to 400 mg/dL.

f. *Assay cut-off:*

Not Applicable.

2. Comparison studies:

a. *Method comparison with predicate device:*

Performance of the Carbon Dioxide (CO₂) Reagent assayed on the T60 analyzer was compared with the results generated for the predicate device, Roche CO₂-L, Bicarbonate Liquid (k032377) using 100 samples. The samples consisted of 71 serum (range: 9.1 – 49.5 mmol/L) and 29 Li-heparin plasma (range: 11.4 – 45.2 mmol/L). Comparison of the data based on two methods for serum, plasma and samples as a total gave correlation coefficients of 0.9835, 0.9816, and 0.9825, respectively. Deming regression analysis for serum, plasma and samples as a total resulted in the following equations, $Y = 0.972X + 1.4$; $Y = 1.046X - 0.24$; and $Y = 0.978X + 1.23$, respectively.

b. *Matrix comparison:*

The sponsor conducted independent studies using serum and plasma to demonstrate that the performance of the Carbon Dioxide Reagent is substantially equivalent to the predicate, as described above.

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 of CO₂ given for adult (22 – 29 mmol/L) were based on literature. The sponsor recommends in the labeling that each laboratory determine its own reference range.

* Burtis, CA and Ashwood, ER (ed.), Tietz Fundamentals of Clinical Chemistry, 5th edition, WB saunders Company, Philadelphia, 2001, p. 732, 966.

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.