

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

A. 510(k) Number:

k093611

B. Purpose for Submission:

Modification to a marketed device (k802376)

C. Measurand:

Carbon dioxide

D. Type of Test:

Quantitative, potentiometric

E. Applicant:

Ortho-Clinical Diagnostics, Inc.

F. Proprietary and Established Names:

VITROS Chemistry Products CO₂ DT Slide assay
Bicarbonate / carbon dioxide assay

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 indication(s) for use below.

2. Indication(s) for use:

VITROS Chemistry Products CO₂ DT Slides quantitatively measure carbon dioxide (CO₂) concentration in serum and plasma using VITROS DT60 and DT60 II Chemistry Systems. Total carbon dioxide measurements are used in the diagnosis and treatment of numerous potentially serious disorders associated with changes in body acid-base balance. For *in vitro* diagnostic use only.

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

For use on the VITROS DT60 and DT60 II Chemistry Systems only

I. Device Description:

The VITROS CO₂ DT Slide method is performed using the VITROS CO₂ DT Slides and the VITROS Chemistry Products DT Calibrator Kit on VITROS DT60/DT60 II Chemistry Systems.

The VITROS DT60/ DT60II Chemistry Systems and reagents are designed specifically for use with the VITROS Chemistry Products range of products. The following materials are required to perform a carbon dioxide test on the VITROS DT60/DT60 II Chemistry System:

- VITROS DT60/ DT60 II Chemistry System
- VITROS Chemistry Products CO₂ DT Slides:

Reactive ingredients

Silver 0.4 mg; silver chloride 0.2 mg; sodium chloride 0.2 mg; potassium chloride 63 µg; trioctylpropylammonium chloride 0.5 mg; and decyltrifluoroacetophenone 0.8 mg.

Other ingredients

Binders, plasticizers, surfactants, stabilizer, buffers, nickel-chromium and cross-linking agent.

- VITROS Chemistry Products DT Calibrator Kit (cleared under k841503)
- VITROS Chemistry Products DT Electrolyte Diluent
- VITROS DT Reference Fluid

J. Substantial Equivalence Information:

1. Predicate device name(s):

VITROS Chemistry Products CO₂ DT Slides

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

k802376

3. Comparison with predicate:

Similarities		
Item	New Device VITROS Chemistry Products CO₂ DT Slide (Modified)	Predicate Device VITROS Chemistry Products CO₂DT Slide
Intended Use	Same	For <i>in vitro</i> diagnostic use only. VITROS CO ₂ DT Slides quantitatively measure carbon dioxide (CO ₂) concentration in serum and plasma.
Fundamental scientific technology	Same	Dry, multilayered slide utilizing direct potentiometry
Reactive Ingredients per square cm	Same	Silver 0.4 mg; silver chloride 0.2 mg; sodium chloride 0.2 mg; potassium chloride 63 µg; trioctylpropylammonium chloride 0.5 mg; and decyltrifluoroacetophenone 0.8 mg.
Sample type	Same	Serum, plasma
Instrumentation	Same	VITROS DT Systems
Measuring Range	Same	5 – 50 mmol/L
Reference Range	Same	22 – 30 mmol/L

Differences		
Item	New Device VITROS Chemistry Products CO₂ DT Slide (Modified)	Predicate Device VITROS Chemistry Products CO₂DT Slide
Manufacturing Process of the ISE baseweb (Ag/AgCl and Support Layers of the Na ⁺ DT Slide)	Magnetic sputter deposition	Electron beam evaporation
Composition of ISE baseweb component	Ag/AgCl concentration: No change; Nickel Stripes: NiCr (80% Nickel, 20% Chromium)	Ag/AgCl concentration: Silver 0.4 mg and silver chloride 0.2 mg Nickel Stripes: Ni (99+% Nickel)

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

- Interference Testing in Clinical Chemistry; Approved Guideline (CLSI EP 7-A)
- Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline (CLSI EP09-A2)
- Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline (CLSI EP5-A)
- Protocols for Determination of Limits of Detection and Limits of Quantitation (CLSI EP17-A)

L. Test Principle:

The VITROS CO₂ DT Slide method is performed using the VITROS CO₂ DT Slides and the VITROS Chemistry Products DT Calibrator Kit on VITROS DT60/DT60 II Chemistry Systems. The VITROS CO₂ DT Slide is a multilayered, analytical element coated on a polyester support that uses direct potentiometry for measurement of ionic carbon dioxide.

The slide consists of two ion-selective electrodes, each containing a buffer layer, an ion selective membrane layer, a reference layer, and a silver and a silver chloride layer coated on a polyester support. The buffer layer adjusts the sample pH to 8.4 and maintains CO₂, HCO₃⁻, and CO₃⁻² in proper equilibrium. The ion-selective membrane layer contains an ion exchanger trioctylpropylammonium chloride (TOPA Cl) and a CO₃⁻² ionophore decyltrifluoroacetophenone (DTFA). A drop of patient sample and a drop of VITROS DT Reference Fluid on separate halves of the slide results in migration of both fluids toward the center of the paper bridge. A stable liquid junction is formed connecting the reference electrode to the sample indicator electrode. Each electrode produces an electrical potential in response to the concentration of carbon dioxide applied to it. The potential difference poised between the two electrodes is proportional to the carbon dioxide concentration in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

The precision study was performed using two quality control fluids and two levels of calibrator fluids. Samples were analyzed in duplicate, twice a day for 21 days. One VITROS DT 60 II instrument was used to collect the data. Results are summarized below:

Concentration (mmol/L)	Within Day SD	Within Day CV%	Within Lab SD	Within Lab CV%	n
10	0.2	2.0	0.2	2.0	84
20	0.6	3.0	0.6	3.0	84
25	0.6	2.4	0.7	2.8	84
36	0.7	1.9	0.9	2.5	84

b. *Linearity/assay reportable range:*

The measuring range of the CO₂ assay is 5 – 50 mmol/L. A linearity study was performed as follows. Two serum pools were prepared with total carbon dioxide concentrations near the extremes of the calibration range. The high pool was 7% BSA with an approximate CO₂ concentration of 62.7 mmol/L. The low pool was 7% BSA with an approximate CO₂ concentration of 0.5 mmol/L. The low and high pools were mixed to obtain six admixtures of intermediate concentrations. Two to four determinations of the six admixtures were tested on the VITROS DT60 II Chemistry System. The experiment was performed three times, each test using one reagent lot of CO₂ slides. The measured CO₂ values were plotted as the dependent variable against the % high pool values as the independent variable. Linear regression produced the following:

$$\begin{array}{ll}
 \text{Lot 1} & y = 0.94x + 3 & r = 0.999 \\
 \text{Lot 2} & y = 0.96x + 3 & r = 0.999 \\
 \text{Lot 3} & y = 0.94x + 4 & r = 0.999
 \end{array}$$

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

Unopened VITROS CO₂ DT Slides are stable until the expiration date on the carton when stored refrigerated (2-8 °C) or frozen (≤-18 °C), and for less than 48 hours when stored at room temperature (18–28 °C). Once opened, the VITROS CO₂ Slides are stable at room temperature (18–28 °C) for up to 15 minutes.

d. *Detection limit:*

The sponsor performed Limit of Blank (LOB), Limit of Detection (LOD) and Limit of Quantitation (LOQ) studies based on the CLSI EP17-A guideline.

LOB determinations were made using an ultra filtered plasma sample devoid of analyte on four reagent lots of VITROS CO₂ DT Slides. Sample was assayed in 20 replicates per day for five test days on one VITROS DT60II Chemistry System for a total of 100 replicates for each lot. LOB was determined to be 5.0 mmol/L.

LOD and LOQ was determined for four reagent lots of VITROS CO₂ DT Slides by evaluation of three low plasma samples having concentrations near or greater than the LOB by increments of approximately two standard deviations. Samples were assayed 10 replicates per day over five days on two VITROS DT60 II Chemistry Systems for a total of 50 replicates. LOD and LOQ were determined to be 5.0 mmol/L.

The claimed measuring range of the candidate device is 5 to 50 mmol/L.

e. Analytical specificity:

Interference studies were performed using clinical serum samples to determine the effect of various endogenous and exogenous substances using VITROS DT 60 II analyzer. The following equations were used by the sponsor to calculate bias:

For exogenous substances: Bias = (“spike”: mean concentration of interfering substance pool) – (“blank”: mean concentration of “control” pool).

For endogenous substances: Bias = (mean concentration of VITROS method) – (mean concentration of reference method).

The following substances were tested with the VITROS CO₂ DT Slides at a carbon dioxide concentration of 28 mmol/L and found to cause a bias of ≤ 2 mmol/L at the concentration shown.

Compound	Concentration	
acetaminophen	20 mg/dL	1.3 mmol/L
acetylsalicylic acid	35 mg/dL	1.9 mmol/L
alprazolam	20 µg/dL	648 nmol/L
5 - aminosalicylic acid	23 mg/dL	1.5 mmol/L
amitriptyline	1 µg/mL	3.6 µmol/L
amoxicillin	1500 µg/mL	4.1 mmol/L
ascorbic acid	3 mg/dL	170 µmol/L
atenolol	20 µg/mL	75.1 µmol/L
bilirubin	40 mg/dL	684 µmol/L
calcium	16 mg/dL	4 mmol/L

Compound	Concentration	
carbamazepine	60 µg/mL	254 µmol/L
cephalexin	400 µg/mL	1.2 mmol/L
ciprofloxacin	5 mg/dL	151 µmol/L
clarithromycin	25 mg/dL	334 µmol/L
codeine	4 µg/mL	13.4 µmol/L
dextran	3000 mg/dL	750 µmol/L
dextromethorphan	3.8 µg/mL	14.0 µmol/L
digoxin	3 µg/dL	38.4 nmol/L
diltiazem	5 µg/mL	12.1 µmol/L
diphenhydramine	10 µg/mL	39.1 µmol/L
enalapril	1.2 µg/mL	3.2 µmol/L
ethanol	394 mg/dL	85.7 mmol/L
fluoxetine	0.8 mg/dL	25.9 µmol/L
furosemide	10 mg/dL	302 µmol/L
gentisic acid	0.5 mg/dL	32.4 µmol/L
glucose	600 mg/dL	33.3 mmol/L
glutathione	1 mg/dL	32.5 µmol/L
glyburide	6.4 µg/mL	13.0 µmol/L
guaifenesin	100 mg/dL	5 mmol/L
hemoglobin	1000 mg/dL	10 g/L
hydrochlorothiazide	2 mg/dL	67.2 µmol/L
hydrocodone	250 ng/mL	835 nmol/L
ibuprofen	70 mg/dL	3.4 mmol/L
intralipid	800 mg/dL	8 g/L
isoniazid	0.4 mg/dL	29.2 µmol/L
L-dopa	0.6 mg/dL	30.4 µmol/L
lithium	1 mEq/L	1 mmol/L
loratadine	100 ng/mL	261 nmol/L
magnesium	4.5 mg/dL	1.85 mmol/L
meprobamate	2 mg/dL	91.6 µmol/L
6-mercaptopurine	1.5 mg/dL	98.5 µmol/L
naproxen	900 µg/mL	3.9 mmol/L
nifedipine	0.2 mg/dL	5.8 µmol/L
omeprazole	20 mg/dL	579 µmol/L
phenobarbital	3 mg/dL	129 µmol/L
phenytoin	10 mg/dL	396 µmol/L
phospholipids as lecithin	500 mg/dL	5 g/L
prednisone	0.1 mg/dL	2.8 µmol/L
propoxyphene	0.4 mg/dL	11.8 µmol/L
pseudoephedrine	20 µg/mL	121 µmol/L
ranitidine	20 µg/mL	63.8 µmol/L

Compound	Concentration	
simvastatin	500 mg/L	1.2 mmol/L
sulfamethoxazole	40 mg/dL	1.6 mmol/L
sulfathiazole	6 mg/dL	235 µmol/L
terazosin	1 mg/dL	25.8 µmol/L
tolbutamide	22 mg/dL	814 µmol/L
total protein	4 g/dL	40 g/L
total protein	10 g/dL	100 g/L
triamterene	6 mg/dL	237 µmol/L
triglycerides	800 mg/dL	9 mmol/L
trimethoprim	40.1 µg/mL	138 µmol/L
tyrosine	24 mg/dL	1.3 mmol/L
urea	214 mg/dL	35.7 mmol/L
warfarin	10.7 mg/dL	347 µmol/L

Iodide was tested at a carbon dioxide concentration of 25 mmol/L and found to cause a bias of 6 mmol/L CO₂ at an iodide concentration of 2 mmol/L. This is noted in the labeling.

In the labeling, the sponsor also notes the following:

- Lactate, hippurate, and other organic acids at significantly elevated concentrations have been reported to increase CO₂ results.
- Bromide from therapeutic drugs and ointments may cause a positive bias of approximately 2 mmol/L for each mmol of bromide.
- Nitrate may cause a positive bias of approximately 3 mmol/L for each mmol of nitrate.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

A comparison of 119 samples, ranging in concentration from 8 to 49 mmol/L, was performed using the new device on the VITROS DT 60 II analyzer and the predicate. Spiked, diluted, and unaltered clinical samples were analyzed. The linear regression line was calculated, with the following results:

$$y = 0.975x + 0.48$$

$$r^2 = 0.978$$

b. *Matrix comparison:*

The assay may be performed using serum, lithium heparin plasma, or sodium heparin plasma. To demonstrate this, the sponsor performed a study in which five tube types (plain serum red top, serum separator tubes (SST), LiHep tubes, NaHep tubes, and LiHep plasma separator tubes (PST)) were collected from each of 10 individual donors. Serum or plasma was separated from the cells. The bias for each tube type was calculated using the plain serum red top as the reference when analyzed using the VITROS DT 60 II analyzer. Across all tube types, 63% of the comparisons to the reference red top tube were with ± 1 mmol/L, 89% were ± 2 mmol/L, and 100% were within ± 3 mmol/L.

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:

22 – 30 mmol/L from Tietz NW (ed). *Fundamentals of Clinical Chemistry*. ed. 4. Philadelphia: WB Saunders; 780; 1996.

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.