

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

**A. 510(k) Number:**

k073223

**B. Purpose for Submission:**

New device

**C. Measurand:**

Total Carbon Dioxide

**D. Type of Test:**

Quantitative, Photometric

**E. Applicant:**

Alfa Wassermann Diagnostic Technologies, Inc.

**F. Proprietary and Established Names:**

S-Test Carbon Dioxide (CO<sub>2</sub>) Reagent Cartridge

**G. Regulatory Information:**

<b>Product Code</b>	<b>Classification</b>	<b>Regulation Section</b>	<b>Panel</b>
KHS – Bicarbonate/carbon dioxide test system	Class II	862.1160	75, Chemistry

**H. Intended Use:**

1. Intended use(s):

See Indications for use below

2. Indication(s) for use:

The S-Test Carbon Dioxide Reagent is intended for the quantitative determination of carbon dioxide concentration in serum or heparin plasma using the S40 Clinical Analyzer. Bicarbonate/carbon dioxide measurements are used in the diagnosis and treatment of numerous potentially serious disorders associated with changes in body acid-base balance. The test is intended for use in clinical laboratories or physician's office laboratories. For in vitro diagnostic use only.

3. Special conditions for use statement(s):

For Prescription Use only

4. Special instrument requirements:

S40 Clinical Chemistry Analyzer

**I. Device Description:**

The Carbon Dioxide (CO<sub>2</sub>) is a single use reagent cartridge having two reagent cells, Photometric reaction cuvette, film seal and a 2-D code label. The reagent cells contain the following reagents; Reagent 1 – water and preservative, Reagent 2 - Phosphoenolpyruvate (PEP), Nicotinamide adenine dinucleotide (NADH) analog, reduced, Phosphoenol pyruvate carboxylase (PEPC) (Microbial), Malate dehydrogenase (MD) (Mammalian), Buffer (pH 7.2, 25°C), Activators, Stabilizers, Surfactant and Preservative.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):

ACE plus ISE/Clinical Chemistry System, Alfa Wassermann  
Vitros Fusion Clinical Chemistry Analyzer, Ortho Clinical Diagnostics  
Piccolo xpress Chemistry Analyzer, Abaxis Inc.

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

k930104, k001133 and k950164 respectively

3. Comparison with predicate:

The device and the predicate devices share a similar intended use, analytes measured, analysis temperature, reactive ingredients and sample type.

<b>Differences</b>				
<b>Item</b>	<b>S-Test Carbon dioxide reagent on the S40 Chemistry Analyzer</b>	<b>ACE plus ISE/ clinical chemistry analyzer</b>	<b>Vitros Fusion Clinical Chemistry Analyzer</b>	<b>Piccolo xpress Chemistry Analyzer</b>
Sample volume	5 µL	6 µL	6 µL	100 µL
Linearity range	5-45 mEq/L	2-50 mEq/L	5-40 mEq/L	5-40 mEq/L
Detection limit	5 mEq/L	2 mEq/L	5 mEq/L	5 mEq/L
Reaction Type	Enzymatic endpoint	Kinetic	Enzymatic endpoint	Kinetic

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

CLSI EP5-A2: Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Second Edition (2004)  
 CLSI EP10-A: Preliminary Evaluation of Quantitative Clinical Laboratory Methods; Approved Guideline –Second Edition (2002)  
 CLSI EP6-A: Evaluation of Linearity of Quantitative Measurement Procedures, A Statistical Approach: Approved Guideline (2003)  
 CLSI EP7-A: Interference Testing in Clinical Chemistry; Approved Guideline (2002)  
 CLSI EP17-A: Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline (2004)  
 CLSI EP9-A2: Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline (2002)  
 CLSI C28-A2: How to Define and Determine Reference Intervals in the Clinical Laboratory; Approved Guideline-Second Edition (2000), Section 8.2: Transference and Validation

**L. Test Principle:**

Carbon dioxide in sample reacts with PEP in the presence of PEPC and magnesium to yield oxaloacetic acid and phosphate. In the presence of MD the reduced cofactor absorbs strongly at 405 nm. The difference in absorbance between the final and first reading which is measured bichromatically at 405/508 nm is directly proportional to the carbon dioxide concentration in the sample.

**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:

a. *Precision/Reproducibility:*

Precision studies were conducted in-house and at three Physician Office Laboratories (POL) (with three trained operators typically found in these settings) by testing three serum samples. The samples were run once a day, three times per run for five days using one instrument at each site. The results are presented below:

Lab	CO2 mEq/L			
	Sample	Mean	% CV	
			Within Run	Total
In-House	1	18	2.2%	2.8%
POL 1	1	21	3.9%	5.7%
POL 2	1	19	3.8%	3.7%
POL 3	1	19	3.6%	3.5%
In-House	2	23	1.3%	3.0%
POL 1	2	25	2.8%	2.8%
POL 2	2	23	1.7%	2.0%
POL 3	2	25	2.4%	5.3%
In-house	3	27	6.6%	6.6%
POL 1	3	32	4.0%	5.6%
POL 2	3	33	2.8%	6.4%
POL 3	3	33	4.2%	5.9%

b. *Linearity/assay reportable range:*

Linearity across the assay range was confirmed by testing commercial linearity standards with 9 levels with know concentrations of CO2. Each level was tested in replicates of four. Results are presented below:

<b>Total Carbon Dioxide</b>			
Sample	Assigned Value mg/dL	Measured Value mg/dL	% Recovery
1	3	4	+1 mEq/L
2	7	6	-1 mEq/L
3	13	14	104%
4	18	17	96%
5	24	24	101%
6	28	27	96%
7	33	33	101%
8	38	37	97%
9	43	43	100%
Linear regression $y = 0.988x + 0.02$ , $r^2 = .9964$			

The reportable range of 5-43 mEq/L is based on linearity, detection limit and method comparison.

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

The S Test Carbon dioxide cartridge is factory calibrated by using standard material with an assigned value which is traceable to the NIST standard Reference material SRM351. The 2-D barcode printed on each cartridge provides the analyzer with lot-specific calibration data.

Real time stability studies have been conducted. Protocols and acceptance criteria were described and found to be acceptable. The manufacturer claims the following expiration date:

When stored at 2-8 °C the assay reagent is good until the expiration date.

d. *Detection limit:*

The Limit of Blank and Limit of Detection was determined by running a low sample (five different samples) and a BSA sample, (7.5% in saline) for 3 days, 4 replicates/day, for each low sample and 20 replicates/day, for the true blank sample, for a total of 60 results. The testing was split between two instruments. The detection limit is 5.0 mEq/L CO<sub>2</sub>.

e. *Analytical specificity:*

Interference studies to determine the effects of Unconjugated Bilirubin, Hemolysis were performed using seven serum pools containing approximately 24.0 mg/dl CO<sub>2</sub> which were spiked with varies concentrations of unconjugated bilirubin (0-50 mg/dL), hemoglobin (0-1000 mg/dL). To test Lipemia interference three lipemic serum samples were used.

Sponsor states that interference is considered to be significant if the analyte result is different from the control by  $\pm 10\%$ . There was no significant interference from bilirubin, hemoglobin or Lipemia.

*f. Assay cut-off:*

Not applicable

2. Comparison studies:

*a. Method comparison with predicate device:*

Clinical correlation studies were performed comparing the S-Test CO<sub>2</sub> results generated on the S40 Clinical analyzer against the results from the ACE Clinical analyzer using a total of 94 serum sample Of the 94 serum samples (9 were diluted and 8 were spiked samples). All the samples were measured in singlet and only one specimen per patient was obtained.

The correlation study between the device and the predicate yielded the following results.

Test	n	Slope	Intercept	r	Sample range (mEq/L)
S Test Carbon Dioxide	94	0.985	0.42	0.984	6-41.8

Performance for the S Test Carbon Dioxide was evaluated at three Physician Office Laboratories with a total of three operators who are typical operators at these sites. Operators ran from 39 or more unaltered clinical serum samples obtained from each site as well as 8 diluted and 4 spiked samples. The S Test Carbon dioxide test results were compared to the ACE results. The correlation study between the device and the predicate for serum yielded the following results.

		n	Slope	Intercept	r	Sample range (mEq/L)
Carbon Dioxide	Lab A	57	0.995	.15	0.948	5.3 – 38.9
	Lab B	47	0.941	-0.08	0.937	5.3 – 38.9
	Lab C	57	1.000	-0.76	0.980	5.3 – 38.9

b. *Matrix comparison:*

A serum / plasma comparison test was performed for the S-Test CO2 assay. Thirty-five paired samples were assayed on the S40 System. Seven of the samples were spiked and four samples were diluted to help cover the assay range. The correlation is as follows:

$$y = 0.998x - 0.40, r = 0.962, \text{ range } 10-42$$

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:

Forty-five (45) normal serum samples for CO2 were evaluated on the S40 Clinical Analyzer to determine if the reference ranges of the predicate (Ortho Clinical Fusion) could be transferred to the new assay. The sponsor's acceptance criterion is 90% of the assay results for the normal samples are within the predicate range. Analysis confirmed sufficient agreement (6.7% non-congruent results for CO2, sponsor specification  $\leq 10\%$ ) to transfer the reference range.

CO2 – 22-30 mEq/L

**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.

