

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

A. 510(k) Number:

k072356

B. Purpose for Submission:

New device

C. Measurand:

Calcium

D. Type of Test:

Quantitative, Photometric

E. Applicant:

Alfa Wassermann Diagnostic Technologies, Inc.

F. Proprietary and Established Names:

S-Test Calcium Reagent Cartridge

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
CJY – Calcium test system	Class II	862.1145	75, Chemistry

H. Intended Use:

1. Intended use(s):

See Indications for use below

2. Indication(s) for use:

The S-Test Calcium Reagent is intended for the quantitative determination of calcium concentration in serum or heparin plasma using the S40 Clinical Analyzer. Calcium measurements are used in the diagnosis and treatment of parathyroid disease, a variety of bone diseases, chronic renal disease and tetany (intermittent muscular contractions or spasms). 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 Calcium (CA) is a single use reagent cartridges having two reagent cells, Photometric reaction cuvette, film seal and a 2-D code label. The reagent cells contain the following reagents; Reagent 1 – Monoethanolamine buffer and Hydroxquinoline, Reagent 2 - o-Cresolphthalein complexone

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):

k931786, k946090 and k950164 respectively

3. Comparison with predicate:

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

Differences				
Item	S-Test Calcium reagent on the S40 Chemistry Analyzer	ACE plus ISE/ clinical chemistry analyzer	Vitros Fusion Clinical Chemistry Analyzer	Piccolo xpress Chemistry Analyzer
Sample volume	10 µL	3 µL	10 µL	100 µL
Reportable range	2.3-13.6 mg/dL	0.3-15 mg/dL	1.0-14.0 mg/dL	4-16 mg/dL
Detection limit	2.3 mg/dL	0.3 mg/dL	1.0 mg/dL	4 mg/dL
Reactive ingredients	0-cresolphthalein complexone	Arsenazo III	Arsenazo III dye	Arsenazo III, sodium salt

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:

Calcium in the sample combines with o-cresolphthalein complexone in alkaline medium to form a reddish-purple color, which is measured bichromatically at 600/660 nm. The intensity of color produced is directly proportional to the calcium 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	CA mg/dL			
	Sample	Mean	% CV	
			Within Run	Total
In-House	1	6.3	3.0%	3.0%
POL 1	1	6.2	1.4%	1.9%
POL 2	1	6.4	0.8%	1.0%
POL 3	1	6.2	2.0%	2.8%
In-House	2	9.9	1.4%	1.6%
POL 1	2	9.8	1.5%	1.5%
POL 2	2	9.9	0.8%	1.0%
POL 3	2	9.7	2.3%	2.5%
In-house	3	14.4	0.4%	0.7%
POL 1	3	14.1	1.0%	1.3%
POL 2	3	14.2	0.4%	0.7%
POL 3	3	14.0	3.9%	4.3%

b. *Linearity/assay reportable range:*

Linearity across the assay range was confirmed by testing 6 levels of commercial linearity standards with known concentrations of calcium. Each level was tested in replicates of four. Results are presented below:

Calcium			
Sample	Assigned Value mg/dL	Measured Value mg/dL	% Recovery
1	0	0.2	+0.2 mg/dL
2	2.93	2.83	97%
3	5.85	5.95	102%
4	8.78	8.95	102%
5	11.70	12.05	103%
6	14.63	14.63	100%
Linear regression $y = 1.004x + 0.090$, $r^2 = 0.9987$			

The reportable range of the assay is 2.3-14.6 mg/dL.

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

The S Test CA cartridge is factory calibrated and traceable to the NIST standard Reference material SRM915b. 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. 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 were determined by running a low sample (five different samples) and a BSA sample, (7.5% in saline). Each low sample was run for 3 days, 4 replicates/day. The blank sample was run 20 replicates/day for 4 days. The testing was split between two instruments. The Limit of Detection was determined to be 2.3 mg/dL Ca^{2+} .

e. Analytical specificity:

Interference studies to determine the effects of Unconjugated Bilirubin, Hemolysis and Lipemia were performed. Seven serum pools containing approximately 11.0 mg/dl CA were spiked with varies concentrations of unconjugated bilirubin (0-50 mg/dL), hemoglobin (0-1000 mg/dL) and Intralipids (0-2000 mg/dl). 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 or Lipemia. No significant interference of hemoglobin to 500 mg/dL. A negative bias (17%) occurred at 1000 mg/dL hemoglobin.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

Clinical correlation studies were performed comparing the S-Test Calcium results generated on the S40 Clinical analyzer against the results from the ACE Clinical analyzer using a total of 181 serum samples. Of the 181 serum samples (18 were diluted and 16 were spiked samples). All the samples were measured in singlet.

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

Test	n	Slope	Intercept	r	Sample range (U/L)
S Test CA	181	0.977	-0.07	0.978	2.4 – 14.5

Performance for the S Test CA was evaluated at four Physician Office Laboratories with a total of four operators who are typical operators at these sites. Operators ran from 52 or more unaltered clinical serum samples obtained from each site as well as 8 diluted and 6 spiked samples. The S Test CA 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 (U/L)
CA	Lab A	54	0.948	0.28	0.929	2.7 -11.7
	Lab B	54	0.953	0.38	0.944	2.7 -11.7
	Lab C	52	0.929	0.64	0.934	2.7 -11.7
	Lab D	55	0.946	0.60	0.965	2.7 -11.7

b. *Matrix comparison:*

A serum / plasma comparison study was performed for the S-Test CA assay. Thirty paired samples were assayed on the S40 System. Two samples were spiked and four samples were diluted to help cover the assay range. The correlation was as follows:

$$y = 0.962x + 0.4, r = 0.985, \text{ range } 4.1-14.5$$

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:

Eighty-four (84) normal serum samples for CA were evaluated on the S40 Clinical Analyzer to determine if the reference ranges of the predicate (ACE Clinical Analyzer) could be transferred to the new assays. The sponsors' acceptance criterion is 90% of the assay results for the normal samples are within the predicate range. Analysis confirmed sufficient agreement (6.0% non-congruent results for calcium, sponsor specification $\leq 10\%$) to transfer the reference range.

Expected values – 8.5-10.5 mg/dL

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.