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

A. 510(k) Number:

k080073

B. Purpose for Submission:

New device

C. Measurand:

Creatinine (CRE)

D. Type of Test:

Quantitative

E. Applicant:

Alfa Wassermann Diagnostic Technology, Inc.

F. Proprietary and Established Names:

S Test Creatinine (CRE)

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
JFY - Creatinine	Class II	21 CFR§ 862.1225	75 Chemistry

H. Intended Use:

1. Intended use(s):

   See Indications for Use below.

2. Indication(s) for use:

   The S-Test Creatinine Reagent is intended for the quantitative determination of Creatinine concentration in serum or heparin plasma using the S40 Clinical

Analyzer. Creatinine measurements are used in the diagnosis and treatment of renal diseases, in monitoring renal dialysis, and as a calculation basis for measuring other urine analytes. This test is intended for use in clinical laboratories or physician 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 Analyzer

I. Device Description:

Creatinine is a catabolic end-product produced by an irreversible loss of water from the creatine molecule and is an intermediate in energy generation for muscle contraction. Because the concentration of creatinine in blood increases with kidney failure, uremia, etc., it is a key factor in diagnosis of these diseases and judging their progress. The S-Test Creatinine Assay is based on enzymatic measurement of creatinine, after removal of creatine from the sample.

J. Substantial Equivalence Information:

1. Predicate device name(s):

ACE plus ISE/Clinical Chemistry System, Alfa Wassermann

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

k930104

3. Comparison with predicate:

Creatinine (CRE):

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

Differences		
Item	S40 Clinical Analyzer S Test ALP Reagent	ACE plus ISE Clinical Chemistry System
Sample Volume	12 µL	20 µL
Measuring Range	0.3-15 mg/dL	0.2-25 mg/dL
Detection Limit	0.3 mg/dL	0.2 mg/dL

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)
LSI 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:

S Test CRE - In the first reaction, the sample creatine (which interferes with enzymatic creatinine measurements) is decomposed into water and oxygen by creatine amidinohydrolase, sarcosine oxidase, and catalase. In the second reaction, the creatinine in the sample is converted to creatine by creatinine amidohydrolase and is then converted to sarcosine by creatine amidinohydrolase. The hydrogen peroxide produced by sarcosine oxidase, N-ethyl-N-sulfobutyl-m toluidine (ESBmT) and 4-aminoaminoantipyrine are oxidized and condensed to a reddish-purple pigment via peroxidase enzyme. Creatinine concentration is determined by measuring the absorbance of the produced quinine pigment.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

    a. *Precision/Reproducibility:*
       In-house precision studies were conducted by testing human serum pools at three levels. The samples were run three times a day five days using one instrument. The three levels were assayed 2 times per run, 2 runs per day, for a total of 22 days. Results are summarized below.

CRE

Sample 1 Mean = 0.61 mg/dL CRE	Within Run	Between Run	Between Day	Total
Coefficient of Variation	9.6%	8.7%	11.4%	17.2%

Sample 2 Mean = 1.70 mg/dL CRE	Within Run	Between Run	Between Day	Total
Coefficient of Variation	2.9%	4.2%	3.6%	6.3%

Sample 3 Mean = 6.43 mg/dL CRE	Within Run	Between Run	Between Day	Total
Coefficient of Variation	1.3%	3.4%	2.2%	4.3%

Precision studies were also conducted at three Physician Office Laboratories (POL) with four trained operators typically found in these settings. Human serum pools at three concentrations were tested three times a day for five days on four instruments (one at each lab). The results are presented below:

Lab	Sample	Mean	%CV	
			Within-Run	Total
In-House	1	1.0	5.2%	5.2%
POL 1	1	1.0	10.1%	10.8%
POL 2	1	1.0	2.6%	2.6%
POL 3	1	1.0	4.0%	4.6%
In-House	2	3.5	3.7%	3.7%
POL 1	2	3.5	2.3%	2.4%
POL 2	2	3.4	1.2%	1.4%
POL 3	2	3.5	2.6%	2.7%
In-House	3	12.7	1.2%	1.3%
POL 1	3	12.5	2.1%	2.0%
POL 2	3	12.6	1.0%	1.7%
POL 3	3	12.7	1.3%	1.7%

b. *Linearity/assay reportable range:*

The reportable range for creatinine is 0.3 to 14.8 mg/dL. This range is supported by the limit of detection study (section M.1.d below), the method comparison (section M.2.a below), and the linearity shown below.

Linearity across the assay range was confirmed by testing commercial linearity standards, 5 levels each with known commercial concentrations of creatinine. The assigned value of the highest sample was set to its mean value. The assigned values of the other levels were calculated by multiplying the mean value by the ratios obtained from the manufacturer. Each level was tested in replicates of four. Results are presented below:

CRE			
Sample	Assigned Value mg/dL	Measured Value mg/dL	% Recovery
1	0.00	0.00	NA
2	0.98	0.98	99%
3	4.92	4.93	100%
4	9.83	9.85	100%
5	14.75	14.75	100%
Linear Regression: $y = 1.001x - 0.000$, $r^2 = 0.9999$			

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

The S Test BUN cartridges are factory calibrated and traceable to the NIST standard reference material SRM914.

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 ℃ the assay reagent is good until the expiration date.

d. *Detection limit:*

The Limit of Blank and Limit of Detection was determined for each analyte by running a low sample and true blank sample for 3 days, 20 replicates/day for a total of 60 results. The testing was split between two instruments. The limit of detection was determined to be 0.3 mg/dL.

e. *Analytical specificity:*

Interference studies to determine the effects of Unconjugated Bilirubin, Hemolysis and Lipemia were performed. The sponsor states that interference is considered to be significant if the analyte recovery changes by more than 10%.

Assay performance claims have been established on the S40 clinical analyzer by testing a serum pool containing approximately 0.9 mg/dL creatinine to the following concentrations of each interferent: Unconjugated Bilirubin - 50 mg/dL; Hemolysis - 1000 mg/dL; Triglycerides - 1210 mg/dL.

Bilirubin: No significant interference below 12.5 mg/dL. Concentrations greater than 12.5 mg/dL bilirubin may cause interference.

Hemolysis: Negative interference occurred at all levels tested. Any level of hemolysis may cause interference. Do not use hemolyzed specimens.

Triglycerides: Negative interference occurred at all levels tested. Any level of lipemia may cause interference. Do not use lipemic specimens.

Lipemia (Intralipid): No significant interference.

f. *Assay cut-off:*

Not applicable

2. <u>Comparison studies:</u>

a. *Method comparison with predicate device:*
A series of 65 serum specimens with CRE values ranging from 0.6 to 14.6 mg/dL were assayed in singlicate on the S40 Clinical Analyzer using S-Test CRE Reagent (RC0011) (y) and the ACE Clinical Chemistry System (x). Least-squares regression analysis (Deming) yielded the following results:

Regression Equation	y = 1.016x – 0.15
Correlation Coefficient	0.9984
Std Error Est.	0.16
Confidence Interval Slope	1.002 to 1.031
Confidence Interval Intercept	-0.20 to -0.10

Further studies were done in four separate POL sites. These studies were conducted by personnel without formal medical technology education. The

studies consisted of running 49 or more serum samples with varying levels of creatinine in singlicate on the S40 Clinical Analyzer and the ACE Clinical Chemistry System, with the following linear regression data:

Lab	n	Range	Regression Equation	Correlation Coefficient	Standard Error	Confidence Interval Slope	Confidence Interval Intercept
A	49	0.5-13.9	y = 1.032x - 0.12	0.9987	0.25	1.017 to 1.048	-0.20 to -0.03
B	50	0.7-14.6	y = 1.033x - 0.04	0.9965	0.34	1.008 to 1.058	-0.18 to 0.10
C	50	0.6-14.6	y = 1.040x - 0.28	0.9977	0.29	1.019 to 1.060	-0.38 to -0.18
D	50	0.4-14.6	y = 1.021x - 0.06	0.9983	0.25	1.003 to 1.038	-0.14 to 0.03

b. *Matrix comparison:*

A study was performed by running 29 CRE determinations on paired samples drawn from the same patients in serum and heparin plasma tubes at two POL labs. These collections occurred on five separate days. Because samples with high CRE levels occur very rarely at POL sites, six samples were spiked with a solution containing a high level of creatinine. The serum results ranged from 0.6 to 13.6 mg/dL. Least-squares regression analysis (Deming) yielded the following results:

Regression Equation	y = 1.004x - 0.02
Correlation Coefficient	0.9983
Std. Error Est.	0.21
Confidence Interval Slope	0.980 to 1.027
Confidence Interval Intercept	-0.14 to 0.09

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. <u>Clinical cut-off</u>**:**

Not applicable

5. <u>Expected values/Reference range:</u>

CRE: 0.4-1.2 mg/dL at 37ºC[1]

[1] Creatinine levels were determined on 168 normal apparently healthy individuals. The 2.5th and 97.5th percentile values were 0.4 and 1.2 mg/dL, respectively.

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.