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

A. 510(k) Number:

k072141

B. Purpose for Submission:

New device

C. Measurand:

Inorganic Phosphorous (IP) and Uric Acid (UA)

D. Type of Test:

Quantitative, Photometric

E. Applicant:

Alfa Wassermann Diagnostic Technology, Inc.

F. Proprietary and Established Names:

S Test Inorganic Phosphorous (IP) Reagent cartridge
S Test Uric Acid (UA) Reagent cartridge

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
CEO – Phosphorous	Class I reserved	21 CFR§ 862.1580	75 Chemistry
KNK – Uric Acid	Class I reserved	21 CFR§ 862.1775	75 Chemistry

H. Intended Use:

1. Intended use(s):

   See indications for use below.

2. Indication(s) for use:

   The S Test Inorganic Phosphorous Reagent is intended for the quantitative determination of inorganic phosphorous concentration in serum or heparin plasma using the S40 Clinical Analyzer. Measurements of phosphours (inorganic) are used in the diagnosis and treatment of various disorders, including parathyroid gland and kidney diseases and vitamin D imbalance. This test is intended for use in clinical laboratories or physician office laboratories. For in vitro diagnostic use only.

   The S Test Uric Acid Reagent is intended for the quantitative determination of uric acid concentration in serum or heparin plasma using the S40 Clinical Analyzer. Uric Acid are used in the diagnosis and treatment of numerous renal and metabolic disorders, including renal failure, gout, leukemia, psoriasis, starvation or other wasting conditions and of patients receiving cytotoxic drugs. This test is intended for the 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 Chemistry Analyzer

I. Device Description:

The Inorganic Phosphorous (IP) and Uric Acid (UA) are 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:

IP Reagent 1 – p-methylaminophenol sulfate and nonionic surface=active reagent, Reagent 2 – Ammonium molybdate and Sulfuric acid

UA Reagent 1 - N-ethyl-N-(2-hydroxy-3-sulfopropyl)-m-toluidine, sodium salt (TOOS),Peroxidase (POD) and 2-(N-morpholino) ethanesulfonic acid buffer (pH 6.9), Reagent 2 - Uricase (derived from yeast), 4-aminoantipyrine and 2-(N-morpholino) ethanesulfonic acid buffer (pH 6.9)

J. Substantial Equivalence Information:

1. Predicate device name(s):

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

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

   k931786 and k950164 respectively

3. Comparison with predicate:

   Inorganic Phosphorous:

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

Differences			
Item	S40 Clinical Analyzer S Test ALP Reagent	ACE plus ISE Clinical Chemistry System	Piccolo xpress Chemistry Analyzer
Sample Volume	12 µL	3 µL	100 µL
Measuring Range	1.2-9.9 mg/dL	0.2-20 mg/dL	0.2-20 mg/dL
Detection Limit	1.2 mg/dL	0.2 mg/dL	0.2 mg/dL

   Uric Acid (UA):

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

Differences			
Item	S40 Clinical Analyzer S Test ALP Reagent	ACE plus ISE Clinical Chemistry System	Piccolo xpress Chemistry Analyzer
Sample Volume	12 µL	3 µL	100 µL
Measuring Range	1.4-20.4 mg/dL	0.9-16 mg/dL	1-15 mg/dL
Detection Limit	1.4 mg/dL	0.9 mg/dL	1 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)
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:

S Test IP – Inorganic Phosphorous in a sample under acidic conditions reacts with ammonium molybdate to form an unreduced phosphomolybdate complex. The rate of increase in absorbance at 600 nm/700 nm is directly proportional to phosphorous concentration in the sample.

S Test UA – Uric Acid in a sample is oxidized by uricase to allantoin and hydrogen peroxide. The hydrogen peroxide oxidizes and condenses 4-aminoantipyrine and n-ethyl-N-(2-hydroxy-3-sulopropyl)-m-touluidine under the influence of peroxidase to produce a reddish-purple pigment. The rate of increase at absorbance at 600/800 nm, is directly proportional to the uric acid concentration in the sample.

M. Performance Characteristics (if/when applicable):

1. <u>Analytical performance:</u>

   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:

	IP mg/dL			
			%CV or SD (unit)	
Lab	Sample	Mean	Within Run	Total
In-House	1	1.9	2.1%	2.4%
POL 1	1	1.9	2.2%	2.2%
POL 2	1	1.9	1.9%	1.9%
POL 3	1	1.8	3.4%	3.4%
In-House	2	4.1	1.9%	2.1%
POL 1	2	4.2	1.4%	1.5%
POL 2	2	4.1	1.2%	1.3%
POL 3	2	4.1	1.5%	1.8%
In-House	3	8.3	1.7%	1.6%
POL 1	3	8.5	0.9%	1.2%
POL 2	3	8.4	1.4%	1.7%
POL 3	3	8.3	1.3%	1.4%
	UA mg/dL			
			%CV or SD (unit)	
Lab	Sample	Mean	Within Run	Total
In-House	1	2.9	2.1%	2.3%
POL 1	1	3.0	2.2%	2.2%
POL 2	1	2.9	1.4%	1.6%
POL 3	1	2.9	1.5%	1.5%
In-House	2	6.0	2.2%	2.2%
POL 1	2	6.2	1.3%	1.3%
POL 2	2	6.1	0.7%	0.7%
POL 3	2	6.1	1.0%	1.2%
In-House	3	15.5	1.0%	1.0%
POL 1	3	15.7	1.0%	1.1%
POL 2	3	15.8	0.3%	0.9%
POL 3	3	15.6	0.8%	1.2%

b. Linearity/assay reportable range:

Linearity across the assay range was confirmed by testing commercial linearity standards with 5 levels each with known concentrations of IP and UA. Each level was tested in replicates of four. Results are presented below:

Inorganic Phosphorous			
Sample	Assigned Value mg/dL	Measured Value mg/dL	% Recovery
1	0.71	0.90	+0.2 mg/dL
2	2.84	3.35	+0.5 mg/dL
3	5.67	5.70	100.5%
4	7.09	7.63	+0.5 mg/dL
5	9.93	9.93	100%
Linear regression $y = 0.9739x + 0.366$, $r^2 = 0.9928$			
Uric Acid			
1	0.92	0.90	98%
2	2.76	2.70	98%
3	4.22	3.48	-0.7 mg/dL%
4	6.79	6.30	-0.5 mg/dL
5	11.64	11.35	98%
6	16.49	16.03	97%
7	20.39	20.38	100%
Linear regression $y = 1.005x – 0.264$, $r^2 = 0.9984$			

The reportable range is 1.2–9.9 mg/dL for Inorganic Phosphorous (IP) and 1.4-20.4 mg/dL for Uric Acid (UA).

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

The S Test IP and S Test UA cartridges are factory calibrated and traceable to the NIST standard Reference materials 200a and 913a respectively. 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 ºC the assay reagent is good until the expiration date.

d. Detection limit:

The Limit of Blank and Limit of Detection were determined for each analyte by running a low sample and saline sample for 3 days, 20 replicates/day for a total of 60 results. The testing was split between two instruments. The limits of detection were determined to be 1.2 mg/dL for inorganic phosphorus and 1.4 mg/dL for uric acid.

e. Analytical specificity:

Interference studies to determine the effects of Unconjugated Bilirubin, Hemolysis and Lipemia were performed. Seven serum pools containing approximately 3.6 mg/dL IP and 4.8 mg/dL UA were spiked with various 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%.

IP – There was no significant interference from bilirubin. No significant interference of lipemia at concentration of 63,125 and 250 mg/dl. There was a positive interference of (>17%) at 500 mg/dL and above. Hemoglobin testing showed a positive interference (>14%) at all levels. The sponsor states that users should not use hemolyzed specimens.

UA - There was no significant interference from bilirubin. A positive interference at any level of hemoglobin was observed. The sponsor states that users should not use hemolyzed specimens. Intralipid of 250 mg/dL and above may cause interference. There was a positive interference of (>14%) at 500 mg/dL and above.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Clinical correlation studies were performed comparing the S-Test IP and UA results generated on the S40 Clinical analyzer against the results from the ACE Clinical analyzer using 95 IP and 183 UA serum samples. Of the 95 IP samples (77 were unaltered clinical patient samples, 9 were dilutes and 9 were spiked samples) and 183 UA samples (143 were unaltered clinical patient samples, 16 were dilutes and 24 were spiked samples). All the samples were measure in singlet.

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

Test	n	Slope	Intercept	r	Sample range (U/L)
S Test IP	95	1.088	0.16	0.976	1.1-8.9
S Test UA	183	1.045	-0.76	0.974	2.9-20.2

Performance for the S Test IP and S Test UA was evaluated at three Physician Office Laboratories with a total of three operators who are typical operators at these sites. Operators ran for IP 40-41 unaltered clinical serum samples, site one also ran 8 diluted and 7 spiked, site 2 ran 8 diluted and 9 spiked and site 3 ran 8 diluted and 8 spiked samples. The UA assay all sites ran 40 unaltered clinical samples, site 1 additional ran 9 diluted and 5 spiked, site 2 ran 8 diluted and 8 spiked and site 3 ran 8 dilutes and 6 spiked samples. The S Test IP and UA 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)
IP	Lab A	57	1.044	0.15	0.998	0.9- 8.9
	Lab B	56	1.053	0.19	0.995	1.0-9.1
	Lab C	56	1.101	0.16	0.992	1.2-8.4
UA	Lab A	54	1.062	-1.03	0.995	2.6-17.6
	Lab B	56	1.016	-0.60	0.992	3.0-18.9
	Lab C	54	1.085	-0.18	0.967	2.8-14.7

b. Matrix comparison:

A serum / plasma comparison test was performed for the S-Test IP and S-Test UA assays. Thirty- three paired IP and thirty-two paired UA samples were assayed on the S40 System. The IP comparison eight of the samples were spiked and one sample was diluted, and the UA comparison had 8 spiked samples to help cover the assay range. The correlation is as follows:

IP $y = 1.043x - 0.08$, $r = 0.996$, range 1.2-9.5 mg/dL

UA $y = 1.052 – 0.21$, $r = 0.9975$, range 1.7-17.1 mg/dL

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:

   Eighty-one (81) normal serum samples for IP and UA 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 (9.9% IP and 2.4% UA non-congruent results, sponsor specification ≤10%) to transfer the reference range.

   IP – 2.7-4.5 mg/dL
   UA – 2.6-7.2 mg/dL (3.5-7.2 male and 2.6-6.0 female)

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.