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

A. 510(k) Number:

k050652

B. Purpose for Submission:

Notification of intent to market 3 assays: SpotChem II Creatinine, Amylase and Alkaline Phosphatase (ALP).

C. Measurand:

Creatinine, Amylase and Alkaline Phosphatase (ALP)

D. Type of Test:

Quantitative, Colorimetric

E. Applicant:

Arkray, Inc.

F. Proprietary and Established Names:

Spotchem II Creatinine
Spotchem II Amylase
Spotchem II Alkaline Phosphatase (ALP)

G. Regulatory Information:

1. Regulation section:

   Creatinine - 21CFR §862.1225; Creatinine test system
   Amylase - 21CFR §862.1070; Amylase test system
   ALP - 21CFR §862.1050; Alkaline phosphatase or isoenzymes test system

2. Classification:

   Class II

3. Product code:

   Creatinine – CGX, Alkaline Picrate, Colorimetry, Creatinine
   Amylase – CIJ, Saccharogenic, Amylase
   ALP – CJE, Nitrophenylphosphate, Alkaline Phosphatase or isoenzymes

4. Panel:

   75 (Chemistry)

H. Intended Use:

1. Intended use(s):

   See indications for use below.

2. Indication(s) for use:

   The SPOTCHEM II Creatinine test is intended to measure the concentration of creatinine in serum, plasma and whole blood. 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.

   The SPOTCHEM II Amylase test is intended to measure amylase activity in serum, plasma and whole blood. Amylase measurements are used primarily for the diagnosis and treatment of pancreatitis (inflammation of the pancreas).

   The SPOTCHEM II ALP test is intended to measure ALP activity in serum, plasma and whole blood. Measurements of alkaline phosphatase or its isoenzymes are used in the diagnosis and treatment of liver, bone, parathyroid and intestinal diseases.

3. Special conditions for use statement(s):

   For Prescription use only

4. Special instrument requirements:

   These assays are intended for use on the SpotChem EZ Analyzer (k040332).

I. Device Description:

The SpotChem II Creatinine, Amylase and ALP assays are in vitro diagnostic procedures intended to measure creatinine, amylase and ALP quantitatively in human serum and plasma on the SpotChem EZ Analyzer.

The device is composed of a plastic strip to which a multi-layered test field is affixed. The layers consist of a sample-retention layer, a layer containing the reagent and a support layer.

A fixed amount of serum or plasma is placed on the test field of the reagent strip. The serum or plasma spreads in a uniform fashion across the entire surface of the sample retention layer. The serum or plasma then permeates into the reagent layer where the reaction is initiated.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Vitros Creatinine Slides, 821 2763
   PolyChem Amylase kit, AMY500
   PolyChem ALP kit, ALP500

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

   k001769
   k020852
   k020852

3. Comparison with predicate:

	Creatinine	Amylase	ALP
Predicate Methodology	Colorimetric, enzyme-based	Colorimetric enzyme-based	Colorimetric
Test Methodology	Colorimetric	Colorimetric, enzyme-based	Colorimetric
Predicate Reagent Storage	2-8 °C	2-8 °C	2-8 °C
Test Reagent Storage	2-8 °C	2-8 °C	2-8 °C
Predicate Sample types	Serum/Plasma, Urine	Serum/Plasma, Urine	Serum/Plasma,
Test Sample Types	Serum/Plasma, Whole blood	Serum/Plasma, Whole blood	Serum/Plasma, Whole blood
Predicate Controls	Recommended	Recommended	Recommended
Test Controls	Recommended	Recommended	Recommended

Correlation with Predicate device	N = 50. Samples spanned from 0.7 – 11.8 mg/dL. The regression equation was y = 0.926x + 0.184 and r = 0.997.	N = 40. Samples spanned from 17 – 738 IU/L. The regression equation was y = 1.059x – 6.206 and r = 0.998	N = 40. Samples spanned from 43 - 814 IU/L. The regression equation was y = 0.971x – 0.218 and r = 0.990.

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

None referenced

L. Test Principle:

Creatinine in serum or plasma reacts with 3,5-dinitrobenzoic acid under alkaline conditions to form a red color. During the reaction, the reagent layer is completely dissolved and absorbed by the sample-retention layer. These two layers thus form a single detection layer. The intensity of the red chromogen at 550 nm by reflectance spectrophotometry is directly proportional to the creatinine concentration in the sample.

α-amylase in serum or plasma reacts with the substrate, benzylidene-p-nitrophenol-maltoheptaoside (BG_7-pNP) and hydrolyzes it to form G_n-pNP (n=1-5). The G_n-pNP is rapidly hydrolyzed by the conjugate enzymes, glucoamylase and α-glucosidase, to liberate p-nitrophenol. During the reaction, the reagent layer is completely dissolved and is absorbed by the sample-retention layer. These two layers thus form a single detection layer. The rate, at which the yellow color is generated as measured at 405 nm by reflectance spectrophotometry, is directly proportional to the amylase activity in the sample.

ALP in serum or plasma reacts with the substrate, p-nitrophenylphosphate and hydrolyzes it to p-nitrophenol and phosphate. During the reaction, the reagent layer is completely dissolved and is absorbed by the sample-retention layer. These two layers thus form a single detection layer. The rate, at which the yellow color is generated as measured at 405 nm by reflectance spectrophotometry, is directly proportional to ALP activity in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. *Precision/Reproducibility:*

      Intra-assay precision was assessed by assaying three control samples twenty times in one run. Acceptance criteria is a CV of <5%. Inter-assay precision

was assessed by assaying three control samples in duplicate in ten runs over five days. Acceptance criteria is a CV<10%. The results are presented in the tables below:

Intra Assay Precision on SpotChem EZ Analyzer

Analyzer SpotChem		Level 1	Level 2	Level 3
Creatinine	N	20	20	20
	Mean (mg/dL)	1.23	1.51	4.45
	SD	0.055	0.060	0.076
	%CV	4.5	4.0	1.7
Amylase	Mean (mg/dL)	69.2	298.4	506.7
	SD	3.28	13.59	10.73
	%CV	4.7	4.6	2.1
ALP	Mean (mg/dL)	59.7	223.6	431.2
	SD	1.95	7.95	14.12
	%CV	3.3	3.6	3.3

Inter Assay Precision on SpotChem EZ Analyzer

Analyzer SpotChem		Level 1	Level 2	Level 3
Creatinine	Days	5	5	5
	n	20	20	20
	Mean (mg/dL)	1.29	1.50	4.40
	SD	0.091	0.069	0.110
	%CV	7.1	4.6	2.5
Amylase	Mean (mg/dL)	69.5	290.1	494.1
	SD	2.28	7.28	18.17
	%CV	3.3	2.5	3.7
ALP	Mean (mg/dL)	58.7	222.4	425.9
	SD	1.79	5.65	16.60
	%CV	3.0	2.5	3.9

Whole blood samples with known levels of Creatinine, Amylase and ALP were mixed. Ten replicates of each sample within one run. Acceptance criteria is a CV of <5%. The results are presented in the table below:

Analyzer SpotChem	Creatinine	Amylase	ALP
Mean	2.66	46	307.2
Minimum	2.5	43	294
Maximum	2.9	49	321
Std. Dev	0.126	2.26	8.57
% CV	4.74	4.91	2.78
Std Error	0.04	0.71	2.71

b. *Linearity/assay reportable range:*

The linearity was assessed by assaying serial dilutions. The linearity claim is based on a percent deviation of $\leq$ 5% at the two highest analyte concentrations. The results obtained were as follows: Creatinine up to 37.9 mg/dL, Amylase up to 800 IU/L and ALP up to 859.3 IU/L.

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

The calibration set points are fixed by the manufacturer and are unique with each reagent lot and stored on the magnetic card provided with each kit lot.

The principle of the calibration is to fix a two-point calibration curve for a given lot into the memory of the instrument. The sample absorbances are then read off this fixed curve by the instrument and the concentration is calculated and the results are provided by the software.

The magnetic card has values of the basic calibration curve (Cal-Low (a) and Cal-High (b)) and its own measured value (Cal-Low (A) and Cal-High (B)). During calibration, the SpotChem EZ reads these 4 values from magnetic card, and calculates the calibration to be A->a, B->b. To assign A and B: average on n=18 tests x High (for B) and Low (for A) in each lot with Calibrator (A and B indicated value of calibrator).

The value of the calibrator is assigned by the manufacturer by assessing the mean value of 3 lots x n=6 x 5 days x 2 instruments x High (for b) and Low (for a).

Control values are determined using previously cleared control material (k942458). The value assignment protocol is as follows: a minimum of five vials of each control level is required for value assignment. One vial is required for each day and will be tested on three different instruments to produce a minimum of 10 replicates on each instrument. Each instrument will be calibrated each testing day for five testing days.

d. *Detection limit:*

Functional sensitivity was assessed by diluting a pool to 10 different concentrations below the lower limit of the analyte range. Each dilution was assayed in replicates of ten. The mean, standard deviation and percent coefficient of variation were calculated for the ten replicates of each dilution. The functional sensitivity of the test was defined at the value of the dilution where the CV is approximately 20% (taking into consideration that the actual mean was within $\pm$10% of the expected target). It was determined that functional sensitivity was 0.66 mg/dL with a CV of 7.8% for creatinine, 12.6

IU/L with a CV of 4.1% for amylase and 25.4 IU/L with a CV of 2.8% for ALP.

e. *Analytical specificity:*

Studies were performed to assess common or known substances that could interfere with the method. A summary of the data for know interferents appears for the common interferents in the table below:

Sample	Creatinine Highest Level Tested with No Interference	Amylase Highest Level Tested with No Interference	ALP Highest Level Tested with No Interference
Hemoglobin	300 mg/dL	100 mg/dL	250 mg/dL
Bilirubin	15.21 mg/dL	3.16 mg/dL	7.56 mg/dL
Triglycerides	285 mg/dL	337.4 mg/dL	423 mg/dL

f. *Assay cut-off:*

Not applicable.

2. Comparison studies:

a. *Method comparison with predicate device:*

Clinical correlation studies were performed comparing the SpotChem II amylase and ALP results generated on the SpotChem EZ analyzer against the results from the PolyChem Analyzer using serum samples. The creatinine results were generated on the SpotChem EZ analyzer against results from the Vitros 750 creatinine slides using serum samples. The correlations are as follows:

Creatinine $y = 0.926x + 0.184$, $r = 0.997$, $n = 50$, range 0.7–11.8 mg/dL
Amylase $y = 1.059x – 6.206$, $r = 0.998$, $n = 40$, range 17-738 IU/L
ALP $y = 0.971x-0.218$ $r = 0.990$, $n = 40$, range 43-814 IU/L

b. *Matrix comparison:*

Clinical correlation studies were performed comparing the creatinine, amylase and ALP results generated on the SpotChem EZ analyzer for serum (on the y axis) and whole blood (on the x axis). The correlations are as follows:

Creatinine $y = 0.961x + 0.085$, $r = 0.996$, $n = 23$, range 0.8-10.0 mg/dL
Amylase $y = 0.958x +1.393$, $r = 0.990$, $n = 20$, range 35-138 IU/L
ALP $y = 0.998x +2.760$, $r = 0.992$, $n = 20$, range 34-158 IU/L

Clinical correlation studies were performed comparing creatinine, amylase and ALP results generated on the SpotChem EZ analyzer for plasma (on the y axis) and whole blood (on the x axis). The correlations are as follows:

Creatinine y = 1.004x +0.037, r = 0.998, n = 23, range 0.8-9.7 mg/dL
Amylase y = 0.941x +3.857, r = 0.993, n = 20, range 32-138 IU/L
ALP y = 991x +1.513, r = 0.990, n = 20, range 35-158 IU/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:

   The following literature reference values are provided;
   Creatinine – Adult male 0.7-1.3 mg/dL, 62-115 µmol/L
                   Adult female 0.6 -1.1 mg/dL, 53 – 97 µmol/L
   Amylase –   25-125 IU/L, 0.42 -2.09 µkat/L
   ALP -   40-150 IU/L, 0.67 – 2.50 µkat/L

   1. Tietz, N.W., Fundamentals of Clinical Chemistry, Second Edition, W.B. Saunders Company, 1976.

   2. Tietz, N.W. Textbook of Clinical Chemistry, Second Edition, W.B Saunders Company, 1994

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.