

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

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

k051648

**B. Purpose for Submission:**

Notification of intent to market three assays – SpotChem II Inorganic Phosphorous, SpotChem II CPK, SpotChem II Uric Acid - on an existing device.

**C. Measurand:**

Phosphorus (Inorganic)  
Creatine phosphokinase  
Uric Acid

**D. Type of Test:**

Quantitative, colorimetric

**E. Applicant:**

Arkray, Inc.

**F. Proprietary and Established Names:**

SPOTCHEM II Inorganic Phosphorus  
SPOTCHEM II CPK  
SPOTCHEM II Uric Acid

**G. Regulatory Information:**

1. Regulation section:  
21CFR 862.1580: Phosphorus (inorganic) test system  
21CFR 862.1215: Creatine phosphokinase/creatine kinase  
21CFR 862.1775: Uric acid test system
2. Classification:  
Phosphorus (Inorganic) – Class I(reserved)  
Creatine phosphokinase/creatine kinase – Class II  
Uric Acid – Class I(reserved)

3. Product code:  
CEO - Phosphorus (inorganic)  
CGS - Creatine phosphokinase/creatine kinase  
KNK - Uric acid test system

4. Panel:

Chemistry (75)

#### **H. Intended Use:**

1. Intended use(s):

See indications for use.

2. Indication(s) for use:

The SPOTCHEM II Inorganic Phosphorus test is intended to measure inorganic phosphorous in serum, plasma, and whole blood. Measurements of inorganic phosphorous are used in the diagnosis and treatment of various disorders, including parathyroid gland and kidney disease, and vitamin D imbalance.

The SPOTCHEM II CPK test is intended to measure the activity of the enzyme creatine phosphokinase in serum, plasma, and whole blood. Measurements of creatine phosphokinase and isoenzymes are used in the diagnosis and treatment of myocardial infarction and muscle diseases such as progressive, Duchenne-type muscular dystrophy.

The SPOTCHEM II Uric Acid test is intended to measure uric acid in serum, plasma, and whole blood. Measurements of 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.

3. Special conditions for use statement(s):

For prescription use only.

4. Special instrument requirements:

SPOTCHEM EZ analyzer

## **I. Device Description:**

The SpotChem II Inorganic Phosphorus, CPK, and Uric assays are in vitro diagnostic procedures intended to measure inorganic phosphorus, CPK, and uric acid 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):  
PolyChem Inorganic Phosphorus, PHO500  
PolyChem CK, TCK500  
PolyChem Uric Acid, URA500
2. Predicate 510(k) number(s):  
PolyChem Inorganic Phosphorus: K020852/A002  
PolyChem CK: K020852/A007  
PolyChem Uric Acid: K020852/A025

3. Comparison with predicate:

	Inorganic Phosphorus	CPK	Uric Acid
Predicate Methodology	Colorimetric	Colorimetric enzyme-based	Colorimetric
Submitted Methodology	Colorimetric	Colorimetric enzyme-based	Colorimetric enzyme-based
Predicate Storage Temperature	2-8 °C	2-8 °C	2-8 °C
Submitted Storage Temperature	2-8 °C	2-8 °C	2-8 °C
Predicate Sample Matrix	Serum/Urine	Serum/Plasma, Urine	Serum/Plasma, Urine
Submitted Sample Matrix	Serum/Plasma, Whole blood	Serum/Plasma, Whole blood	Serum/Plasma, Whole blood
Predicate Controls	Recommended	Recommended	Recommended
Submitted Test Controls	Recommended	Recommended	Recommended
Correlation with Predicate device	N = 41. Samples spanned from 1.8 - 12.6 mg/dL. The regression equation was $y = 0.912x - 0.187$ and $r = 0.997$	N = 41. Samples spanned from 57 - 774 IU/L. The regression equation was $y = 0.948x - 1.056$ and $r = 0.992$	N = 41. Samples spanned from 1.7 - 11.9 mg/dL. The regression equation was $y = 0.991x - 0.239$ and $r = 0.996$

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

None referenced.

**L. Test Principle:**

Phosphorus in the sample is combined with molybdate to form a phosphomolybdate complex. In the presence of ascorbic acid, a reducing agent, this complex forms a strongly colored “molybdenum blue”. The rate at which the blue color is generated, as measured at 610 nm by reflectance spectroscopy, is directly proportional to the concentration of inorganic phosphorous in the patient sample.

In the presence of CPK, creatine phosphate reacts with ADP to form creatine and ATP. ATP is utilized in a subsequent reaction involving glucose and hexokinase to generate glucose-6-phosphate. Glucose-6-phosphate reacts with NADP in the presence of G6PDH to form NADPH. NADPH reacts with the dye tetrazolium violet to form the strongly colored purple chromogen complex. The rate at which the purple chromogen complex is formed, measured at 550 nm, is proportional the amount of CPK originally in the sample.

In the presence of uricase, uric acid reacts with oxygen and generates hydrogen peroxide. This generated hydrogen peroxide subsequently reacts with 4-aminoantpyrine and N-Ethyl-N-(2-hydroxy-3-sulfopropyl)-m-toluidine to form a red-purple reaction product. The absorbance of this product, measured at 550 nm, is proportional the concentration of uric acid in the sample. Ascorbic acid, a reducing agent that would interfere with this assay by reacting with the hydrogen peroxide, is removed from the sample by a comparatively fast reaction with Ascorbate oxidase.

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

1. Analytical performance:

*a. Precision/Reproducibility:*

Intra-assay precision was assessed by assaying three levels of control samples twenty times in one run. The company used an acceptance criterion of 5% CV. The results:

		Level 1	Level 2	Level 3
Number of Samples		20	20	20
Inorganic Phosphorus	Mean (mg/dL)	2.07	4.26	8.25
	SD (mg/dL)	0.080	0.106	0.150
	%CV	3.9%	2.5%	1.8%
CPK	Mean (IU/L)	64.9	158.9	505.1
	SD (IU/L)	2.78	6.96	20.95
	%CV	4.3%	4.4%	4.2%
Uric Acid	Mean (mg/dL)	3.34	6.04	9.46
	SD (mg/dL)	0.067	0.088	0.139
	%CV	2.0%	1.5%	1.5%

The company determined the intra-assay precision of their devices using whole blood. They performed 10 replicate measurements of one pooled blood sample in one day. The company used an acceptance criterion of 5% CV. The results:

		Whole Blood
Inorganic Phosphorus	Mean (mg/dL)	8.58
	SD (mg/dL)	0.204
	%CV	2.4%
CPK	Mean (IU/L)	265.9
	SD (IU/L)	12.31
	%CV	4.6%
Uric Acid	Mean (mg/dL)	7.89
	SD (mg/dL)	0.152
	%CV	1.9%

Inter-assay precision was assessed by assaying three levels of samples in duplicate in ten runs over 5 days. The company's acceptance criteria was a CV < 10%. The results:

		Level 1	Level 2	Level 3
Number of Samples		20	20	20
Inorganic Phosphorus	Mean (mg/dL)	1.99	4.22	7.99
	SD (mg/dL)	0.075	0.088	0.184
	%CV	3.8%	2.1%	2.3%
CPK	Mean (IU/L)	76.4	183.5	393.2
	SD (IU/L)	3.44	6.22	12.96
	%CV	4.5%	3.4%	3.3%
Uric Acid	Mean (mg/dL)	3.38	6.04	10.14
	SD (mg/dL)	0.079	0.088	0.223
	%CV	2.3%	1.5%	1.5%

*b. Linearity/assay reportable range:*

The linearity was assessed by assaying serial dilutions covering the concentration range of the assay. Serial dilutions sets were prepared using 7% BSA. The linearity claim is based on a percent deviation of < 5% at the two highest analyte concentrations. The inorganic phosphorous assay was shown to be linear up to 18.7 mg/dL. The CPK assay was found to be linear up to 993 IU/L. The uric acid assay was found to be linear up to 12.8 mg/dL.

*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. 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 absorbencies are then read off this fixed curve by the instrument, 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. The values of A and B are determined by the manufacture based on the average of 18 measurements each of the high and low calibrator. The value of the calibrator is assigned by the manufacturer by assessing the mean value of 3 lots measured 6 times a day for 5 days on 2 instruments for each level of calibrator.

Real time studies of the assay strips confirm a shelf life in excess of 25% of the shelf life claimed on the package insert when stored at 2-8 °C.

Control values are determined using previously cleared control material (k0942458). Values for the control material are obtained by sampling a minimum of five vials from a lot across 3 instruments and measured 10 times per instrument and vial. Each instrument is calibrated daily during the value assignment.

*d. Detection limit:*

Functional sensitivity was assessed by diluting a pool to 10 different concentrations below the lower limit of the normal 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 +10% of the expected target). The company determined that the functional sensitivity of the inorganic phosphorous was 0.64 mg/dL with a CV of 10.9%. The functional sensitivity of the CPK assay was 48.7 IU/L with a CV of 1.9%. The uric acid assay had a functional sensitivity of 1.63 mg/dL with a CV of 5.1%.

*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 in the table below:

	Inorganic Phosphorus	CPK	Uric Acid
Interference			
Hemoglobin	50 mg/dL	150 mg/dL	200 mg/dL
Bilirubin	8.76 mg/dL	6.54 mg/dL	2.18 mg/dL
Triglycerides	354.5 mg/dL	280.8 mg/dL	396.8 mg/dL

*f. Assay cut-off:*

Not applicable for a device of this type

2. Comparison studies:

*a. Method comparison with predicate device:*

Clinical correlation studies were performed comparing the SpotChem II Inorganic Phosphorus, CPK, and Uric acid results generated on the SpotChem EZ analyzer against the results from the PolyChem analyzer using serum and plasma samples. The correlations were as follows:

Inorganic Phosphorus:  $y = 0.912x - 0.187$ ,  $r = 0.9967$ ,  $n = 41$ , range: 1.8 – 12.6 mg/dL

CPK:  $y = 0.948x - 1.056$ ,  $r = 0.9921$ ,  $n = 41$ , range: 57- 774 IU/L

Uric Acid:  $y = 0.964x - 0.297$ ,  $r = 0.983$ ,  $n = 41$ , range 0.7-5.3 mg/dL

*b. Matrix comparison:*

Clinical correlation studies were performed comparing the inorganic phosphorus, CPK, and uric results generated with serum and whole blood samples when performed on the SpotChem EZ analyzer. The correlations were as follows:

Inorganic Phosphorus:  $y = 0.994x - 0.019$ ,  $r=0.9814$ ,  $n=21$

CPK:  $y = 1.098x - 1.843$ ,  $r=0.9991$ ,  $n=20$

Uric Acid:  $y = 1.004x - 0.099$ ,  $r=0.9969$ ,  $n = 20$

3. Clinical studies:

*a. Clinical Sensitivity:*

Not applicable for a device of this type

*b. Clinical specificity:*

Not applicable for a device of this type

*c. Other clinical supportive data (when a. and b. are not applicable):*

Not applicable for a device of this type

4. Clinical cut-off:

Not applicable for a device of this type

5. Expected values/Reference range:

Inorganic Phosphorus<sup>(1)</sup>: 2.5-4.5 mg/dL

Uric acid<sup>(1)</sup>: 3.5 – 7.2 mg/dL (male)  
2.6 – 6.0 mg/dL (female)

CPK<sup>(2)</sup>: 10-80 IU/L male  
10-70 IU/L female

<sup>(1)</sup> Tietz, N.W., "Textbook of Clinical Chemistry 2<sup>nd</sup> ed.", W.B. Saunders Co., Philadelphia (1994)

<sup>(2)</sup> Szasz, G., Gruger, W., Bernt, E., Clin. Chem, 22(5): 650-656 (1976)

**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.



