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

A. 510(k) Number:

K051432

B. Purpose for Submission:

Notification of intent to market 3 assays: SpotChem II Total Bilirubin, Total Protein and Albumin tests.

C. Measurand:

Total Bilirubin, Total Protein and Albumin

D. Type of Test:

Quantitative, Colorimetric

E. Applicant:

Arkray, Inc.

F. Proprietary and Established Names:

Spotchem II Total Bilirubin
Spotchem II Total Protein
Spotchem II Albumin

G. Regulatory Information:

1. <u>Regulation section:</u>

   Total Bilirubin - 21CFR §862.1110; Bilirubin (total or direct) test system
   Total Protein - 21CFR §862.1635 Total Protein test system
   Albumin - 21CFR §862.1035; Albumin test system

2. <u>Classification:</u>

   Class II

3. Product code:

Total Bilirubin – CIG, Diazo Colorimetry, Bilirubin
Total Protein – CEK, Biuret (Colorimetric), Total Protein
Albumin – CIX, Bromcresol Green Dye-Binding, Albumin

4. Panel:

75 (Chemistry)

H. Intended Use:

1. Intended use(s):

See indications for use below.

2. Indication(s) for use:

The SPOTCHEM II Total Bilirubin test is intended to measure the levels of
bilirubin in serum, plasma and whole blood. Measurements of the levels of
bilirubin are used in the diagnosis and treatment of liver, hemolytic hematological
and metabolic disorders including hepatitis and gall bladder block.

The SPOTCHEM II Total Protein test is intended to measure Total Protein in
serum, plasma and whole blood. Measurements of Total Protein are used in the
diagnosis and treatment of a variety of diseases involving the liver, kidney, or
bone marrow as well as other metabolic and nutritional disorders.

The SPOTCHEM II Albumin test is intended to measure Albumin concentration
in serum, plasma and whole blood. Measurements of Albumin are used in the
diagnosis and treatment of numerous diseases involving the liver or kidneys.

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 Total Bilirubin, Total Protein and Albumin assays are in vitro diagnostic procedures intended to measure Total Bilirubin, Total Protein and Albumin quantitatively in human serum and plasma (whole blood) 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 Total Bilirubin, TLB500
   PolyChem Total Protein, TPR500
   PolyChem Albumin, ALB500

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

   k020852/A036, k020852/A019 and k020852/A003 respectively

3. Comparison with predicate:

	Total Bilirubin	Total Protein	Albumin
Predicate Methodology	Colorimetric,	Colorimetric	Colorimetric
Test Methodology	Colorimetric	Colorimetric	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	Serum/Plasma	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 = 41. Samples spanned from 0.4 – 8.8 mg/dL. The regression equation was y = 0.918x + 0.125 and r = 0.997.	N = 41. Samples spanned from 3.5 – 10.7 g/dL. The regression equation was y = 0.993x – 0.037 and r = 0.979.	N = 42. Samples spanned from 1.6 - 5.7 g/dL. The regression equation was y = 1.087x – 0.530 and r = 0.957.

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

None referenced

L. Test Principle:

Both indirect and direct bilirubin in serum or plasma reacts with diazonium salt in the presence of dyphylline and an acidic buffer to form a red azobilirubin as a final product. 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 color at 550 nm by reflectance spectrophotometry is proportional to the concentration of Total Bilirubin in the sample.

Protein in serum or plasma reacts with copper ion at high pH to form a blue-purple color. 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 intensity of the blue-purple color as measured at 550 nm by reflectance spectrophotometry, is proportional to the concentration of Total Protein in the sample.

Albumin in serum or plasma is combined with bromcresol green (BCG) in acidic conditions to form a blue-green complex. 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 intensity of the blue-green color as measured at 610 nm by reflectance spectrophotometry, is proportional to the concentration of Albumin in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. *Precision/Reproducibility:*

   Intra-assay precision was assessed by three control samples. Twenty replicates of each sample within 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
Total Bilirubin	N	20	20	20
	Mean (mg/dL)	0.69	1.68	6.5
	SD	0.031	0.062	0.266
	%CV	4.5	3.7	4.1
Total Protein	Mean (mg/dL)	5.19	7.57	9.49
	SD	0.107	0.232	0.290
	%CV	2.1	3.1	3.1
Albumin	Mean (mg/dL)	2.47	4.90	5.30
	SD	0.073	0.147	0.103
	%CV	3.0	3.0	1.9

Inter Assay Precision on SpotChem EZ Analyzer.

Analyzer SpotChem		Level 1	Level 2	Level 3
Total Bilirubin	Days	5	5	5
	n	20	20	20
	Mean (mg/dL)	0.70	1.64	6.28
	SD	0.000	0.088	0.231
	%CV	0.0	5.4	3.7
Total Protein	Mean (mg/dL)	5.11	7.47	9.49
	SD	0.137	0.237	0.323
	%CV	2.7	3.2	3.4
Albumin	Mean (mg/dL)	2.45	4.84	5.31
	SD	0.061	0.135	0.112
	%CV	2.5	2.8	2.1

Intra assay precision was assessed using a whole blood sample. Ten replicates of the same sample within one run. Acceptance criteria is a CV of <5%. The results are presented in the table below:

Analyzer SpotChem	Mean	SD	% CV
Total Bilrubin	4.09	0.166	4.1%
Total Protein	8.92	0.326	3.7%
Albumin	5.37	0.263	4.9%

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: Total Bilirubin up to 16.4 mg/dL, Total Protein up to 10.7 g/dL and Albumin up to 6.6 g/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 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 $\pm10\%$ of the expected target). It was determined that functional sensitivity was 0.3 mg/dL with a CV of 0.0% for Total Bilirubin, 2.7 g/dL with a CV of 2.5% for Total Protein and 0.6 g/dL with a CV of 0.0% for Albumin.

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:

	Total Bilirubin	Total Protein	Albumin
Sample	Highest Level Tested with No Interference	Highest Level Tested with No Interference	Highest Level Tested with No Interference
Hemoglobin	150 mg/dL	300 mg/dL	150 mg/dL
Bilirubin	N/A	7.63 mg/dL	7.63 mg/dL
Triglycerides	302 mg/dL	334.6 mg/dL	436.1 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 Total Bilirubin, Total Protein and Albumin against the results from the PolyChem analyzer using serum samples. The correlations were as follows:

Total Bilirubin $y = 0.918x + 0.125$, $r = 0.997$, $n = 41$, range 0.4-8.8 mg/dL
Total Protein $y = 0.993x - 0.037$, $r = 0.979$, $n = 41$, range 3.5-10.7 g//dL
Albumin $y = 1.087x - 0.530$, $r = 0.957$, $n = 42$, range 1.6-5.7 g/dL

b. Matrix comparison:

Clinical correlation studies were performed comparing the Total Bilirubin, Total Protein and Albumin results generated on the SpotChem EZ analyzer for the specimen types of serum (on the y axis) and whole blood (on the x axis). The correlations were as follows:

Total Bilirubin $y = 0.977x + 0.004$, $r = 0.962$, $n = 20$
Total Protein $y = 1.055x - 0.125$, $r = 0.963$, $n = 22$
Albumin $y = 0.973x + 0.260$, $r = 0.917$, $n = 23$

Clinical correlation studies were performed comparing Total Bilirubin, Total Protein and Albumin results generated on the SpotChem EZ analyzer for the specimen types of plasma (on the y axis) and whole blood (on the x axis). The correlations were as follows :

Total Bilirubin $y = 0.988x - 0.004$, $r = 0.9897$, $n = 20$
Total Protein $y = 1.019x - 0.098$, $r = 0.9614$, $n = 22$
Albumin $y = 0.940x + 0.255$, $r = 0.9705$, $n = 23$

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 were provided;
Total Bilirubin; 0.2–1.0 mg/dL   3.4–17.1 mmol/L
Total Protein; 6.0-7.8 g/dl   60-78 g/L
Albumin; 3.5-5.0 g/dL   35-50 g/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.