

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

A. 510(k) Number: k050077

B. Purpose for Submission: Notification of intent to market 3 assays: SpotChem II Calcium, Magnesium and Blood Urea Nitrogen (BUN).

C. Measurand: Calcium, Magnesium and Blood Urea Nitrogen (BUN)

D. Type of Test: quantitative, colorimetric

E. Applicant: Arkray, Inc.

F. Proprietary and Established Names:

Spotchem II Calcium
Spotchem II Magnesium
Spotchem II Blood Urea Nitrogen (BUN)

G. Regulatory Information:

1. Regulation section:

Calcium 21CFR §862.1145; Calcium test system
Magnesium 21CFR §862.1495; Magnesium test system
BUN 21CFR §862.1770; Urea nitrogen test system

2. Classification:

Class II, Class I (reserved) and Class II; respectively

3. Product code:

Calcium – CIC, Cresolphthalein Complexone, Calcium
Magnesium – JGJ, Photometric, Magnesium
BUN – JGZ, o-Phthalaldehyde, Urea Nitrogen

4. Panel:

75 (Chemistry)

H. Intended Use:

1. Intended use(s):

The SpotChem II Calcium, Magnesium and BUN tests are in vitro diagnostic procedures intended to measure calcium, magnesium and BUN quantitatively in human serum and plasma on the SpotChem EZ analyzer.

2. Indication(s) for use:

Calcium measurements are used in the diagnosis and treatment of parathyroid disease, a variety of bone diseases, chronic renal disease and tetany (intermittent muscular contractions or spasms).

Magnesium measurements are used in the diagnosis and treatment of hypomagnesemia (abnormally low plasma levels of magnesium) and hypermagnesemia (abnormally high plasma levels of magnesium).

Blood Urea Nitrogen (BUN) measurements are used in the diagnosis and treatment of certain renal and metabolic 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 Calcium, Magnesium and BUN assays are in vitro diagnostic procedures intended to measure calcium, magnesium and Bun 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 Calcium kit CAL500
 Vitros BUN/UREA slides, 174 3418
 Vitros Mg slides, 825 5093

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

k020852
 k001885
 k023876

3. Comparison with predicate:

| | Calcium | BUN | Magnesium |
|-----------------------------------|---|---|--|
| Predicate Methodology | Colorimetric | Colorimetric enzyme-based | 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/Urine | Serum/Plasma, Urine | Serum/Plasma, Urine |
| 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. Range spanned from 5.6 – 16.0 mg/dL. The regression equation was $y = 1.048x - 0.719$ and $r = 0.984$ | N = 38. Range spanned from 7 – 85 mg/dL. The regression equation was $y = 1.037x - 0.411$ and $r = 0.995$ | N = 44. Range spanned from 0.7 - 5.3 mg/dL. The regression equation was $y = 0.964x - 0.297$ and $r = 0.983$. |

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

None referenced

L. Test Principle:

Calcium in the sample is combined with 0-cresolphthalein complexone (OCPC) under strong alkaline conditions to form a purple chelate. The intensity of the blue chromogen as measured at 575 nm by reflectance spectrophotometry is directly proportional to the calcium concentration in the sample.

Urea in the sample reacts with o-phthalaldehyde to produce 1,3-dihydroxyisoindoline (DHI). The carbonium ion of DHI reacts with N-1-naphthyl-N'-diethylethylenediamineoxalic acid under strong acidic conditions 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 chromogen as measured at 610 nm by reflectance spectrophotometry is directly proportional to the blood urea nitrogen concentration in the sample.

Magnesium in the sample is combined with o-cresolphthalein complexone (OCPC) under strong alkaline conditions to form a purple chelate. The intensity of the blue chromogen as measured at 575 nm by reflectance spectrophotometry is directly proportional to magnesium concentration in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

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

| Analyzer SpotChem | | Level 1 | Level 2 | Level 3 |
|-------------------|--------------|---------|---------|---------|
| Calcium | n | 20 | 20 | 20 |
| | Mean (mg/dL) | 8.00 | 10.46 | 12.41 |
| | SD | 0.290 | 0.404 | 0.554 |
| | %CV | 3.6% | 3.9% | 4.5% |
| BUN | Mean (mg/dL) | 15.3 | 23.4 | 69.4 |
| | SD | 0.47 | 0.67 | 2.30 |
| | %CV | 3.1% | 2.9% | 3.3% |
| Magnesium | Mean (mg/dL) | 0.97 | 2.14 | 3.97 |
| | SD | 0.047 | 0.088 | 0.142 |
| | %CV | 4.9% | 4.1% | 3.6% |

Inter Assay Precision on SpotChem EZ Analyzer.

| Analyzer SpotChem | | Level 1 | Level 2 | Level 3 |
|-------------------|--------------|---------|---------|---------|
| Calcium | Days | 5 | 5 | 5 |
| | n | 20 | 20 | 20 |
| | Mean (mg/dL) | 7.88 | 10.08 | 12.3 |
| | SD | 0.346 | 0.309 | 0.453 |
| | %CV | 4.4% | 3.1% | 3.7% |
| BUN | Mean (mg/dL) | 14.9 | 23.3 | 67.5 |
| | SD | 0.45 | 0.85 | 1.88 |
| | %CV | 3.0% | 3.7% | 2.8% |
| Magnesium | Mean (mg/dL) | .99 | 2.12 | 3.87 |
| | SD | 0.064 | 0.089 | 0.157 |
| | %CV | 6.5% | 4.2% | 4.1% |

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: Calcium up to 16.9 mg/dL, BUN up to 169.7 mg/dL and Magnesium up to 6.27 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 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 absorbences 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 $A \rightarrow a, B \rightarrow b$. 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 4.9 mg/dL with a CV of 3.3% for calcium, 6.6 mg/dL with a CV of 7.8% for BUN and 0.2 mg/dL with a CV of 0.0% for Magnesium.

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:

| | Calcium | BUN | Magnesium |
|---------------|---|---|---|
| Sample | Highest Level Tested with No Interference | Highest Level Tested with No Interference | Highest Level Tested with No Interference |
| Hemoglobin | 300 mg/dL | 300 mg/dL | 300 mg/dL |
| Bilirubin | 11.8 mg/dL | 12.0 mg/dL | 10.14 mg/dL |
| Triglycerides | 394 mg/dL | 285 mg/dL | 295.8 mg/dL |
| Magnesium | 5.3 mg/dL | | |
| Calcium | | | 15.5 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 Calcium results generated on the SpotChem EZ analyzer against the results from the PolyChem analyzer using serum and plasma samples and on the BUN and Magnesium results generated on the SpotChem EZ analyzer against results from the Vitros 750 BUN/UREA slides and Mg slides using serum and plasma samples. The correlations were as follows:

Calcium $y = 1.048x - 0.719$, $r = 0.984$, $n = 41$, range 5.6-16.0 mg/dL

BUN $y = 1.037x - 0.411$, $r = 0.995$, $n = 38$, range 7-85 mg/dL

Magnesium $y = 0.964x - 0.297$, $r = 0.983$, $n = 44$, range 0.7-5.3 mg/dL

b. *Matrix comparison:*

Clinical correlation studies were performed comparing the Calcium, BUN and Magnesium results generated against serum and whole blood samples when performed on the SpotChem EZ analyzer. The correlations were as follows:

Calcium $y = 1.002x - 0.062$, $r = 0.9846$, $n = 23$

BUN $y = 0.994x - 0.755$, $r = 0.9977$, $n = 21$

Magnesium $y = 1.095x - 0.088$, $r = 0.9755$, $n = 23$

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;

Calcium – 8.10-10.4 mg/dL, 2.02-2.60 mmol/L

BUN – 8-20 mg/dL, 2.9-7.1 mmol/L

Magnesium - 1.6-2.4 mg/dL, 0.70-0.99 mmol/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:

1. The submitted information in this premarket notification is complete and supports a substantial equivalence decision.