

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

A. 510(k) Number:

k061575

B. Purpose for Submission:

Clearance of a new device

C. Measurand:

Calcium

D. Type of Test:

Quantitative Absorbance Assay

E. Applicant:

Olympus America Inc.

F. Proprietary and Established Names:

Olympus Calcium Arsenazo reagent, OSR60117/OSR61117/OSR65117

G. Regulatory Information:

1. Regulation section:
21 CFR §862.1145 Calcium test system
2. Classification:
Class II
3. Product code:
CJY
4. Panel:
75 (Chemistry)

H. Intended Use:

1. Intended use(s):
Reagent for the quantitative determination of calcium in human serum, plasma and urine on automated clinical chemistry analyzers.
2. Indication(s) for use:
Olympus System reagent for the quantitative determination of calcium concentrations in human serum, plasma and urine on OLYMPUS analyzers. Measurement of calcium is used in the diagnosis and treatment of parathyroid disease, a variety of bone diseases, chronic renal disease and tetany (intermittent muscular contractions or spasms).
3. Special conditions for use statement(s):
For prescription use.

4. Special instrument requirements:
Olympus AU400/AU400E, AU600/AU640/AU640E, and AU2700/AU5400 Clinical Chemistry Analyzers.

I. Device Description:

Calcium Arsenazo III reagent consists of a solution containing 0.1-0.2% Arsenazo III, imidazol pH 6.9, Triton X-100 and preservatives.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Olympus Calcium Arsenazo III Reagent; Olympus Calcium oCPC Reagent
2. Predicate 510(k) number(s):
k982035; k922233.
3. Comparison with predicate:
The Olympus Calcium Arsenazo reagent is identical to the predicate (k982035) in the following ways: intended use, test principle, calibrator traceability and expected values. The reagent differs from the predicate (k982035) in the following ways:

Differences		
	Predicate device k982035	Proposed Reagent
Matrix	Serum/plasma	Serum, plasma and urine
Linearity (serum)	4-16 mg/dL	4-18 mg/dL
Interfering substances	Lipemia <10% up to 300 mg/dL Intralipid	Lipemia <10% up to 1000mg/dL Intralipid
On-board stability	30 days	90 days

The Olympus Calcium Arsenazo reagent is identical to the predicate (k922233) in the following ways: intended use, matrices, linear range for urine samples, calibrator traceability, and expected values. The reagent differs from the predicate (k922233) in the following ways:

Differences		
	Predicate device k922233	Proposed Reagent
Reagent	o-Cresolphthalein-complexone	Arsenazo III
Linearity (serum)	0-18 mg/dL	4-18 mg/dL
On-board stability	30 days	90 days

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

Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline (CLSI EP09-A2)

Interference Testing in Clinical Chemistry; Approved Guideline (CLSI EP 7-A)

Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline (CLSI EP5-A)

Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline (CLSI EP6-A)

L. Test Principle:

$\text{Ca}^{2+} + \text{Arsenazo III} \rightarrow \text{Ca-Arsenazo III complex (purple)}$

Calcium ions (Ca^{2+}) react with Arsenazo III (2,2'-[1,8-Dihydroxy-3,6-disulphonaphthylene-2,7-bisazo]-bisbenzenear-sonic acid) to form an intense purple-colored complex.

In this method, the absorbance of the Ca-Arsenazo III complex is measured bichromatically at 660/700nm. The resulting increase in absorbance of the reaction mixture is directly proportional to the calcium concentration in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Precision studies were run based on CLSI EP5-A recommendations, which consisted of running serum-based control material or urine-based control material over a multiple day period utilizing the new Olympus Calcium Arsenazo reagent. The results of these studies are shown below:

Serum:

AU400:

N=80	Within run		Total	
Mean, mg/dL	SD	CV%	SD	CV%
6.67	0.06	0.84	0.11	1.62
9.78	0.06	0.57	0.12	1.22
16.63	0.11	0.63	0.21	1.27

AU600/AU640E:

N=80	Within run		Total	
Mean, mg/dL	SD	CV%	SD	CV%
6.77	0.05	0.80	0.06	0.93
10.10	0.05	0.46	0.07	0.72
17.52	0.09	0.50	0.13	0.76

AU2700/AU5400:

N=80	Within run		Total	
Mean, mg/dL	SD	CV%	SD	CV%
6.45	0.04	0.57	0.06	0.95
10.06	0.07	0.65	0.10	0.96
16.77	0.08	0.48	0.16	0.94

Urine:

AU400:

N=80	Within run		Total	
Mean, mg/dL	SD	CV%	SD	CV%
0.50	0.07	13.31	0.05	10.68
22.26	0.26	1.15	0.37	1.66
37.51	0.36	0.95	0.57	1.52

AU600/AU640E:

N=80	Within run		Total	
Mean, mg/dL	SD	CV%	SD	CV%
0.45	0.01	2.14	0.02	3.67
22.72	0.14	0.61	0.27	1.18
38.12	0.24	0.62	0.47	1.23

AU2700/AU5400:

N=80	Within run		Total	
Mean, mg/dL	SD	CV%	SD	CV%
0.44	0.01	2.05	0.01	2.60
22.10	0.22	1.00	0.27	1.21
37.33	0.41	1.09	0.52	1.40

b. *Linearity/assay reportable range:*

Linearity evaluations were performed according to CLSI Document EP6-P. A series of at least ten analyte concentrations, covering the measuring range were prepared by dilution of a high pool sample. Each dilution was assayed in quadruplicate and the mean analytical results were plotted versus the relative analyte concentrations. The best fit line was calculated by linear regression and the deviations of the data from linearity were evaluated.

Serum: Data generated during this study indicate an acceptable assay recovery across the measuring range (4-18 mg/dL) for serum samples with percent recoveries within 3% of the predicted values.

Urine: Data generated during this study indicates an acceptable assay recovery across the measuring range (0.1 - 40 mg/dL) for urine samples with percent recoveries within 5% of the predicted values.

Samples with results in excess of the linear range should be repeated after dilution. Accurate dilution of samples using the recommended diluent (deionized water) was demonstrated by diluting multiple elevated samples at a 1:1.75 (serum) or 1:5 (urine) ratio. All samples tested recovered within 5% (serum) or 15% (urine) of the expected value.

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

On-board Stability: The stability of the reagent after storage on-board the instrument for maximum allowable time was tested by checking linearity and recovery. Results for reagents on-board the analyzer for 90 days were within the acceptance criteria set by the manufacturer. Protocols and acceptance criteria were reviewed and found to be acceptable.

d. *Detection limit:*

Functional Sensitivity: Precision results (40-fold determination) for a calcium concentration below 4.0 mg/dL, the lower limit of the measuring range for serum samples, were shown to have a CV of <20% for each instrument.

	Mean Concentration (mg/dL)	SD	CV %
AU400	0.24	0.039	16.7
AU2700	0.09	0.009	10.1
AU640	0.07	0.006	9.2

The results of this study support the functional sensitivity claim of <4.0 mg/dL of the proposed new Olympus Calcium Arsenazo reagent for use on the Olympus analyzers with serum samples.

Lowest Detectable Level - urine: Twenty consecutive measurements of a sample devoid of calcium were tested on the Olympus analyzers. The lowest detectable level was calculated as mean recovery plus three standard deviations. These measurements support the claimed measuring range of 0.1 - 40 mg/dL for urine.

	Lowest Detectable Level (mg/dL)
AU640	0.02
AU400	0.02
AU2700	0.07

e. Analytical specificity:

The Olympus Calcium Arsenazo assay was evaluated for interference using a protocol developed according to CLSI Document EP7-P. A pooled sample with an analyte level corresponding to a medical decision point for the assay was used. The sample was spiked with different levels of the potential interferent up to the maximum level which could be present in samples and tested four-fold at each level. The mean analytical result at each level was compared with that for the non-spiked sample. Interference from Bilirubin up to 40 mg/dL, Hemolysis up to 500 mg/dL hemolysate, and Lipemia up to 1000 mg/dL Intralipid was evaluated. No interference was observed for these substances.

f. Assay cut-off:
Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

Serum: A split sample method comparison was conducted with 107 serum samples using the Calcium Arsenazo OSR61117 assay compared to the predicate, the Olympus Calcium Arsenazo OSR6176 assay, on the AU640 Olympus analyzer.

Linear Regression equation: $Y = 1.003 X - 0.068$
Correlation coefficient: 0.999

Urine: A split sample method comparison was conducted with 118 urine samples using the Calcium Arsenazo OSR61117 assay compared to the predicate, the Olympus oCPC Calcium assay, on the AU640 Olympus analyzer.

Linear Regression equation: $Y = 1.020 X - 0.066$
Correlation coefficient: 0.999

Olympus Analyzers: Using the AU600/AU640E as the reference analyzer, a series of studies was conducted which consisted of running patient samples on the Olympus clinical chemistry analyzers using the new Olympus Calcium Arsenazo Reagent. This study yielded the following linear regression statistics:

Olympus Analysers – Serum:

Y Method	AU400	AU2700/AU5400
X Method	AU640	AU640
Slope	1.010	1.008
Intercept	0.095	0.057
Correlation Coeff.	0.999	0.999
No. of Samples	112	112

Olympus Analysers – Urine:

Y Method	AU400	AU2700/AU5400
X Method	AU640	AU640
Slope	0.971	0.995
Intercept	-0.022	-0.042
Correlation Coeff.	0.999	0.999
No. of Samples	118	138

b. *Matrix comparison:*

A split sample method comparison was conducted with fifty-one matched serum and lithium heparin plasma samples using the Calcium Arsenazo OSR61117 assay.

Linear Regression equation: $Y = 1.009 X - 0.037$
Correlation coefficient: 0.998

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:

Serum² : 8.2 - 10.0 mg/dL

Urine¹ : 100 - 300 mg/day

1. Tietz, N.W., Fundamentals of Clinical Chemistry, 3rd Edition, W.B. Saunders, 720: 1987.

2. Olympus America Inc. data on samples collected from 200 blood donors in North Texas.

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.