

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

A. 510(k) Number:

k061944

B. Purpose for Submission:

New device

C. Measurand:

Creatinine

D. Type of Test:

Quantitative, Enzymatic Colorimetric

E. Applicant:

Polymedco Inc.

F. Proprietary and Established Names:

Poly-Chem Creatinine

G. Regulatory Information:

1. Regulation section:
Creatinine test system- 21CFR §862.1225
2. Classification:
Class II
3. Product code:
JFY
4. Panel:
75 (Chemistry)

H. Intended Use:

- 1 Intended use(s):
See indications for use below.
- 2 Indication(s) for use:

The Poly-Chem Creatinine is intended to measure the creatinine levels in serum and urine. 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.

3 Special conditions for use statement(s):

For Prescription use only

4 Special instrument requirements:

Poly-Chem Chemistry Analyzer

I. Device Description:

The Poly-Chem Creatinine test has two reagents, R1 and R2. R1 contains 27 mL of the following ingredients: Good's buffer 30 mM, Creatinase 9 U/mL, Sarcosine oxidase 4 U/mL, Catalase 100 U/mL, Ascorbate oxidase 1 U/mL, and N-Ethyl-N-(2-hydroxy-3-sulfo-propyl)-3-methylaniline 1.4mM. R2 contains 33 mL of the following ingredients: Good's buffer 30 mM, Creatininase 40 U/mL, Peroxidase 4 U/mL, and 4-AA 5.9 mM.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Arkray SpotChem II Creatinine and Ortho-Clinical VITROS Creatinine

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

k050652 and k001769

3. Comparison with predicate:

Similarities and Differences for Creatinine			
	Poly-Chem Creatinine test (New device)	Arkray SpotChem II Creatinine (Predicate device)	Ortho-Clinical VITROS Creatinine (Predicate device)
Indications for use	To measure the creatinine levels in serum and urine. 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.	To measure the creatinine levels 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.	For <i>in vitro</i> diagnostic use only. VITROS CREA slides quantitatively measure creatinine concentration in serum, plasma, and urine.
Methodology	Enzymatic colorimetric	Colorimetric	Colorimetric
Reagent storage temperature	2-8°C	2-8°C	2-8°C
Sample types	Serum and Urine	Serum/Plasma, Whole	Serum, plasma, and

		Blood	urine
Detection limits	Serum: 0.46mg/dL Urine: 11 mg/dL	Serum: 0.66 mg/dL	Serum: 0.05mg/dL Urine: 1.05 mg/dL
Measuring range	Serum: 0.46- 34.2 mg/dL Urine: 11- 1300 mg/dL	Serum: 0.66-37.9 mg/dL	Serum: 0.05-14.0 mg/dL Urine: 1.05-346.5 mg/dL
Expected range	Serum: <u>Male:</u> 0.7–1.3 mg/dL(62-115µmol/L) <u>Female:</u> 0.6–1.1 mg/dL (53-97 µmol/L) Urine: <u>Male:</u> 14-26(mg/d)/kg [124-230 (µmol/d)/kg] <u>Female:</u> 11-20(mg/d)/kg [97-177 (µmol/d)/kg]	Serum: <u>Male:</u> 0.7–1.3 mg/dL(62-115µmol/L) <u>Female:</u> 0.6–1.1 mg/dL (53-97 µmol/L)	Serum: <u>Male:</u> 0.8–1.5 mg/dL(72-113µmol/L) <u>Female:</u> 0.7–1.2 mg/dL (62-106 µmol/L) Urine: <u>24 hrs:</u> 800-2800 mg/day

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

Application of Kinetic Models and Arrhenius Methods to Product Stability Evaluation, MD&DI, April 1984.

L. Test Principle:

Creatinine in serum or urine sample is hydrolyzed to creatine, which is then hydrolyzed to sarcosine and urea. Sarcosine is oxidized to formaldehyde, glycine, and hydrogen peroxide. Finally, a peroxidase-catalyzed reaction produces a dye that can be measured by the instrument. The intensity of the dye, when read at 546 nm, is proportional to the amount of creatinine in the patient sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Intra-assay precision was determined by analyzing three control samples for both serum and urine controls twenty times in one run. The results are presented in the tables below:

Poly-Chem Creatinine	Serum Level 1	Serum Level 2	Serum Level 3
Mean (mg/dL)	0.922	2.546	6.521
SD	0.042	0.104	0.115
CV (%)	4.5	4.1	1.8
N	20	20	20

	Urine Level 1	Urine Level 2	Urine Level 3
Mean (mg/dL)	17.66	64.68	155.70
SD	0.790	2.721	2.867
CV (%)	4.5	4.2	1.8
N	20	20	20

Inter-assay precision was determined by analyzing duplicates of three different samples in different runs over 5 days. The acceptance criteria are CV of $\leq 10\%$. The results are presented in the tables below:

Poly-Chem Creatinine	Serum Level 1	Serum Level 2	Serum Level 3
Mean (mg/dL)	0.957	2.600	6.624
SD	0.073	0.081	0.182
CV (%)	7.6	3.1	2.8
N	20	20	20
	Urine Level 1	Urine Level 2	Urine Level 3
Mean (mg/dL)	39.94	206.58	322.76
SD	1.972	7.233	13.752
CV (%)	4.9	3.5	4.3
N	20	20	20

b. Linearity/assay reportable range:

The linearity was determined by assaying serial dilutions using a pool that spanned the linear range of the test. The results at each level were averaged and the linear fit was calculated. The sponsor's acceptance criteria are deviation of $\leq 5\%$ at the two highest analyte concentrations. This test is linear up to 34.2 mg/dL with serum and 1300 mg/dL with urine. The results of the linearity study were shown in the tables below:

Table 1: Summary of the Serum Creatinine Linearity Study, lower concentrations. Means in mg/dL.

Theoretical Level	Mean Actual Level	Standard Deviation	%CV	Deviation from Theoretical	% Deviation	% Recovery
0.59	0.60	0.05	8.8	0.01	2.4	102.4
1.17	1.14	0.04	3.2	-0.03	-2.7	97.3
1.76	1.72	0.06	3.2	-0.03	-1.9	98.1
2.34	2.30	0.03	1.4	-0.04	-1.7	98.3
2.93	2.88	0.02	0.6	-0.05	-1.7	98.3
3.51	3.55	0.08	2.2	0.04	1.0	101.0
4.10	4.09	0.07	1.8	-0.01	-0.2	99.8
4.69	4.70	0.06	1.2	0.02	0.4	100.4

5.27	5.22	0.05	1.0	-0.05	-1.0	99.0
5.86	5.86	0.06	0.9	0.00	0.0	100.0
			Linear Fit Parameters			
			Slope:		1.002	
			Intercept:		-0.02	
			r:		0.9999	

Table 2: Summary of the Serum Creatinine Linearity Study, higher concentrations. Means in mg/dL.

Theoretical Level	Mean Actual Level	Standard Deviation	%CV	Deviation from Theoretical	% Deviation	% Recovery
3.42	3.28	0.11	3.2	-0.15	-4.3	95.7
6.85	6.73	0.12	1.8	-0.12	-1.7	98.3
10.27	9.98	0.08	0.8	-0.29	-2.8	97.2
13.69	13.56	0.11	0.8	-0.13	-1.0	99.0
17.12	16.90	0.17	1.0	-0.21	-1.2	98.8
20.54	20.52	0.35	1.7	-0.02	-0.1	99.9
23.96	24.25	0.09	0.4	0.29	1.2	101.2
27.38	27.46	0.15	0.5	0.08	0.3	100.3
30.81	31.11	0.17	0.5	0.30	1.0	101.0
34.23	34.23	0.33	1.0	0.00	0.0	100.0

Linear Fit Parameters

Slope: 1.013

Intercept: -0.275

r: 0.9999

Table 3: Summary of the Urine Creatinine Linearity Study with urine samples. Means in mg/dL.

Theoretical Level	Mean Actual Level	Standard Deviation	%CV	Deviation from Theoretical	% Deviation	% Recovery
66.7	69.50	4.00	5.8	2.80	4.2	104.2
133.4	129.17	5.69	4.4	-4.23	-3.2	96.8
266.8	258.83	7.57	2.9	-7.97	-3.0	97.0
400.2	399.17	4.80	1.2	-1.03	-0.3	99.7
533.6	522.50	13.03	2.5	-11.10	-2.1	97.9
667.0	667.00	11.14	1.7	0.00	0.0	100.0
800.4	791.50	16.30	2.1	-8.90	-1.1	98.9
933.8	944.33	5.62	0.6	10.53	1.1	101.1
1067.2	1057.50	6.06	0.6	-9.70	-0.9	99.1
1200.6	1175.50	4.77	0.4	-25.10	-2.1	97.9
1334.0	1299.83	9.00	0.7	-34.17	-2.6	97.4
			Linear Fit Parameters			
			Slope:		0.983	

			Intercept:	-3.556
			r:	0.9997

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

The Poly-Chem Creatinine test was standardized to NIST SRM 909b. The calibration set points are fixed by the manufacturer and are unique with each calibrator lot. The stability of the recommended calibrators on the Poly-Chem instrument is 4 days. The calibrators can be stored at 2 – 8°C until expiration date. A calibration is recommended at least once every 4 days, with each reagent lot or bottle change, or as indicated by quality control.

The recommended control and calibrator materials were 510(k) cleared previously and are sold separately from the creatinine reagents.

d. Detection limit:

Functional sensitivity was determined by diluting a pool sample to 10 different concentrations below the lower limit of the normal test range for the analyte. 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). The manufacturer determined that functional sensitivity was 0.46 mg/dL with a CV of 12.5% for serum creatinine and 11.0 mg/dL with a CV of 7.6% for urine creatinine.

e. Analytical specificity:

Studies were performed to determine common or known substances that could interfere with the method. The interfering substances were evaluated in serum pools that had creatinine concentrations of approximately 1.0, 3.3, and 6.6 mg/dL. The acceptable established criteria are that the analyte recovery should not vary from the base recovery by $\pm 10\%$. The summary of the results of the recovery studies is provided in the table below:

Substances	Highest Level Tested with No Interference
Hemoglobin	150 mg/dL
Bilirubin	9.84 mg/dL
Triglycerides	302.5 mg/dL

Urine interference studies were performed on samples with creatinine concentrations of approximately 63.9 mg/dL. The summary of the results of the recovery studies is provided in the table below:

Substances	Highest Level Tested with No Interference
Glucose	5 g/L
Citric acid	500 mg/dL
Tartaric acid	500 mg/dL
Oxalic acid	500 mg/dL
Uric acid	140 mg/dL
Ascorbic acid	500 mg/dL
Human serum albumin	1 g/dL
Creatine	100 mg/dL
Calcium	500 mg/dL

Urine samples with creatinine concentrations of approximately 76.7 mg/dL were tested from pH 2 to 11 and no interference was observed.

The labeling includes a literature source for the statement “Known drug interferences include levodopa, methyldopa, and nitrofurantoin derivatives, which may cause falsely elevated urine creatinine levels.”

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

A method correlation study was performed comparing the Poly-Chem creatinine and SpotChem II creatinine results using serum samples. The 60 serum samples tested spanned from 0.65 mg/dL to 18.9 mg/dL. The regression equation was $y = 1.082x - 0.061$ and $r = 0.9977$. (y = Poly-Chem creatinine and x = SpotChem II creatinine)

Another method correlation study was performed comparing the Poly-Chem creatinine and Ortho-Clinical VITROS creatinine results using urine samples. The 49 urine samples tested spanned from 11.0 mg/dL to 1127.2 mg/dL. The regression equation was $y = 1.038x + 3.737$ and $r = 0.9941$. (y = Poly-Chem creatinine and x = Ortho-Clinical VITROS creatinine)

b. Matrix comparison:

Not applicable

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):

None

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

The sponsor cites reference range from “Tietz, N.W. Textbook of Clinical Chemistry,” Second Edition, W.B Saunders Company, 1994

Serum: Male: 0.7–1.3 mg/dL(62-115 μ mol/L)

Female: 0.6–1.1 mg/dL (53-97 μ mol/L)

Urine: Male: 14-26(mg/d)/kg [124-230 (μ mol/d)/kg]

Female: 11-20(mg/d)/kg [97-177 (μ mol/d)/kg]

The sponsor recommends in the labeling that each laboratory establish its own reference range to reflect the age, sex, diet and geographical location of the population.

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.