

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

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

k110818

**B. Purpose for Submission:**

New device

**C. Measurand:**

Albumin, BUN, Calcium, Carbon Dioxide, Creatinine

**D. Type of Test:**

Quantitative, Photometry

**E. Applicant:**

Polymedco, Inc.

**F. Proprietary and Established Names:**

Poly-Chem 90 Albumin, Poly-Chem 90 BUN, Poly-Chem 90 Calcium, Poly-Chem 90 Carbon Dioxide, Poly-Chem 90 Creatinine

**G. Regulatory Information:**

<b>Product Code</b>	<b>Name and Regulation Section</b>	<b>Class</b>	<b>Panel</b>
CIX	Albumin test system 21 CFR 862.1035	II	75 Clinical Chemistry
CDQ	Urea Nitrogen test system 21 CFR 862.1770	II	75 Clinical Chemistry
CIC	Calcium test system 21 CFR 862.1145	II	75 Clinical Chemistry
KHS	Bicarbonate/carbon dioxide test system 21 CFR 862.1160	II	75 Clinical Chemistry
CGX	Creatinine Test System 21 CFR 862.1225	II	75 Clinical Chemistry

## **H. Intended Use:**

1. Intended use(s):

See indications for use below.

2. Indication(s) for use:

The Poly-Chem 90 Albumin test system is an in vitro diagnostic procedure intended to measure the albumin concentration in human serum on the Poly-Chem 90 analyzer. Albumin measurements are used in the diagnosis and treatment of numerous diseases involving primarily the liver or kidneys.

The Poly-Chem 90 BUN test system is an in vitro diagnostic procedure intended to measure urea nitrogen (an end product of nitrogen metabolism) in human serum on the Poly-Chem 90 analyzer. Measurements obtained by this device are used in the diagnosis and treatment of certain renal and metabolic diseases.

The Poly-Chem 90 Calcium test system is an in vitro diagnostic procedure intended to measure the total calcium level in human serum on the Poly-Chem 90 analyzer. 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).

The Poly-Chem 90 Carbon Dioxide test system is an in vitro diagnostic procedure intended to measure bicarbonate/carbon dioxide in human serum on the Poly-Chem 90 analyzer. Bicarbonate/carbon dioxide measurements are used in the diagnosis and treatment of numerous potentially serious disorders associated with changes in body acid-base balance.

The Poly-Chem 90 Creatinine test system is an in vitro diagnostic procedure intended to measure creatinine levels in human serum on the Poly-Chem 90 analyzer. 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 90 Analyzer (k090703)

## **I. Device Description:**

**Albumin** consists of the following *in vitro* diagnostic reagents: Succinate buffer; pH 4.2, Bromocresol green, Brij 35 and methylisothiazolon as a preservative.

**BUN** consists of the following *in vitro* diagnostic reagents: R1-**Coenzyme**, Capso Buffer, pH 9.65 and NADH. R2-**Enzymes/Substrate**, Bicine Buffer, Urease, GLDH and  $\alpha$ -oxoglutarate.

**Calcium** consists of the following *in vitro* diagnostic reagents: R1-Buffer, Ethanolamine Buffer. R2-Chromogen, O-Cresolphthalein complexone, 8-Hydroxyquinoline and Hydrochloric Acid.

**Carbon Dioxide** consists of the following *in vitro* diagnostic reagents: Phosphoenolpyruvate (PEP), NADH analog, Phosphoenolpyruvate Carboxylase (PEPC), and Malate Dehydrogenase (MDH)

**Creatinine** consists of an R1 and an R2 reagent. R1 reagent contains Sodium Hydroxide, R2 reagent contains Picric Acid.

**J. Substantial Equivalence Information:**

1. Predicate device name(s)

Poly-Chem Albumin, Poly-Chem BUN, Poly-Chem Calcium, Poly-Chem Carbon Dioxide, and Poly-Chem Creatinine

2. Predicate 510(k) number(s)

k020852, previously cleared as: Radox Albumin (k984494), Radox BUN ( k923506), Radox Calcium (k000375), Radox Carbon Dioxide (k951221), Radox Creatinine ( k973993)

3. Comparison with predicate:

<b>Similarities and Differences Albumin</b>		
<b>Item</b>	<b>Device Poly-Chem 90 Albumin</b>	<b>Predicate Poly-Chem Albumin</b>
Intended Use	For the quantitative <i>in vitro</i> determination of Albumin in serum.	Same
Sample Type	Serum	Serum and Plasma
Measuring range	0.2 – 5.0 mg/dL	0.47 – 5.0 mg/dL
Storage/stability	Stable until expiration date when stored at 15-25° C. On-board stability is 30 days at 10°C.	Same
Analyzer	Poly-Chem 90	Poly-Chem 180

<b>Similarities and Differences BUN</b>		
<b>Item</b>	<b>Device Poly-Chem 90 BUN</b>	<b>Predicate Poly-Chem BUN</b>
Intended Use	For the quantitative <i>in vitro</i> determination of blood urea nitrogen in serum	Same
Sample Type	Serum	Serum, plasma, urine
Measuring Range	5.5 – 160.1 mg/dL	4.1 - 142 mg/dL
Storage/stability	R1 reagent - Stable until expiration date when stored at 2-8°C. Once opened reagent is stable for 30 days on board the analyzer at 10°C. R2 reagent- Stable until expiration date when stored at 2-8°C. Once opened the reagent is stable for 28 days on board the analyzer at 10°C.	Same
Analyzer	Poly-Chem 90	Poly-Chem 180

<b>Similarities and Differences Calcium</b>		
<b>Item</b>	<b>Device Poly-Chem 90 Calcium</b>	<b>Predicate Poly-Chem Calcium</b>
Intended Use	For the quantitative <i>in vitro</i> determination of the total Calcium in serum.	Same
Sample Type	Serum	Serum and Urine
Measuring Range	0.7 – 20.0 mg/dL	0.76 – 20.04 mg/dL
Storage/Stability	Stable until expiration when stored at 15 - 25°C. Once opened the reagent is stable for 28 days on board the instrument at 10°C.	Same
Analyzer	Poly-Chem 90	Poly-Chem 180

<b>Similarities and Differences Carbon Dioxide</b>		
Item	Device Poly-Chem 90 Carbon Dioxide	Predicate Poly-Chem Carbon Dioxide
Intended Use	For the quantitative <i>in vitro</i> determination of Carbon Dioxide in serum.	Same
Sample Type	Serum	Serum and Plasma
Measuring Range	5-49 mmol/L	2.9 – 50 mmol/L
Storage/Stability	Stable until expiration date on the label when unopened and stored at 2-8°C.	Same
Analyzer	Poly-Chem 90	Poly-Chem 180

<b>Similarities and Differences Creatinine</b>		
Item	Device Poly-Chem 90 Creatinine	Predicate Poly-Chem Creatinine
Intended Use	For the quantitative <i>in vitro</i> determination of Creatinine in serum.	Same
Sample Type	Serum	Serum and urine
Measuring Range	0.3 – 20.7 mg/dL	0.31 – 22 mg/dL
Storage/Stability	R1 and R2 Reagents- Stable until expiration date on label when stored at 15-25°C. Once opened the reagent should be capped and stored in the refrigerator at 2-8°C overnight or when not in use. On-board stability is 3 days at 10°C.	Same
Analyzer	Poly-Chem 90	Poly-Chem 180

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

CLSI EP5-A2: Evaluation of Precision Performance of Quantitative Measurement Methods;

Approved Guideline-Second Edition

CLSI EP6-A: Evaluation of Linearity of Quantitative Measurement Procedures, A Statistical Approach: Approved Guideline

CLSI EP17-A: Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline

## L. Test Principle:

**Albumin:** The measurement of serum albumin is based on its quantitative binding to the indicator 3,3',5,5'-tetrabromo-m-cresol sulphonphthalein (bromocresol green). The albumin-BCG-complex absorbs maximally at 578 nm.

**BUN:** The measurement of BUN in serum is based on the hydrolysis of urea in the presence of water and urease to produce ammonia and carbon dioxide. The ammonia produced in the first reaction combines with  $\alpha$ -oxoglutarate and NADH in the presence of glutamate-dehydrogenase to yield glutamate and  $\text{NAD}^+$ .

**Calcium:** The measurement of calcium in serum is based on calcium ions forming a violet complex with O-cresolphthalein complexone in an alkaline medium

**Carbon Dioxide:** The measurement of carbon dioxide in serum is an enzymatic procedure employing phosphoenolpyruvate carboxylase (PEPC) and a stabilized NADH analog. PEPC catalyzes the first reaction which produces oxaloacetate. In the presence of MDH, the reduced cofactor is oxidized by oxaloacetate. The decrease in concentration of the reduced cofactor is monitored between 405 and 415 nm and is proportional to the total carbon dioxide concentration in the sample.

**Creatinine:** The measurement of creatinine in serum is based on creatinine in an alkaline solution reacting with picrate to form a colored complex. The rate of formation of the complex is measured.

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

### 1. Analytical performance:

#### a. *Precision/Reproducibility:*

Precision studies were performed at three levels of each test on two separate Poly-Chem 90 analyzers over 10 days. Samples were tested in duplicate twice a day (n=80) for each level tested for each analyte. Results for inter-assay precision are summarized in the tables below.

<i>Albumin</i> Sample	Instrument	Mean (mg/dl)	Within run		Between run	
			SD	%CV	SD	%CV
1	1	1.46	0.025	1.68	0.037	2.52
	2	1.47	0.016	1.11	0.036	2.48
2	1	2.86	0.035	1.22	0.060	2.09
	2	2.88	0.018	0.63	0.062	2.15
3	1	4.66	0.076	1.63	0.099	2.12
	2	4.71	0.022	0.47	0.083	1.76

<i>Bun</i> Sample	Instrument	Mean (mg/dl)	Within run		Between run	
			SD	%CV	SD	%CV
1	1	16.6	0.66	4.0	0.88	5.3
	2	16.7	0.33	2.0	0.45	2.7
2	1	52.4	0.85	1.6	1.01	1.9
	2	51.7	0.53	1.0	0.80	1.6
3	1	112.1	0.76	0.7	1.27	1.1
	2	110.0	0.64	0.6	1.87	1.7

<i>Calcium</i> Sample	Instrument	Mean (mg/dl)	Within run		Between run	
			SD	%CV	SD	%CV
1	1	4.07	0.155	3.81	0.251	6.18
	2	4.11	0.138	3.36	0.201	4.90
2	1	8.55	0.198	2.32	0.286	3.35
	2	8.56	0.137	1.60	0.214	2.51
3	1	15.01	0.122	0.82	0.366	2.44
	2	15.07	0.136	0.90	0.351	2.33

<i>Carbon Dioxide</i> Sample	Instrument	Mean (mmol/l)	Within run		Between run	
			SD	%CV	SD	%CV
1	1	8.7	0.42	4.8	0.80	9.2
	2	8.8	0.27	3.1	0.77	8.7
2	1	18.6	0.39	2.1	0.83	4.5
	2	18.7	0.50	2.7	0.86	4.6
3	1	42.0	0.61	1.46	2.71	6.4
	2	42.6	0.35	0.83	2.27	5.3

<i>Creatinine</i> Sample	Instrument	Mean (mg/dl)	Within run		Between run	
			SD	%CV	SD	%CV
1	1	0.65	0.022	3.40	0.033	4.99
	2	0.65	0.016	2.44	0.045	6.93
2	1	1.35	0.025	1.83	0.035	2.60
	2	1.30	0.026	2.00	0.046	3.57
3	1	3.80	0.040	1.06	0.084	2.22
	2	3.86	0.041	1.07	0.067	1.75
4	1	15.14	0.103	0.68	0.372	2.46
	2	15.54	0.091	0.58	0.291	1.88

Intra-assay precision was performed with three serum samples at different concentrations of the analyte on two Poly-Chem 90 analyzers. Twenty replicates of each sample were tested within one instrument run. Results are summarized in the table below:

<i>Albumin</i> Replicate	Level 1		Level 2		Level 3	
	INSTR 1	INSTR 2	INSTR 1	INSTR 2	INSTR 1	INSTR 2
Mean (mg/dL)	1.46	1.48	2.86	2.91	4.61	4.72
SD	0.043	0.010	0.045	0.012	0.050	0.032
%CV	2.9	0.7	1.6	0.4	1.1	0.7
Minimum	1.42	1.46	2.74	2.90	4.47	4.67
Maximum	1.63	1.49	2.92	2.94	4.67	4.78
Range	0.21	0.03	0.18	0.04	0.20	0.11

<i>BUN</i> Replicate	Level 1		Level 2		Level 3	
	INSTR 1	INSTR 2	INSTR 1	INSTR 2	INSTR 1	INSTR 2
Mean (mg/dL)	16.8	16.9	52.0	52.0	109.2	110.5
SD	0.90	0.36	1.27	0.48	1.56	0.81
%CV	5.3	2.1	2.5	0.9	1.4	0.7
Minimum	15.3	16.2	49.5	51.3	104.9	108.4
Maximum	18.5	18.0	54.3	52.8	111.7	111.7
Range	3.2	1.8	4.8	1.5	6.8	3.3

  

<i>Calcium</i> Replicate	Level 1		Level 2		Level 3	
	INSTR 1	INSTR 2	INSTR 1	INSTR 2	INSTR 1	INSTR 2
Mean (mg/dL)	4.3	4.3	8.8	8.8	15.1	15.3
SD	0.08	0.08	0.03	0.05	0.24	0.18
%CV	1.8	1.9	0.3	0.5	1.6	1.2
Minimum	4.2	4.1	8.8	8.7	14.6	15.0
Maximum	4.4	4.4	8.9	8.9	15.4	15.5
Range	0.2	0.3	0.1	0.2	0.8	0.5

<i>Carbon Dioxide</i> Replicate	Level 1		Level 2		Level 3	
	INSTR 1	INSTR 2	INSTR 1	INSTR 2	INSTR 1	INSTR 2
Mean (mg/dL)	9	9	19	19	44	43
SD	0.6	0.4	0.2	0.4	0.7	0.8
%CV	6.8	4.0	1.2	1.9	1.6	1.9
Minimum	8	9	19	18	43	41
Maximum	10	10	20	19	45	44
Range	2	1	1	1	2	3

<i>Creatinine</i> Replicate	Level 1		Level 2		Level 3	
	INSTR 1	INSTR 2	INSTR 1	INSTR 2	INSTR 1	INSTR 2
Mean (mg/dL)	0.64	0.65	3.67	3.83	15.09	15.59
SD	0.024	0.031	0.028	0.036	0.101	0.105
%CV	3.7	4.8	0.8	0.9	0.7	0.7
Minimum	0.59	0.60	3.63	3.77	14.92	15.41

Maximum	0.68	0.71	3.73	3.90	15.37	15.80
Range	0.09	0.11	0.10	0.13	0.45	

b. *Linearity/assay reportable range:*

The linearity of each analyte on the Poly-Chem 90 system was tested by mixing human serum containing the analyte to several levels of the test to obtain 7 concentration levels for each analyte (Albumin 0.17-6.67 g/dL; BUN 5.4-160.1 mg/dL; Calcium 0.7-20.1 mg/dL; Carbon Dioxide 5-49 mmol/L; Creatinine 0.3-20.7 mg/dL). Recoveries ranged from 91.3 to 108.0% for Albumin; 96.7-100% for BUN; 93.7-101.3% for Calcium; 100-101.4% for Carbon Dioxide and from 96.5-100% for Creatinine. The summary of linear regression analysis of data is given in the table below.

Test	Range Tested	Slope (95% CI)	Intercept (95% CI)
Albumin	0.2 – 6.7 g/dL	0.90 (0.87-0.93)	0.20 (0.08 – 0.31)
BUN	5.4 – 160.1 mg/dL	1.01 (1.00- 1.01)	-0.27 (-0.75 – 0.21)
Calcium	0.7-20.1 mg/dL	1.03 (1.02-1.04)	-0.24 (-0.36 - -0.13)
Carbon Dioxide	5.0 – 49.0 mmol/L	1.02 (0.99-1.05)	0.37 (-0.50 – 1.23)
Creatinine	0.3-20.7 mg/dL	1.00 (1.00 – 1.01)	0.04 (-0.03 – 0.11)

The linearity studies support the sponsor’s claimed measuring range as follows:

Albumin: 0.2- 5.0 g/dL

BUN: 5.5 – 160.1 mg/dL

Calcium: 0.7 – 20.1 mg/dL

Carbon Dioxide: 5- 49 mmol/L

Creatinine: 0.3 – 20.7 g/dL

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

The tests are traceable through the appropriate recommended calibrator (Polymedco calibration serum previously cleared under *k955489* and *CO<sub>2</sub>* Standard Verichem previously cleared under *k975285*) to the Reference material/methods listed in the table below:

<b>Reagent</b>	<b>Reference Material/Method</b>
Albumin	DA470
BUN	NIST909b
Calcium	NIST 909b,SRM956b, Atomic absorption
Carbon Dioxide	Sodium Carbonate Alkameric Standard
Creatinine	NIST 909b/SRM 967

*d. Detection limit:*

A limit of detection study was performed according to the CLSI EP17-A guideline. LoB was conducted using a blank sample measured 60 times. LoD and LoQ were conducted using five serum samples containing very low concentrations of the analyte to be tested in replicates of three over four days. LoQ is defined as the concentration at which inter-assay precision is  $\leq 10\%$  CV. LoB, LoD and LoQ are summarized in the table below.

<b>Analyte</b>	<b>LoB</b>	<b>LoD</b>	<b>LoQ</b>	<b>Measuring Range</b>
Albumin	0.0076 g/dL	0.015g/dL	0.18g/dL	0.2 – 5.0 g/dL
BUN	0.431 mg/dL	1.27 mg/dL	5.5 mg/dL	5.5 – 160.1 mg/dL
Calcium	0.123 mg/dL	0.246 mg/dL	0.7 mg/dL	0.7 – 20.1 mg/dL
Carbon Dioxide	0.000 mmol/L	0.78mmol/L	5 mmol/L	5.0 – 49.0 mmol/L
Creatinine	0.000 mg/dL	0.039 mg/dL	0.29 mg/dL	0.3 – 20.7 mg/dL

*d. Analytical specificity:*

An endogenous interfering substances study was performed according to the CLSI EP7-A guideline. Serum samples containing the analyte at three levels of the test were spiked with the potentially interfering substance—hemoglobin, bilirubin and triglyceride—to several concentrations. Samples were then run in triplicate using the Poly-Chem 90 test. The recovery of the test at each concentration of interferents was calculated by comparing the mean result of testing with no interferents to the mean result at each level tested. The sponsor defines non-significant interference as bias  $< 10\%$  between the spiked and unspiked samples. The highest level tested with no significant interference is listed in the table below.

Analyte	Highest level tested with no interference		
	Hemoglobin	Bilirubin	Triglyceride
Albumin	200 mg/dL	70.7 mg/dL	612 mg/dL
BUN	600 mg/dL	25 mg/dL	694 mg/dL
Calcium	500 mg/dL	25 mg/dL	554 mg/dL
Carbon Dioxide	300 mg/dL	25 mg/dL	839 mg/dL
Creatinine	100 mg/dL	25 mg/dL	740 mg/dL

The sponsor has the following limitation in their labeling on all the 5 assays based on the hemoglobin study above:

“Do not use hemolyzed samples. Hemolyzed samples will cause erroneous results.”

f. *Assay cut-off:*

Not applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

Patient serum samples with values across the range of the assays were analyzed on the Poly-Chem 180 instrument (predicate device) vs. the Poly-Chem 90 instrument. Samples were run in singlicate for both devices. Samples were as follows: 45 samples (1 spiked, 7 diluted) for Albumin, 50 samples (3 spiked, 1 diluted) for BUN, 50 samples (6 spiked and 4 diluted) for Calcium, 43 samples (5 spiked, 3 diluted) for Carbon Dioxide and 43 samples (2 spiked, 1 diluted) for Creatinine. Results obtained from each instrument were compared using Passing-Bablok analysis. Results are summarized in the table below.

Test	n	Range of samples	Slope (95%CI)	Intercept (95% CI)	r
Albumin	45	0.97-4.81	0.99 (0.97 - 1.01)	0.02 (-0.07 - 0.11)	0.9969
BUN	50	6.0 – 147.0	1.03 (1.01 - 1.04)	-0.20 (-0.69 - 0.43)	0.9988
Calcium	50	2.2-18.5	1.03 (1.00 - 1.07)	-0.18 (-0.53 - 0.10)	0.9948
Carbon Dioxide	43	7 – 49	1.00 (1.00 - 1.04)	1.00 (-0.08 - 1.00)	0.9966
Creatinine	43	0.30 – 19.00	1.03 (1.02 - 1.06)	-0.13 (-0.20 - 0.07)	0.9995

*b. Matrix comparison:*

Serum is the only sample type indicated.

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):*

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

The expected values are stated within the labeling for each analyte based on the literature. The manufacturer recommends, within the labeling, each laboratory establish its own reference range o reflect the age, sex, diet and geographical location of the population.

Albumin<sup>1</sup>: Adult Serum 3.8-5.0 g/dl

BUN<sup>2</sup>: Serum 5-23 mg/dl

Calcium<sup>3</sup>: Serum 8.10 – 10.4 mg/dl

CO<sub>2</sub><sup>4</sup>: Serum 20 – 29 mmol/l

Creatinine<sup>5</sup>: Serum Men 0.6 – 1.1 mg/dl

Serum Women 0.5 – 0.9 mg/dl

<sup>1</sup>Doumas, B.T., Watson, W.A., Biggs, H.G. Clin. Chem. Acta. 1971;31:87.

<sup>2</sup>Kerscher, L; Tieqenhorn, J; “Methods of enzymatic Analysis”, H.U. Bergmeyer Ed., VCH Verlagsgesellschaft, Weinham, 1985 3<sup>rd</sup> Ed; Vd VII

<sup>3</sup>Barnett, R.N., et al. (1973) Amer. J. Clin. Path.59:836

<sup>4</sup>Tietz, NW (Ed.) Fundamentals of clinical chemistry, W.B. Saunders, Co., Toronto, 636-638, 937 (1970)

<sup>5</sup>Schirmeister, J.,H. Willman, and H. Kiefer. (1964). Dtsch. Med. Wschr. 89:1018.

**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.