510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

k100550

B. Purpose for Submission:

New device

C. Measurand:

HDL Cholesterol, LDL Cholesterol, Cholesterol, Triglycerides

D. Type of Test:

Quantitative enzymatic, photometric assay

E. Applicant:

Polymedco, Inc.

F. Proprietary and Established Names:

Poly-Chem 90 Direct HDL-Cholesterol, Poly-Chem 90 Direct LDL-Cholesterol, Poly-Chem 90 Cholesterol and Poly-Chem 90 Triglycerides

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
LBS	Class I, meets limitations per 21 CFR 862.9(c)(4)	21 CFR 862.1475 Lipoprotein test system	75 Clinical Chemistry
MRR	Class I, meets limitations per 21 CFR 862.9(c)(4)	21 CFR 862.1050 System, Test, Low Density Lipoprotein	75 Clinical Chemistry
CHH	Class I, meets limitations per 21 CFR 862.9(c)(4)	21 CFR 862.1175, Cholesterol test system	75 Clinical Chemistry

Product Code	Classification	Regulation Section	Panel
CDT	Class I, meets limitations per 21 CFR 862.9(c)(4)	21 CFR 862.1705 Triglyceride test system	75 Clinical Chemistry

H. Intended Use:

1. Intended use(s):

   See indications for use below.

2. Indication(s) for use:
   The Poly-Chem 90 Direct HDL cholesterol test system is an in vitro diagnostic procedure intended to measure high density lipoproteins quantitatively in human serum on the Poly-Chem 90 analyzer. HDL Cholesterol results are used in the diagnosis and treatment of lipid disorders (such as diabetes mellitus), atherosclerosis and various other liver and renal diseases, and for the assessment for the risk of developing cardiovascular disease.

   The Poly-Chem 90 Direct LDL cholesterol test system is an in vitro diagnostic procedure intended to measure low density lipoproteins quantitatively in human serum on the Poly-Chem 90 analyzer. LDL Cholesterol results are used in the diagnosis and treatment of lipid disorders (such as diabetes mellitus), atherosclerosis and various other liver and renal diseases, and for the assessment for the risk of developing cardiovascular disease.

   The Poly-Chem 90 cholesterol test system is an in vitro diagnostic procedure intended to measure cholesterol quantitatively in human serum on the Poly-Chem 90 analyzer. Cholesterol measurements are used in the diagnosis and treatment lipid, lipoprotein metabolism disorders and atherosclerosis.

   The Poly-Chem 90 triglyceride test system is an in vitro diagnostic procedure intended to measure triglyceride quantitatively in human serum on the Poly-Chem 90 analyzer. Triglycerides measurements are used in the diagnosis and treatment of disease involving lipid metabolism and various endocrine disorders e.g. diabetes mellitus, nephrosis and liver obstruction.

3. Special conditions for use statement(s):

   For prescription use only.

4. Special instrument requirements:

Poly-Chem 90 Analyzer (k090703)

I. Device Description:

Direct HDL Cholesterol consists of the following *in vitro* diagnostic reagents:

R1, Enzyme Reagent 1:

N,N-Bis(2-hydroxyethyl) - 100 mmol/l, pH 7.0
2-aminoethanesulfonic acid HDAOS 0.7 mmol/l
N-(2-hydroxy-3-Sulfopropyl)-3,5-dimethoxyaniline)
Cholesterol Esterase >800 U/l [E.C.3.1.1.13. Pseudomonas]
Cholesterol Oxidase >500 U/l [E.C.1.1.3.6. Nocardia]
Catalase >300 KU/l [E.C.1.11.1.6. Bovine Liver]

R2, Enzyme Reagent 2:

N,N-Bis(2-hydroxyethyl)- 100 mmol/l, pH 7.0
2-aminoethanesulfonic acid
4-Amino antipyrine 4 mmol/l
Peroxidase >4 KU/l [E.C.1.11.1.7, Horse Radish]
Sodium Azide 0.09% (w/v)

Direct LDL Cholesterol consists of the following *in vitro* diagnostic reagents:

R1, Enzyme Reagent 1:

PIPES Buffer 50 mmol/l, pH 7.0
Piperazine-1,4-bis(2-ethanesulfonic acid) TOOS 2.0 mmol/l
N-Ethyl-N-(2-hydroxy-3-sulfopropyl)-3-methylaniline Cholesterol Esterase ≥600U/l [E.C.3.1.1.13. Pseudomonas]
Cholesterol Oxidase ≥500U/l [E.C.1.1.3.6. Nocardia]
Catalase ≥600KU/l [E.C.1.11.1.6. Bovine Liver]

R2, Enzyme Reagent 2:

PIPES Buffer 50 mmol/l, pH 7.0
Piperazine-1,4-bis(2-ethanesulfonic acid) 4-Amino antipyrine 4 mmol/l
Peroxidase ≥4KU/l [E.C.1.11.1.7, Horse Radish]
Sodium Azide 0.05% (w/v)

Cholesterol consists of the following *in vitro* diagnostic reagents:

Pipes Buffer 80 mmol/l, pH 6.8

4-Aminoantipyrine 0.25 mmol/l
Phenol 6 mmol/l
Peroxidase ≥ 0.5 U/ml (E.C.1.11.1.7, Horse Radish)
Cholesterol esterase ≥ 0.15 U/ml (E.C.3.1.1.13. Pseudomonas)
Cholesterol oxidase ≥ 0.10 U/ml (E.C.1.1.3.6. Nocardia)

Triglyceride consists of the following *in vitro* diagnostic reagents:

R1, Reagent 1 (Buffer):

Pipes Buffer 40 mmol/l, pH 7.5
4-chloro-phenol 5.0 mmol/l
Magnesium-ions 5.0 mmol/l

R2, Enzyme Reagent
4-aminophenazone 0.4 mmol/l
ATP 1.0 mmol/l
Lipases ≥150 U/ml
Glycerol-kinase ≥0.4 U/ml
Glycerol-3-phosphate oxidase ≥1.5 U/ml
Peroxidase ≥0.5 U/ml

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Randox Direct LDL Cholesterol
   Randox HDL Cholesterol
   Randox Cholesterol
   Randox Triglyceride

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

   k982529
   k982341
   k923504
   k923508

3. Comparison with predicate:

Similarities and Differences Direct HDL-cholesterol		
Item	Device	Predicate
Indications for Use	in vitro diagnostic procedure intended to measure high density lipoproteins quantitatively. HDL Cholesterol results are used in the diagnosis and	Same

Similarities and Differences Direct HDL-cholesterol		
Item	Device	Predicate
	treatment of lipid disorders (such as diabetes mellitus), arteriosclerosis and various other liver and renal diseases, and for the assessment for the risk of developing cardiovascular disease.	
Instrument	Poly-Chem 90	Poly-Chem 180
Sample type	serum	Serum and plasma
Assay type	Photometric	same
Throughput	90 tests per hour	180 tests per hour

Similarities and Differences Direct LDL-cholesterol		
Item	Device	Predicate
Indications for Use	in vitro diagnostic procedure intended to measure low density lipoproteins quantitatively. LDL Cholesterol results are used in the diagnosis and treatment of lipid disorders (such as diabetes mellitus), arteriosclerosis and various other liver and renal diseases, and for the assessment for the risk of developing cardiovascular disease.	Same
Instrument	Poly-Chem 90	Poly-Chem 180
Sample type	serum	Serum and plasma
Assay type	Photometric	same
Throughput	90 tests per hour	180 tests per hour

Similarities and Differences Cholesterol		
Item	Device	Predicate
Indications for Use	in vitro diagnostic procedure intended to measure cholesterol quantitatively. Cholesterol measurements are used in the diagnosis and treatment lipid, lipoprotein metabolism disorders and atherosclerosis.	Same
Instrument	Poly-Chem 90	Poly-Chem 180
Sample type	Serum	Serum and plasma

Similarities and Differences Cholesterol		
Item	Device	Predicate
Assay type	Photometric	same
Throughput	90 tests per hour	180 tests per hour

Similarities and Differences Triglyceride		
Item	Device	Predicate
Indications for Use	in vitro diagnostic procedure intended to measure triglyceride quantitatively. Triglycerides measurements are used in the diagnosis and treatment of disease involving lipid metabolism and various endocrine disorders e.g. diabetes mellitus, nephrosis and liver obstruction.	Same
Instrument	Poly-Chem 90	Poly-Chem 180
Sample type	serum	Serum and plasma
Assay type	Photometric	same
Throughput	90 tests per hour	180 tests per hour

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:

Direct HDL-Cholesterol:

The assay consists of 2 distinct reaction steps:

1. Elimination of chylomicron, VLDL-Cholesterol and LDL Cholesterol by cholesterol esterase, cholesterol oxidase and subsequently catalase.

2. Specific measurement of HDL-Cholesterol after release of HDL-Cholesterol by detergents in Reagent 2.

The intensity of the quinone imine dye produced in the reaction is directly proportional to the cholesterol concentration when measured at 600 nm.

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The intensity of quinone imine dye produced in the reaction is directly proportional to the cholesterol concentration when measured at 600 nm.

Cholesterol:

The cholesterol is determined after enzymatic hydrolysis and oxidation. The indicator quinoneimine is formed from hydrogen peroxide and 4-aminoantipyrine in the presence of phenol and peroxidase.

Triglyceride:

The triglycerides are determined after enzymatic hydrolysis with lipases. The indicator is a quinoneimine formed from hydrogen-peroxide, 4-aminophenazone and 4-chlorophenol under the catalytic influence of peroxidase.

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 instruments over 10 days. Samples were tested in duplicate twice a day with n = 80 for each level tested for each analyte.

HDL			Within run		Between run	
Sample	Instrument	Mean	SD	CV	SD	CV
1	1	25.0	0.45	1.8%	0.58	2.3%
	2	25.3	0.40	1.6%	0.54	2.1%
2	1	48.7	0.56	1.1%	0.96	2.0%
	2	49.2	0.38	0.8%	0.70	1.4%
3	1	87.8	0.81	0.9%	1.63	1.9%
	2	88.9	0.60	0.7%	1.04	1.2%
LDL			Within run		Between run	
Sample	Instrument	Mean	SD	CV	SD	CV
1	1	75.6	1.22	1.6%	1.46	1.9%
	2	75.1	0.90	1.2%	1.77	2.4%
2	1	189.2	1.98	1.1%	2.53	1.3%
	2	188.1	1.47	0.8%	4.32	2.3%
3	1	701.1	7.66	1.1%	14.59	2.1%
	2	685.0	9.48	1.4%	16.68	2.4%

Cho			Within run		Between run	
Sample	Instrument	Mean	SD	CV	SD	CV
1	1	79.0	0.67	0.9%	1.46	1.9%
	2	79.8	0.95	1.2%	1.53	1.9%
2	1	226.4	3.47	1.5%	4.30	1.9%
	2	227.3	1.67	0.7%	2.94	1.3%
3	1	526.0	3.67	0.7%	6.99	1.3%
	2	528.1	5.14	1.0%	7.67	1.5%
Trig			Within run		Between run	
Sample	Instrument	Mean	SD	CV	SD	CV
1	1	81.4	1.31	1.6%	1.37	1.7%
	2	83.3	0.74	0.9%	1.74	2.1%
2	1	239.2	3.31	1.4%	4.61	1.9%
	2	244.4	2.02	0.8%	2.82	1.2%
3	1	923.4	6.44	0.7%	9.92	1.1%
	2	933.1	5.76	0.6%	11.61	1.2%

b. *Linearity/assay reportable range:*

The linearity of each analyte on the Poly-Chem 90 system was tested by mixing human serum with human serum containing the analyte to several levels of the test to obtain 7 concentration levels for each analyte (HDL cholesterol 5 -115 mg/dL; LDL cholesterol 1.7 to 883 mg/dL; Cholesterol 7-716 mg/dL; Triglycerides 5 - 1049 mg/dL). Recoveries ranged from 94.6 to 108.7% for Direct HDL; from 90.1 to 104.2 % for Direct LDL; from 97.2 to 108.9 % for Cholesterol and from 96.2 to 105.4 % for Triglycerides. The summary of linear regression analysis of data is given in the table below.

Test	Range tested (mg/dL)	Slope (95% CI)	Intercept (95% CI)
Direct-HDL	5 - 115	0.990 (0.974 – 1.01)	-0.333 (-1.347 – 0.681)
Direct-LDL	1.7 - 883	1.003 (0.993 – 1.014)	-6.148 (-11.073 – -1.224)
Cholesterol	7 - 716	0.9999 (0.991 – 1.008)	2.076 (-1.351 – 5.502)
Triglyceride	5 - 1049	0.994 (0.986 – 1.002)	3.15 (-1.25 – 7.55)

The linearity studies support the sponsor's claimed measuring ranges as follows:

Direct HDL: 5 -115 mg/dL

Direct LDL: 9.2 – 883 mg/dL

Cholesterol: 8 – 716 mg/dL

Triglyceride: 5 -1049 mg/dL

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

The tests are traceable through the appropriate recommended calibrator to the Reference material/methods listed in the table below:

Reagent	Reference Material/Method
Direct HDL Cholesterol	Ultracentrifugation
Direct LDL Cholesterol	Ultracentrifugation
Total Cholesterol	NIST 909b NIST 1952a
Triglycerides	ID-GC/MS

The calibrators and controls are not included with the reagent kits, however the labeling recommends using Polymedco Calibration Serum (k955489), Polymedco Lipid Control for Direct HDL and LDL cholesterol (k022591) and Polymedco Assayed Multisera for Cholesterol and Triglycerides (k942458), which are sold separately. The calibrator set points and control ranges are provided for the Poly-Chem 90 analyzer.

The reagent systems have not been tested or certified by the Cholesterol Reference Method Laboratory Network (CRMLN). The labeling for Direct HDL, Direct LDL and Cholesterol contains language that the reagent systems have not been tested or certified by the CRMLN.

d. Detection limit:

Direct HDL-cholesterol
Samples of 0.9% saline solution were tested 60 consecutive times with the assay. The limit of blank was calculated from the results based on CLSI EP17-A. The limit of blank was calculated parametrically as:

LoB = 4.376 mg/dL

Five serum samples containing very low levels of the analyte (serum samples diluted with 0.9% saline) were tested in replicates of three over four days. The results were evaluated to determine the limit of detection for the assay.

The limit of detection was calculated parametrically as

LoD = 4.88 mg/dL

The sponsor set the lower end of the measuring range at 5 mg/dL based on LoD and linearity studies.

Direct LDL-cholesterol
Samples of 0.9% saline solution were tested 60 consecutive times with the assay. The limit of blank was calculated from the results based on CLSI EP17-A. The limit of blank was calculated parametrically as:
The limit of blank was calculated parametrically as:

LoB = 0.040 mg/dL

Five serum samples containing very low levels of the analyte (serum samples diluted with 0.9% saline) were tested in replicates of three over four days. The results were evaluated to determine the limit of detection for the assay.

The limit of detection was calculated parametrically as:
LoD = 0.43 mg/dL

The sponsor set the lower end of the measuring range at 9.2 mg/dL based on LoD and linearity studies.

Cholesterol

Samples of 0.9% saline solution were tested 60 consecutive times with the assay. The limit of blank was calculated from the results based on CLSI EP17-A.

The limit of blank was calculated parametrically as:
LoB = 0.000 mg/dL

Five serum samples containing very low levels of the analyte (serum samples diluted with 0.9% saline) were tested in replicates of three over four days. The results were evaluated to determine the limit of detection for the assay.

LoD = 0.70 mg/dL

The sponsor set the lower end of the measuring range at 8 mg/dL based on LoD and linearity studies.

Triglyceride

Samples of 0.9% saline solution were tested 60 consecutive times with the assay. The limit of blank was calculated from the results based on CLSI EP17-A.

The limit of blank was calculated parametrically as:
LoB = 0.000 mg/dL

Five serum samples containing very low levels of the analyte (serum samples diluted with 0.9% saline) were tested in replicates of three over four days. The results were evaluated to determine the limit of detection for the assay.

The limit of detection was calculated parametrically as

LoD = 0.95 mg/dL

The sponsor set the lower end of the measuring range as 5 mg/dL based on LoD and linearity studies.

e. *Analytical specificity:*

The sponsor conducted interference studies to evaluate the interference from hemoglobin, bilirubin, triglyceride and ascorbic acid for Direct HDL-cholesterol, Direct LDL-cholesterol and Cholesterol. Interference studies for triglyceride tested hemoglobin, bilirubin and ascorbic acid. Samples containing 2 levels of each analyte were used to spike the interfering substances at different concentrations to evaluate the bias in reference to the unspiked samples. Following are the levels of analyte in the un-spiked samples:

Direct HDL-cholesterol

Interferent	Level 1 (mg/dL)	Level 2 (mg/dL)
Hemoglobin	22	76
Bilirubin	29	84
Triglyceride	27	75
Ascorbic acid	28	78

Direct LDL-cholesterol

Interferent	Level 1 (mg/dL)	Level 2 (mg/dL)
Hemoglobin	96	201
Bilirubin	65	167
Triglyceride	66	189
Ascorbic acid	70	196

Cholesterol

Interferent	Level 1 (mg/dL)	Level 2 (mg/dL)
Hemoglobin	83	232
Bilirubin	110	231
Triglyceride	77	220
Ascorbic acid	95	221

Triglyceride

Interferent	Level 1 (mg/dL)	Level 2 (mg/dL)
Bilirubin	81	245
Ascorbic acid	105	237
Hemoglobin	73	304

Based on the acceptable recovery of analytes between 90 and 110% defined by the sponsor as indicating no significant interference, the results summarized in the table below indicate the interference limits.

Test	Highest level tested with no interference			
	Hemoglobin	**Bilirubin**	**Triglyceride**	**Ascorbic Acid**
Direct HDL	1000 mg/dL	15 mg/dL	805 mg/dL	10 mg/dL
Direct LDL	1000 mg/dL	20 mg/dL	805 mg/dL	10 mg/dL
Cholesterol	200 mg/dL	7.5 mg/dL	817 mg/dL	5 mg/dL
Triglycerides	200 mg/dL	5 mg/dL	NA	3 mg/dL

The labeling for the Cholesterol and Triglyceride assays includes the limitation that hemolyzed or icteric samples should not be tested and that high levels of ascorbic acid can interfere.

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 assayed on the Poly-Chem 180 instrument (predicate device, k020852) vs. the Poly-Chem 90 instrument. 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
Direct HDL-Cholesterol	43	22 – 109 mg/dL	1.02 (0.99 to 1.06)	1.08 (-0.89 to 3.19)	0.9957
Direct LDL-Cholesterol	50	17 – 824 mg/dL	1.00 (0.98 to 1.01)	-3.15 (-4.62 to -1.14)	0.9994
Cholesterol	84	15 – 680 mg/dL	0.98 (0.96 to 1.00)	-0.31 (-3.00 to 2.88)	0.9978
Triglycerides	49	14 – 915 mg/dL	1.01 (0.99 to 1.02)	-0.45 (-2.73 to 1.15)	0.9994

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 based on the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III).

   HDL-Cholesterol:

< 40 mg/dL	Low
≥60 mg/dL	High

   LDL-Cholesterol:

< 100 mg/dL	Optimal
100 - 129 mg/dL	Near or above optimal
130 – 159 mg/dL	Borderline high
160 – 189 mg/dL	High
≥ 190 mg/dL	Very high

   Cholesterol:

< 200 mg/dL	Desirable
200 – 239 mg/dL	Borderline high
≥ 240 mg/dL	High
Triglyceride:	
< 150 mg/dL	Normal
150 – 199 mg/dL	Borderline high
200 – 499 mg/dL	High
≥ 500 mg/dL	Very high

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.