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

A. 510(k) Number:

k111036

B. Purpose for Submission:

The purpose of the submission is to add lithium heparin plasma as a sample matrix to the following previously cleared devices:

High Density Lipoprotein (HDL-Cholesterol)	k073497
Low Density Lipoprotein (LDL-Cholesterol)	k090734
Total Cholesterol (CHOL)	k072249
Triglyceride (TRIG)	k080823

C. Measurand:

HDL-Cholesterol, LDL-Cholesterol, Total Cholesterol, Triglyceride

D. Type of Test:

Quantitative spectrophotometric

F. Proprietary and Established Names:

EasyRA HDL Cholesterol Reagent, EasyRA LDL Cholesterol Reagent, EasyRA CHOL Reagent, EasyRA TRIG Reagent

E. Applicant:

Medica Corporation

G. Regulatory Information:

1. Regulation section:

Device Name	Regulation	Name	Class	Product Code
EasyRA HDL Cholesterol Reagent	21 CFR§862.1475	Lipoprotein test system	I, meets limitations per 21 CFR 862.9(c)(4)	LBS

EasyRA LDL Cholesterol Reagent	21 CFR§862.1475	Lipoprotein test system	I, meets limitations per 21 CFR 862.9(c)(4)	MRR
EasyRA CHOL Reagent	21 CFR§862.1175	Cholesterol (total) test system	I, meets limitations per 21 CFR 862.9(c)(4)	CHH
EasyRA TRIG Reagent	21 CFR§862.1705	Triglyceride test system	I, meets limitations per 21 CFR 862.9(c)(4)	CDT

4. Panel:

   Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See Indications for use below.

2. Indication(s) for use:

   EasyRA High Density Lipoproteins (HDL) Cholesterol Reagent:

   The EasyRA HDL Cholesterol reagent is intended for the quantitative determination of High Density Lipoprotein Cholesterol in human serum and plasma on the Medica EasyRA Chemistry Analyzer. The Medica EasyRA HDL-Cholesterol reagent can assist in the diagnosis and treatment of patients at risk of developing coronary heart disease. For in vitro diagnostic use only.

   EasyRA Low Density Lipoproteins (LDL) cholesterol Reagent

   The EasyRA LDL Cholesterol reagent is intended for the quantitative determination of Low Density Lipoprotein Cholesterol in human serum and plasma, using the MEDICA "EasyRA Chemistry Analyzer" in clinical laboratories. The LDL Cholesterol measurements are used in the diagnosis and treatment of lipid disorders (such as diabetes mellitus), atherosclerosis, and various liver and renal diseases. For in vitro diagnostic use only.

   EasyRA Cholesterol (CHOL) Reagent

   The EasyRA CHOL reagent is intended for the quantitative determination of total cholesterol in human serum and plasma, using the MEDICA "EasyRA Chemistry Analyzer" in clinical laboratories. Total cholesterol measurements are used to screen for elevated cholesterol as a risk factor in coronary artery disease. For in vitro diagnostic use only.

EasyRA Triglycerides (TRIG) Reagent

The EasyRA TRIG reagent is intended for the quantitative measurement of triglycerides in human serum and plasma, using the MEDICA "EasyRA Chemistry Analyzer" in clinical laboratories. Measurements obtained by this device are used in the diagnosis and treatment of patients with diabetes mellitus, nephrosis, liver obstruction, other diseases involving lipid metabolism and various endocrine disorders. For in vitro diagnostic use only.

3. Special conditions for use statement(s):

For prescription use

4. Special instrument requirements:

Medica EasyRA chemistry analyzer

I. Device Description:

The Medica HDL cholesterol reagent and the LDL reagents are *in vitro* diagnostic reagent systems consisting of two parts: R1 and R2. The reagents are packaged in wedge shaped containers and are liquid, ready-to-use.

The Medica Cholesterol and Triglyceride reagents are single *in vitro* diagnostic reagent systems. Each reagent is packaged in a wedge shaped container and is liquid, ready-to-use.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Device Name	Predicate 510k	Predicate Name
EasyRA HDL Reagent	k073497	EasyRA HDL Reagent
EasyRA LDL Reagent	k090734	EasyRA LDL Reagent
EasyRA CHOL Reagent	k072249	EasyRA CHOL Reagent
EasyRA TRIG Reagent	k080823	EasyRA TRIG Reagent

3. Comparison with predicate:

HDL-Cholesterol		
Item	Device	Predicate-k073497
Intended Use	Same	The EasyRA High Density Lipoprotein (HDL) reagent is intended for the quantitative determination of High Density Lipoproteins using the MEDICA "EasyRA Chemistry Analyzer" in clinical laboratories.
Sample	Serum, Plasma	Serum
Reagent type	Same	Liquid ready-for-use
Reportable range	Same	2.0 – 150 mg/dL
Wavelength	Same	Primary: 600 nm Secondary: 700 nm
Wavelength	Same	Primary: 600 nm Secondary: 700 nm
Reagent storage	Same	2 – 8 ^{0}C
Test Summary	Same	The HDL-cholesterol reagent 1 precipitates non-high density lipoproteins. The HDL-cholesterol reagent 2 solubilizes and reacts with HDL to develop a chromogen absorbing at 600nm. The absorbance is directly proportional to the HDL level.

–LDL-Cholesterol		
Item	Device	Predicate- k090734
Intended Use	Same	The EasyRA Low Density Lipoprotein (LDL-cholesterol) reagent is intended for the quantitative determination of Low Density Lipoproteins using the MEDICA "EasyRA Chemistry Analyzer" in clinical laboratories.
Sample	Serum, Plasma	Serum
Reagent type	Same	Liquid ready-for-use
Reportable range	Same	6.0 – 540 mg/dL
Wavelength	Same	550 nm
Reaction type	Same	Endpoint
Reagent storage	Same	2 – 8 ^{0}C
Test Summary	Same	Reagent 1 solubilizes only the non LDL particles. The cholesterol realized is consumed by cholesterol esterase/oxidase in a non color forming reaction. Reagent 2 solubilizes the LDL particles and a coupler develops a chromogen that absorbs light at

–LDL-Cholesterol		
Item	Device	Predicate- k090734
		550nm. The EasyRA measures absorbance according to Beer's law.

–Total Cholesterol		
Item	Device	Predicate- k072249
Intended Use	Same	The EasyRA (CHOL) reagent is intended for the quantitative determination of Total Cholesterol using the MEDICA "EasyRA Chemistry Analyzer" in clinical laboratories.
Sample	Serum, Plasma	Serum
Reagent type	Same	Liquid ready-for-use
Reportable range	Same	10 – 600 mg/dL
Wavelength	Same	520 nm
Reaction type	Same	Endpoint
Reagent storage	Same	2 – 8 ^{0}C
Test Summary	Same	Cholesterol esters are hydrolyzed to cholesterol and fatty acids. Cholesterol is oxidized to delta 4-cholestenone with the simultaneous production of hydrogen peroxide. In the presence of peroxidase, hydrogen peroxide oxidizes phenol and 4-aminoantipyrine to give a quinoneimine dye colored red. The intensity of the color produced is proportional to the concentration of cholesterol in the sample.

Triglyceride		
Item	Device	Predicate- k080823
Intended Use	Same	The EasyRA TRIG reagent is intended for the quantitative determination of Triglycerides using the MEDICA "EasyRA Chemistry Analyzer" in clinical laboratories.
Sample	Serum, Plasma	Serum
Reagent type	Same	Liquid ready-for-use
Reportable range	Same	3 – 750 mg/dL
Wavelength	Same	520 nm
Reaction type	Same	Endpoint
Reagent storage	Same	2 – 8 ^{0}C
Test Summary	Same	Triglycerides are hydrolyzed to glycerol and free fatty acids by lipase. The

Triglyceride		
Item	Device	Predicate- k080823
		glycerol is phosphorylated to glycerol-1-phosphate, which is then oxidized by glycerol phosphate oxidase (GPO) to produce hydrogen peroxide. The hydrogen peroxide causes oxidative coupling of p-chlorophenol and 4 amino-antipyrine, which produces a red dye complex. The absorbance of the dye at 520 nm is proportional to the concentration of triglyceride in the sample.

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

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

CLSI EP9-A2: *Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Second Edition*

L. Test Principle:

HDL-C: The Medica HDL cholesterol assay is a two reagent system: R1 and R2. The first step involves the removal of non-high density lipoproteins (non-HDL) via selective reaction with reagent R1. In the second step, the selective detergent in R2 solubilizes the HDL cholesterol, which then reacts with a chromagen to develop a color that can be read optically at 600nm. The intensity of the color is proportional to the concentration of HDL cholesterol in the sample.

LDL-C: The Medica Low Density Lipoprotein (LDL) Reagent is provided in a ready-to-use dual chamber plastic wedge. Reagent 1 solubilizes the **non**-LDL particles. The cholesterol realized is consumed by cholesterol esterase and cholesterol oxidase in a non color forming reaction. Reagent 2 solubilizes the LDL particles and a chromogenic coupler develops a chromogen. The chromogen absorbs light of specific wavelength (550nm), where the EasyRA measures absorbance according to Beer's law.

Cholesterol (CHOL): The Medica EasyRA Cholesterol reagent uses the enzymatic Trinder endpoint reaction, which is based on the work of Allain et al. In this method, cholesterol esters are hydrolyzed by cholesterol esterase to cholesterol and fatty acids. Cholesterol is oxidized by cholesterol oxidase to delta 4-cholestenone with the simultaneous production of hydrogen peroxide. In the

presence of peroxidase, hydrogen peroxide oxidizes phenol and 4-aminoantipyrine to give a quinoneimine dye colored red. The absorbance of the resulting quinoneimine dye is measured at 520 nm with 600 nm as a blanking wavelength. The intensity of the color produced is proportional to the concentration of cholesterol in the sample based on Beer's Law.

Triglyceride: The Medica EasyRA TRIG Reagent is provided in a ready-to-use plastic wedge. Serum triglycerides are hydrolyzed to glycerol and free fatty acids by lipase. In the presence of ATP and glycerol kinase (GK), the glycerol is phosphorylated to glycerol-1-phosphate, which is then oxidized by glycerol phosphate oxidase (GPO) to produce hydrogen peroxide. The hydrogen peroxide causes oxidative coupling of p-chlorophenol and 4 amino-antipyrine, which produces a red colored quinoneimine dye complex. The absorbance of the dye at 520 nm is proportional to the concentration of triglyceride in the sample according to Beer's Law.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Serum and plasma- Precision studies were performed on the EasyRA analyzer in conjunction with the matrix comparison study with lithium heparin tubes. Paired plasma and serum samples were analyzed over a minimum of 7 days. Results were calculated for average SD for 3 partitioned bins covering the ranges tested. The average SD in each of the 3 bins for both plasma and serum are comparable.

HDL- cholesterol	**Low**	**Medium**	**High**
Analytical Range	2 - 45 mg/dL	45 – 60 mg/dL	60– 150 mg/dL
Number of samples	20	29	18
Number of replicates	2	2	2
Serum Mean	34.3	52.1	86.3
Serum SD	0.50	0.44	0.53
Serum CV (%)	1.46%	0.84%	0.61%
Plasma Mean	33.9	51.6	84.0
Plasma SD	0.63	0.60	0.83
Plasma CV (%)	1.86%	1.17%	0.99%

LDL- cholesterol	**Low**	**Medium**	**High**
Analytical Range	6 - 100 mg/dL	100 – 130 mg/dL	130– 540 mg/dL
Number of samples	28	21	19
Number of replicates	2	2	2

Serum Mean,	76.1	112.5	232.6
Serum SD	0.72	1.02	2.07
Serum CV (%)	0.95%	0.91%	0.89%
Plasma Mean	74.3	110.5	229.9
Plasma SD	0.67	1.07	1.85
Plasma CV (%)	0.90%	0.97%	0.80%

Total Cholesterol	**Low**	**Medium**	**High**
Analytical Range	10 - 175 mg/dL	175 – 210 mg/dL	210– 600 mg/dL
Number of samples	29	20	21
Number of replicates	2	2	2
Serum Mean	140.0	191.8	297.2
Serum SD	1.32	1.79	4.15
Serum CV (%)	0.95%	0.93%	1.40%
Plasma Mean	136.4	189.3	295.1
Plasma SD	1.26	1.29	4.63
Plasma CV (%)	0.92%	0.68%	1.57%

Triglyceride	**Low**	**Medium**	**High**
Analytical Range	3 - 100 mg/dL	100 – 150 mg/dL	150– 750 mg/dL
Number of samples	22	17	24
Number of replicates	2	2	2
Serum Mean	72.0	122.0	285.2
Serum SD	0.71	1.10	1.66
Serum CV (%)	0.98%	0.90%	0.58%
Plasma Mean	68.6	117.5	275.9
Plasma SD	0.95	0.92	1.75
Plasma CV (%)	1.39%	0.79%	0.63%

In addition a simplified within-run precision study was performed on the EasyRA analyzer by analyzing 3 plasma patient samples, 20 consecutive times in one run on one day. The within-run precision data is summarized in the table below:

	Mean	**SD**	**CV (%)**
HDL-C	Level 1 – 25.9	Level 1 – 0.31	Level 1 – 1.19
	Level 2 – 54	Level 2 – 0.65	Level 2 – 1.20
	Level 3 – 133.2	Level 3 – 0.89	Level 3 – 0.67
LDL-C	Level 1 – 36.9	Level 1 – 0.49	Level 1 – 1.33
	Level 2 – 93.2	Level 2 – 1.18	Level 2 – 1.27
	Level 3 – 287.7	Level 3 – 1.84	Level 3 – 0.64
Cholesterol	Level 1 – 43.0	Level 1 – 0.51	Level 1 – 1.19
	Level 2 – 154.9	Level 2 – 1.60	Level 2 – 1.03

	Level 3 – 383.2	Level 3 – 3.67	Level 3 – 0.96
Triglyceride	Level 1 – 54.6	Level 1 – 0.60	Level 1 – 1.11
	Level 2 – 410.6	Level 2 – 2.04	Level 2 – 0.50
	Level 3 – 627.1	Level 3 – 2.61	Level 3 – 0.42

b. Linearity/assay reportable range:

Plasma - Linearity studies were not conducted in plasma. See previously cleared linearity data in k073497 (HDL-C), k090734 (LDL-C), k072249 (Chol), and k080823 (Triglyceride) for serum samples. The linear reportable ranges for each assay are summarized below.

Device Name	Measuring Range
EasyRA HDL-C Reagent	2 – 150 mg/dL
EasyRA LDL-C Reagent	6 to 540 mg/dL
EasyRA CHOL Reagent	10 – 600 mg/dL
EasyRA TRIG Reagent	3 mg/dL to 750 mg/dL

Extended linearity studies were performed for LDL, cholesterol and triglyceride to evaluate accuracy and precision. The sponsor recommends a dilution of 1:2 when the LDL-C, cholesterol and triglyceride results in plasma or serum fall outside the upper measuring range of 540 mg/dL, 600 mg/dL and 750 mg/dL, respectively. A dilution study was performed for LDL-C, cholesterol and triglyceride on five different spiked patient plasma samples (one set of 5 for each assay) to increase the LDL level in the range of 540 to 1080 mg/dL, to increase the cholesterol level in the range of 600 to 1200 mg/dL, and to increase triglyceride level in the range from 750 to 1500 mg/dL. Materials used for spiking for LDL-C and cholesterol were derived from bovine material. High triglyceride levels were obtained by spiking with Intralipid.

Each sample was then diluted with saline at 1:2 dilution by the analyzer and compared to a manually diluted sample. Each diluted sample was run in triplicate on two EasyRA analyzers. The % recovery range of the system for each analyte is provided in the table below:

Device Name	EasyRA % Recovery
EasyRA LDL-C Reagent	99.38-101.4 %
EasyRA CHOL Reagent	101.5-102.9 %
EasyRA TRIG Reagent	97.7-104.8 %

In addition, a simplified within-run precision study was performed in the extended linearity range for all analytes by analyzing 3 plasma samples, 20 consecutive times in one run on one day on three instruments using on-board dilution. The within-run precision data is summarized in the table below:

	Mean	SD	CV (%)
LDL-C	Level 1 – 631.5	Level 1 – 7.37	Level 1 – 1.17
	Level 2 – 696.4	Level 2 – 8.8	Level 2 – 1.26
	Level 3 – 837.0	Level 3 – 8.76	Level 3 – 1.05
Cholesterol	Level 1 – 711.3	Level 1 – 6.72	Level 1 – 0.94
	Level 2 – 814.5	Level 2 – 15.3	Level 2 – 1.87
	Level 3 – 916.8	Level 3 – 11.1	Level 3 – 1.21
Triglyceride	Level 1 – 893.2	Level 1 – 6.99	Level 1 – 0.78
	Level 2 – 1014.0	Level 2 – 17.84	Level 2 – 1.76
	Level 3 – 1355.3	Level 3 – 7.53	Level 3 – 0.56

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

Calibrators were previously cleared under k073497 (HDL-C), k090734 (LDL-C), k072249 (Total Cholesterol), k080823 (Triglyceride).

The Easy RA HDL-C, LDL-C and Total Cholesterol devices are not CRMLN certified.

d. Detection limit:

Limit of detection studies were not conducted for plasma. See cleared serum data under k073497 (HDL-C), k090734 (LDL-C), k072249 (Total Cholesterol), k080823 (Triglyceride).

e. Analytical specificity:

Interference studies were not conducted for plasma. See cleared serum data under k073497 (HDL-C), k090734 (LDL-C), k072249 (Total Cholesterol), k080823 (Triglyceride).

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

Serum—See cleared method comparison data under k073497 (HDL-C), k090734 (LDL-C), k072249 (Total Cholesterol), k080823 (Triglyceride). Plasma matrix comparison data are provided below in 2. (b) of this section.

b. Matrix comparison:

Lithium Heparin Plasma - A matrix comparison study was performed in conjunction with CLSI EP9-A2 guidelines using lithium heparin tubes. The study was conducted with human plasma and serum samples. Each sample was evaluated for bias and recovery between the two matrices using the EasyRA chemistry analyzer. 67 paired samples (57 natural and 10 altered through spiking or dilution) were used for HDL-C; 68 paired samples (57 natural and 11 altered through spiking or dilution) were used for LDL-C; 70 paired samples (57 natural and 13 altered through spiking or dilution) were used for cholesterol; and 63 paired samples (56 natural and 7 altered through spiking or dilution) were used for triglyceride. One single set of plasma samples were used as test samples, while duplicate serum samples were used as references. The follow regression equations were obtained:

Analyte	Slope	Intercept	R^2	Sample Range (mg/dL)
HDL-C	0.9767	0.0900	0.9950	3 to 148
LDL-C	0.9954	-1.8888	0.9991	9 to 512
Cholesterol	1.0145	-5.1408	0.9982	11 to 578
Triglyceride	0.9735	-1.9025	0.9992	8 to 706

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:

   All reference ranges in the labeling follow the recommendations set by the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) guidelines as follows:

   HDL-Cholesterol[1]: < 40 mg/dL Low, ≥ 60 mg/dL High

   LDL-Cholesterol[1]:

LDL Cholesterol – Primary Target of Therapy

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

Cholesterol[1]:

Risk Classification	Total Cholesterol
Desirable	< 200 mg/dl (5.18 mmol/L)
Borderline High	200 –239 mg/dl (5.18-6.19 mmol/L)
High	≥ 240 mg/dl (6.22mmol/L)

Triglyceride[1]:

Triglycerides	Primary Target of Therapy
<150 mg/dL	Normal
150-199 mg/dL	Borderline High
200-499 mg/dL	High
>500 mg/dL	Very High

[1] 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). NIH publication No. 01-3670: May 2001.

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.