

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY**

A. 510(k) Number:

k090734

B. Purpose for Submission:

New device

C. Measurand:

Low density lipoprotein (LDL) cholesterol

D. Type of Test:

Quantitative, colorimetric assay.

E. Applicant:

Medica Corporation

F. Proprietary and Established Names:

EasyRA dLDL Reagent

EasyRA dLDL Calibrator

EasyRA EasyQC material

G. Regulatory Information:

Device Name	Product Code	Device Classification	Regulation Number	Panel
EasyRA dLDL Reagent	MRR	I, meets the limitation to the exemption (21 CFR 862.9 (c) (4))	21 CFR 862.1475-System, test, Low Density Lipoprotein	Chemistry (75)
EasyRA dLDL Calibrator	JIX	II	21 CFR 862.1150-Calibrator	Chemistry (75)
EasyRA EasyQC Material	JJY	I	21 CFR 862.1660-Quality control material (assayed and unassayed)	Chemistry (75)

H. Intended Use:

1. Intended use(s):

See Indications for Use below.

2. Indications(s) for use:

The EasyRA dLDL Reagent is intended for the quantitative determination of Low Density Lipoproteins in human serum, using the MEDICA “Easy RA 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.

The EasyRA dLDL Calibrator facilitates measurements of LDL Cholesterol on the EasyRA clinical chemistry analyzer when used in conjunction with Medica’s dLDL reagent. The dLDL calibrator is used to establish a point of reference that is used in the determination of values in the measurement of LDL Cholesterol in human serum.

The EasyRA EasyQC Material validates measurements of LDL Cholesterol on the EasyRA clinical chemistry analyzer when used in conjunction with Medica’s dLDL reagent and calibrator. The EasyQC is used to estimate test precision and to detect systemic analytical deviations that may arise from reagent or analytical instrument variation.

3. Special conditions for use statement(s):

For prescription use only; for professional use only.

Avoid using icteric serum samples.

4. Special instrument requirements:

MEDICA EasyRA Chemistry Analyzer

I. Device Description:

The EasyRA dLDL cholesterol Reagent system is intended for the quantitative measurement of LDL in human serum using the MEDICA EasyRA Chemistry Analyzer in clinical laboratories. Two reagents are provided as usable volumes, R1 (29 mL) and R2 (10 mL). R1 solubilizes the non-LDL lipoproteins. The cholesterol realized is consumed by cholesterol esterase and cholesterol oxidase in a non-color forming reaction. The selective detergent in R2 solubilizes the LDL cholesterol specifically which then reacts with a chromogen. The resulting color can then be read optically at 550 nm by the EasyRA analyzer. R1 and R2 contain reagents, detergents, buffer, and preservatives.

The EasyRA dLDL cholesterol Calibrator is provided as 1 ml vials of lyophilized human serum containing lipoproteins from the various lipoprotein classes including low density lipoprotein.

The EasyQC material contains two levels (Level A and B) of lyophilized, human serum base, multi-constituent QC powder. EasyRA Easy QC is the same material as in the predicate (k080404) with the added assayed value for LDL. Level A and B contain 85 (75-95) and 50 (45-55) mg/dL of dLDL, respectively.

The inserts for the Calibrator and QC material include the following statement: Human source material used in the manufacture of this calibrator has been tested using FDA approved methods and found to be non-reactive for HBsAg, and antibodies to HCV and HIV-1/2.

J. Substantial Equivalence Information:

1. Predicate device name(s):
 Genzyme, N-Geneous LDL Cholesterol Reagent (k971573)
 Genzyme, N-Geneous LDL Cholesterol Calibrator (k971573)
 Medica, EasyQC Chemistry (k080404)
2. Predicate 510(k) number(s):
 k971573, k080404
3. Comparison with predicate:

dLDL Reagent Similarities and Differences		
Item	Device	Predicate (k971573)
Intended Use	The EasyRA direct Low Density Lipoprotein (dLDL) cholesterol reagent is intended for the quantitative measurement of LDL in human serum, using the MEDICA “EasyRA Chemistry Analyzer” in clinical laboratories. Measurement of LDL is used in the diagnosis and treatment of lipid disorders (such as diabetes mellitus), atherosclerosis and various liver and renal diseases.	Clinical chemistry reagent used to provide a direct quantitative measurement of low-density lipoprotein cholesterol (LDL-C) in human serum and plasma, using an automated chemical analyzer.
Test Methodology	A two reagent system where 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	Same

dLDL Reagent Similarities and Differences		
Item	Device	Predicate (k971573)
	remaining LDL particles and a chromogenic coupler develops a chromogen. The chromogen absorbs light of specific wavelength (550 nm), where the EasyRA measures absorbance according to Beer's law.	
Sample type	Serum	Same
Reagent type	Liquid ready-for-use	Same
Linearity range	6-540 mg/dL	6.6-992 mg/dL
Wavelength	550 nm	Same
Reagent Storage	2-8 °C	Same

dLDL Calibrator Similarities and Differences		
Item	Device	Predicate (k971573)
Intended Use	The LDL cholesterol calibrator is for use as the LDL calibrator for the Medica LDL cholesterol test on the Medica EasyRA Chemistry Analyzer.	The LDL cholesterol calibrator facilitates measurements of low density lipoproteins that are used in the diagnosis and treatment of lipid disorders (such as diabetes mellitus), atherosclerosis and various liver and renal diseases.
Test Methodology	The calibrator is used to establish the calibration factor in Beer's equation using a known concentration reagent and the measured absorbance. The calibration factor is used to determine the LDL concentration in the patient sample.	Same
Reagent Storage	2-8 °C	Same

EasyRA Easy QC is the same material as in the predicate (k080404) with the added assayed value for LDL.

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

Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – Second Edition (CLSI EP5-A2).

Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Second Edition (CLSI EP9-A2).

Evaluation of the Linearity of Quantitative Measuring Procedures: A Statistical Approach; Approved Guideline (CLSI EP6-A2).

Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline (CLSI EP17-A).

Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition (CLSI EP7-A2).

Preliminary Evaluation of Quantitative Clinical Laboratory Methods; Approved Guideline-Second Edition (CLSI EP-10A2).

L. Test Principle:

In this two step, two reagent system the non- LDL particles are selectively solubilized in the first step and the realized cholesterol is consumed by cholesterol esterase and cholesterol oxidase in a non-color forming reaction. In the second step the remaining LDL particles are solubilized and a chromogenic coupler develops a chromogen that absorbs light of specific wavelength (550 nm).

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

The sponsor performed Within Run and Total precision studies according to the CLSI EP5-A2 guideline. One lot each of the following human serum based controls: two levels of Medica Quality Control material (85 and 50 mg/dL), a commercially available QC material (Biorad, 130 mg/dL), and a QC material at 193 mg/dL were used. All four levels were tested on one EasyRA analyzer twice a day over a 20 day period. Results from the 40 measurements are summarized below:

	Level 1	Level 2	Level 3	Level 4
Mean (mg/dL)	48.6	83.3	132.6	193.2
Within Run Precision				
Std. Dev.	0.70	0.99	1.59	2.11
CV%	1.44	1.19	1.20	1.10
Total Precision				
Std. Dev.	1.31	1.93	3.03	3.36
CV%	2.7	2.32	2.28	1.75

To verify precision in the extended measuring range a spiked sample with a nominal value of approximately 800 mg/dL was analyzed 20 times on a single EasyRA analyzer to determine the within run precision. Results are summarized below:

Mean (mg/dL)	784.5
Within Run Precision	
Std. Dev.	10.62
CV%	1.35

b. Linearity/assay reportable range:

The sponsor performed linearity studies in accordance with the CLSI EP6-A guideline. A commercially available concentrated LDL stock solution was used to spike a pooled human serum solution to an LDL value of approximately 600 mg/dL. This solution was subsequently diluted with saline to make a total of eight solutions ranging from 2.1 to 599.5 mg/dL covering the entire claimed range of 6 to 540 mg/dL.

The eight samples were assayed in duplicate and the recovered values were plotted against the assigned values. The data was analyzed using linear regression as well as second and third order non-linear fitted polynomial regression. The 1st order regression equation was: $y = 1.00x - 4.03$; $R^2 = 0.9993$.

The linear regression equation supports the sponsor's claimed linearity of 6 to 540 mg/dL.

The extended measuring range (540 to 1080 mg/dL) was evaluated for recovery obtained with the EasyRA on-board dilution compared to manually diluted samples. A fresh serum sample was obtained from a single donor, pre-assayed for LDL cholesterol, and then spiked with a concentrated LDL stock solution to give three different levels of LDL (550, 800, 1000 mg/dL). Half of each sample was manually diluted, then all of the samples were analyzed in triplicate on two different Easy RA analyzers. The % recovery of the on-board dilution compared to the manually diluted samples (96.8% at 1000 mg/dL; 100.9% at 800 mg/dL; 98.6 at 550 mg/dL) validated the extended measuring range of 540 to 1080 mg/dL.

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

Medica dLDL Calibrator and EasyQC Chemistry Level A and B, or EasyQC Chemistry/Electrolytes Level A and B are required materials for the assay specified in the labeling but are not provided with the assay reagent.

The EasyRA Calibrator manufactured by Genzyme Corp. was cleared under k971573. The QC material manufactured by Media Corp. is the same material cleared under k080404 with the added assayed value of LDL.

Traceability:

The reagent insert states that Medica's LDL test has not been certified or tested by the Cholesterol reference Method Laboratory Network (CRLMN). Sponsor attests that the value of the LDL Cholesterol Calibrator is traceable to the National Reference System for Cholesterol (NRS/CHOL).

Value assignment was performed on a minimum of 3 EasyRA analyzers with both levels assayed in triplicate to assign the mean recovery for each analyte. To be acceptable the results must be within $\pm 2SD$ of that assigned to the control used from the manufacturer.

The reagent insert states that Medica recommends the use of additional lipid control material with LDL levels around 160 mg/dL.

Stability:

EasyRA Calibrator: Stability was established in k971573. Calibrator is stable until the expiration date if stored at 2 to 8°C. After reconstitution, the calibrator is stable for 14 days when stored closed at 2 to 8°C. Frozen LDL calibrator aliquots are stable for up to 4 weeks at -80°C and should be thawed only once.

EasyRA QC material: Stability was established in k080404. EasyQC material is stable until the expiration if stored at 2 to 8°C, and after reconstitution the LDL component is stable for 5 days at 2 to 8°C.

d. Detection limit:

The sponsor determined the limit of quantitation (LOQ) according to the CLSI EP-17A guideline. Five independent serum solutions with LDL concentrations of about 5 mg/dL were prepared and tested in duplicate in five runs. The mean value of the 5 solutions tested was obtained and the LOQ was determined to be 4.8 mg/dL.

c. Analytical specificity:

The sponsor performed interference studies according to the CLSI EP7-A guideline. Serum samples containing four concentrations of LDL (50, 96, 156, and 194 mg/dL) were used. Six to seven levels of each interferent were tested in triplicate on the EasyRA analyzer.

The sponsor defined interference as the highest level tested that does not cause greater than $\pm 10\%$ change in recovery (95% confidence). No interference was found for hemoglobin up to 600 mg/dL, lipemia (Intralipid) up to 500 mg/dL, bilirubin (unconjugated) up to 5.5 mg/dL, and ascorbic acid up to 50 mg/dL.

Included in the insert is a warning not to use icteric samples as there is significant interference above 5.5 mg/dL bilirubin. Also included are the following references regarding exogenous drugs and substances that can interfere with clinical chemistry tests:

Young DS. *Effects of Drugs on Clinical Laboratory Tests* 4th ed. Washington, DC: AACC Press; 1995.

Young DS. Effects of Preanalytical Variables on Clinical Laboratory Tests. 2nd ed. Washington, DC. AACC Press; 1997.

d. Assay cut-off:

Not Applicable

2. Comparison studies:

a. Method comparison with predicate device:

Method comparisons to the predicate device were performed in accordance with the CLSI EP9-A2 guideline. A total of 61 human serum samples were tested to fully span the claimed measuring range. Of these 61 samples, 5 were spiked and 2 were diluted to supplement the upper and lower ends of the range. Samples ranging from 7 to 540 mg/dL were analyzed using the Medica dLDL Reagent on Medica's EasyRA analyzer (Y) and were compared to results of samples analyzed in duplicate using the Genzyme LDL Reagent on the Roche Cobas-Mira analyzer (Predicate method, k971573) (X). The comparison resulted in: $y = 0.9904x - 0.3123$; $R^2 = 0.9976$.

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):

Not Applicable

4. Clinical cut-off:

Not Applicable

5. Expected values/Reference range:

The following reference ranges for LDL in serum from the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) guidelines are included in the package insert:

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

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.