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

A. 510(k) Number:

k072249

B. Purpose for Submission:

New Device

C. Measurand:

Calcium and Cholesterol

D. Type of Test:

Calcium: AZO method

Cholesterol: Enzymatic endpoint

E. Applicant:

Medica Corp.

F. Proprietary and Established Names:

EasyRA Quantitative Calcium Reagent

EasyRA Quantitative Cholesterol Reagent

G. Regulatory Information:

1. Regulation section:

   21 CFR 862.1145 Calcium test system

   21 CFR 862.1175 Cholesterol (total) test system

2. Classification:

   Calcium – Class II

   Cholesterol - Class I, meets the limitations to exemption in 21 CFR 862.9(c)(4)

3. Product code:

   CJY - azo dye, calcium

   CHH - enzymatic esterase--oxidase, cholesterol

4. Panel:

   Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See indications for use below

2. Indication(s) for use:

   EasyRA Calcium
   EasyRA Calcium Reagent is intended for the quantitative determination of total calcium concentration in serum using the Medica EasyRA Chemistry 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).
   For *in-vitro* diagnostic use only. For Professional use only.

   EasyRA Cholesterol
   The EasyRA Cholesterol Reagent is intended for the quantitative determination of cholesterol in human serum on the Medica EasyRA Chemistry analyzer to screen for elevated cholesterol as a risk factor in coronary artery disease.
   For *in-vitro* diagnostic use only. For Professional Use Only.

3. Special conditions for use statement(s):

   For prescription use only

4. Special instrument requirements:

   Medica EasyRA chemistry analyzer

I. Device Description:

The calcium assay is a two reagent system where R1 contains Phosphate buffer, 8-Hydroxyquinoline-5-sulfonic acid, Arsenazo III, non-reactive stabilizers, and surfactant. R2 contains hydrochloric acid and surfactant.

The cholesterol reagent contains Pipes buffer, Phenol, Sodium cholate , 4-Aminoantipyrine, Cholesterol esterase, Cholesterol oxidase, and Peroxidase.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Cobas Ready Calcium Reagent

   Cobas Ready Cholesterol Reagent

2. Predicate K number(s):

   k896224

   k896239

3. Comparison with predicate:

Calcium Similarities		
Item	Device	Predicate
Sample	Serum	Serum
Test Methodology	Ready-to-use reagents using AZO methodology	Ready-to-use reagents using AZO methodology

Calcium Differences		
Item	Device	Predicate
Storage	2 – 8°C	15 – 25°C
Measuring range	1- 15 mg/dL	Up to 14 mg/dL

Cholesterol Similarities		
Item	Device	Predicate
Sample	Serum	Serum
Test Methodology	Enzymatic Endpoint	Enzymatic Endpoint
Storage	2 – 8°C	2 – 8°C

Cholesterol Differences		
Item	Device	Predicate
Measuring range	10 – 600 mg/dL	2 – 525 mg/dL

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

None referenced.

L. Test Principle:

Calcium

This reagent utilizes Arsenazo III, which has a high affinity for calcium at neutral pH. Interference from magnesium is eliminated by the addition of 8-hydroxyquinoline-5-sulfonic acid. Arsenazo III reacts with calcium to form a 1:1 blue complex with an absorption maximum at 650 nm. The concentration of calcium is proportional to the intensity of the blue color.

Cholesterol

Cholesterol esters are hydrolyzed by cholesterol esterase to cholesterol and fatty acids. Cholesterol is oxidized by cholesterol oxidase 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.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   Within run imprecision studies were run for EasyRA Calcium and EasyRA Cholesterol. Twenty replicates at three concentrations were tested in the same run. The data is summarized below.

Calcium

QC Level (mg/dL)	Total Imprecision SD (mg/dL)	Total Imprecision CV (%)
12.81	0.23	1.8
9.73	0.19	1.9
5.24	0.17	3.3

Cholesterol

QC Level (mg/dL)	Total Imprecision SD (mg/dL)	Total Imprecision CV (%)
215.9	4.13	1.9
168.05	1.76	1
105.7	1.34	1.3

Total imprecision was determined following CLSI EP5-A2. Three levels of commercial serum-based controls were tested in duplicate twice a day for 20 days on three analyzers. The data is summarized below.

Calcium

QC Level (mg/dL)	Total Imprecision SD (mg/dL)	Total Imprecision CV (%)
9	0.13	1.46
11.8	0.16	1.33
6	0.12	1.95

Cholesterol

QC Level (mg/dL)	Total Imprecision SD (mg/dL)	Total Imprecision CV (%)
168.1	2.5	1.5
302.9	3.6	1.2
102.2	2.3	2.2

b. Linearity/assay reportable range:

Calcium

Linearity studies were performed using commercially available linearity standards. The concentrations tested ranged from 1.1 mg/dL to 20 mg/dL and the observed values demonstrated acceptable recovery compared to the expected values. A linear regression was performed resulting in a slope of 0.97, an intercept of -0.09, and a correlation coefficient of $R^2 = 0.999$. These results demonstrate linearity across the reportable range of 1 – 15 mg/dL.

In order to validate the extended range, several samples were spiked to concentrations between 15 mg/dL and 30 mg/dL and re-tested using the automated procedure with a lower sample volume. These samples were also manually diluted off line and re-tested. The results from the automated re-test were all within ± 5% of the results from the manual off line dilution. The extended range allows the user to measure samples with calcium concentrations up to 30 mg/dL.

Cholesterol

Linearity studies were performed using commercially available linearity standards. The concentrations tested ranged from 10 mg/dL to 667 mg/dL and the observed values demonstrated acceptable recovery compared to the

expected values. A linear regression was performed resulting in a slope of 1.02, an intercept of 1.10, and a correlation coefficient of $R^2 = 0.999$. These results demonstrate linearity across the reportable range of 10 – 600 mg/dL.

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

The reagents are stable up to the expiration dates shown on the label when they are stored as recommended.

The assay is certified by the Cholesterol Reference Method Laboratory Network.

d. Detection limit:

The limit of the blank (LOB) was determined by evaluating a blank sample run n=20 on multiple instruments. The limit of detection (LOD) was calculated by evaluating low level analyte samples n=20 on multiple instruments. For calcium the LOB was determined to be 0.02 mg/dL and the LOD was 0.15 mg/dL. For cholesterol the LOB was determined to be 1.26 mg/dL and the LOD was 1.97 mg/dL.

e. Analytical specificity:

Testing for interfering substances was based on CLSI EP-7A. Calcium and cholesterol samples with increasing amounts of interferent were tested and compared to an interferent free sample. The following substances were tested with calcium and cholesterol: Hemoglobin to 500 mg/dL; Bilirubin to 20 mg/dL; and Intralipid to 2250 mg/dL. Glucose to 600 mg/dL and Ascorbic Acid to 25 mg/dL were tested with cholesterol, but not for calcium. The sponsor defined interference as the highest level tested that does not cause > 10% change in analytical result. The calcium samples showed no interference up to 500 mg/dL hemoglobin, 20 mg/dL bilirubin, and 2250 mg/dL of intralipid. The cholesterol samples showed no interference up to 500 mg/dL hemoglobin, 5 mg/dL bilirubin, 2250 mg/dL intralipid, 600 mg/dL glucose, and 10 mg/dL ascorbic acid.

f. Assay cut-off:

Not Applicable

2. Comparison studies:

a. Method comparison with predicate device:

Calcium

A method comparison with 49 patient samples ranging in concentration from 1.7 mg/dL to 13.2 mg/dL was performed with the Medica Reagent for Calcium on the Medica EasyRA Chemistry Analyzer and the Calcium reagent on the Roche COBAS MIRA Analyzer. Samples were tested in singlicate on the Medica analyzer and in duplicate on the Roche analyzer. The comparison resulted in a slope of 1.06, an intercept of -0.13, and a correlation coefficient of $R^2 = 0.9874$.

Cholesterol

A method comparison with 53 patient samples ranging in concentration from 11 mg/dL to 578 mg/dL was performed with the Medica Reagent for Cholesterol on the Medica EasyRA Chemistry Analyzer and the Cholesterol reagent on the Roche COBAS MIRA Analyzer. Samples were tested in singlicate on the Medica analyzer and in duplicate on the Roche analyzer. The comparison resulted in a slope of 0.97, an intercept of 5.8, and a correlation coefficient of $R^2 = 0.9992$.

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:

Calcium

The reference range for Calcium in serum is as follows:

Normal: 8.8-10.2 mg/dL

Tietz NW. Textbook of Clinical Chemistry, 3rd ed. WB Saunders and Co., Philadelphia, PA, p. 831-832 (1994).

Cholesterol

Risk groups have been studied to classify the acceptable concentrations of total cholesterol in serum. 4 The following risk groups have been identified:

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

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.