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

A. 510(k) Number:

k152327

B. Purpose for Submission:

Modifications of the Calcium test of the previously cleared device (k112788) to perform the ionized calcium test at room temperature (temperature 22 – 25 ^{0}C) instead of at 37^{0}C and to no longer provide a corrected ionized calcium result with pH correction.

C. Measurand:

Ionized calcium (Ca++)

D. Type of Test:

Quantitative, ion-selective electrode

E. Applicant:

Medica Corporation

F. Proprietary and Established Names:

EasyLyte Na/K/Cl/Ca Analyzer

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
JFP	II	862.1145, Calcium Test System	75-Chemistry

H. Intended Use:

1. Intended use(s):

   See indications for use below.

2. Indication(s) for use:

The EasyLyte Na/K/Cl/Ca Analyzer is intended for in-vitro diagnostic testing of sodium (Na), Potassium (K), Chloride (CL), and Ionized Calcium (Ca++) without pH correction.

The ionized calcium test on the EasyLyte Na/K/Cl/Ca analyzer is intended for the quantitative determination of calcium ions (Ca^{++}) in human serum, plasma and whole blood in clinical laboratories.

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).

3. Special conditions for use statement(s):

   For prescription use only.

4. Special instrument requirements:

   EasyLyte Na/K/Cl/Ca analyzer

I. Device Description:

The EasyLyte Na/K/Cl/Ca analyzer is an automated, microprocessor-controlled analyzer for the measurement of sodium, potassium, chloride and ionized calcium. All measurands used specific ion selective electrode for the measurement of the analytes. Calibration of the measurands is automatic and all the calibration solutions are contained in the standard calibration solutions, which are listed below.

The EasyLyte Solution Pack includes:

800 mL Calibrant A
140 mmol/L Na+, 4.00 mmol/L K+, 125 mmol/L Cl-, 1.25mmol/L Ca++, 1.0 mmol/L Li+, buffer, preservative, wetting agent

180 mL Calibrant B
35.0 mmol/L Na+, 16.00 mmol/L K+, 41.0 mmol/L Cl-, 2.50mmol/L Ca++, 0.4 mmol/L Li+, buffer, preservative, and wetting agent

80 mL Wash Solution
0.1 mmol/L Ammonium Bifluoride

There are two modifications made to the current ionized calcium test in the current submission when compared against the previously cleared ionized calcium test in k112788. First modification is no pH corrected ionized calcium result is provided to the user. The second modification is the ionized calcium test is conducted at room temperature (22 – 25 ^{0}C) instead of at 37^{0}C.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   EasyLyte Na/K/Ca/pH analyzer

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

   k112788

3. Comparison to predicate

Items	EasyLyte Na/K/Cl/Ca analyzer for the measurement of ionized calcium (Candidate Device)	EasyLyte Na/K/Ca/pH analyzer for the measurement of ionized calcium (Predicate Device: k112788)
Similarity/Differences		
Intended Use	For the quantitative determination of Ionized calcium in serum, plasma, and whole blood samples	Same
	Clinical laboratory use	Same
Sample modes	Syringe mode or capillary mode	Same
Sample volumes	100 µL for both syringe and capillary modes	Same
Measuring Range	0.1 – 6.0 mmol/L	Same
Sensor type	Ion specific electrode	Same
Sample Type	Serum, Plasma, whole blood	Same
Menu	Fully configurable test menu based on above sensors	Same
Test Temperature	72 – 77 F (22 – 25 ^{0}C)	99 F (37 ^{0}C)
pH Correction	No	Yes

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 EP7-A2: Interference Testing in Clinical Chemistry; Approved Guideline-Second Edition

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

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

CLSI EP25-A: Evaluation of In Vitro Diagnostic Reagents; Approved Guideline – CLSI EP25-A

L. Test Principle:

The Ionized calcium is measured by ion selective electrode. An electrical potential is developed according the Nernst Equation for a specific ion. When compared to a reference electrode, this electrical potential is translated into voltage and then in to the ion concentration of the sample.

The ionized calcium result reported is an un-normalized ionized calcium result. If normalized ionized calcium result is needed, the user can use the following equation to calculate the normalized ionized calcium result:

$$[Ca{+}{+}]_{pH7.40} = [Ca{+}{+}]_{pHx.xx} * 10^{\wedge(-0.23*(7.40-x.xx))}$$

M. Performance Characteristics (if/when applicable):

1. <u>Analytical performance:</u>

   a. Precision/Reproducibility:

   <u>Serum Precision</u>
   Within-run and total precision were determined following CLSI EP5-A2. Three levels of Medica's EasyQC material (cleared under k990971) were tested on one EasyLyte Na/K/Cl/Ca analyzer twice a day over a twenty-day period. The precision data are summarized below.

Sample	Mean (mmol/L)	N	Within-run SD	Within-run %CV	Total precision SD	Total precision %CV
Level 1	1.47	40	0.006	0.4%	0.012	0.8%
Level 2	0.93	40	0.005	0.6%	0.011	1.1%
Level 3	2.05	40	0.010	0.5%	0.016	0.8%

Whole blood Precision

Whole blood samples (with Sodium Heparin) were analyzed twenty consecutive times on two EasyLyte analyzers using two different lots of calibrants and sensors. Only within-run precision was evaluated because of the instability of the whole blood samples. The within-run precision data are summarized below.

Sample	Mean (mmol/L)	N	Within-run SD	Within-run %CV
Level 1	0.99	20	0.012	1.2%
Level 2	1.29	20	0.019	1.5%

b. Linearity/assay reportable range:

A linearity study was evaluated using stripped human serum spiked with Calcium according to CLSI-EP6-A. Twelve (12) concentration levels (0.07, 0.13, 0.60, 1.0, 1.81, 2.32, 2.88, 3.45, 4.10, 4.99, 5.74, 6.20 mmol/L) were analyzed on one EasyLyte Na/K/Cl/Ca analyzer. Linear regression was performed on the results using expected values based on the highest spiked sample prepared. The linearity results are presented in the table below.

Ca++ Linearity on the EasyLyte Na/K/Cl/Ca

Parameter	total # levels	Sample range tested	Claimed measuring range	Slope	Intercept	r
Ca++	12	0.07 – 6.20 mmol/L	0.10-6.0 mmol/L	0.9543	0.0212	0.9996

The data provided in the linearity studies supports the sponsor's claimed measuring range from 0.10 to 6.0 mmol/L.

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

Traceability

The ionized calcium calibration solutions were traceable to an internal prepared standard which is traceable to a highly purified commercially available material. The ionized calcium calibration solutions had been previously cleared in k112788.

d. *Detection limit:*

Refer to the linearity study data above in M. 2.b. for the measuring range claim of Ca++. In addition, the sponsor conducted a Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantitation (LoQ) according to the CLSI EP-17A guideline using human serum.

Limit of Blank (LoB) – Stripped human serum solution was analyzed 20 times on three EasyLyte Na/K/Cl/Ca analyzers and the results were rank ordered to determine the LoB.

Limit of Detection (LoD) – A serum sample was prepared with a calcium value above the LoB. It was analyzed 20 times on three EasyLyte Na/K/Cl/Ca analyzers to determine the typical precision of the low concentration sample. The average standard deviation of the low concentration sample was subsequently used, in conjunction with the previously calculated LoB to determine the LoD. The LoD is equal to the LoB plus 1.653 times the average standard deviation of the low concentration sample based on the calculation formula according to the CLSI EP17-A.

Limit of Quantitation (LoQ) – LoQ was analyzed by using four low concentrations of ionized calcium samples at low concentrations over at least five runs. From this data, the LoQ is calculated based on a CV of 10% or less. Results are summarized in the table below.

	LoB	LoD	LoQ	Claimed Measurement Range
Ca++	0.07 mmol/L	0.09 mmol//L	0.10 mmol/L	0.1 – 6.0 mmol/L

e. *Analytical specificity:*

Human serum samples were used in the interference study. For the initial testing, each interferent was spiked at 20 times the recommended concentration by CLSI EP-7 A2 guideline. Each sample containing interferent was evaluated against the same serum sample without the interferent. If interference was observed, the study was repeated with lower levels to establish the concentration above which interference

occurred. The sponsor's definition of significant interference is within ±10% bias. The following table represents substances that were tested without demonstrating a significant interference on test results:

Substance	Highest Concentration Tested
Ethosuximide	25.0 mg/dL
Valproic Acid-Na salt	60.0 mg/dL
Chlorpromazine-HCl	5.0 mg/dL
Nortrityline-HCl	0.25 mg/dL
Procainamide-HCl	3 mg/dL
Imipramine-HCl	0.25 mg/dL
Dopamine-HCl	0.25 mg/dL
Acetaminophen	0.25 mg/dL
Salicyclic acid	30 mg/dL
Acetylsalicyclic acid (Aspirin)	80 mg/dL
Erythromycin	6.0 mg/dL
Ampicillin	5.5 mg/dL
Na-Thiocyanate	42 mg/dL
Benzalconium Chloride	8.0 mg/dL
Magnesium Acetate	6.2 mg/dL
Hemoglobin	500 mg/dL
Intralipid	1000 mg/dL
Conjugated (Direct) Bilirubin	20 mg/dL
Unconjugated (Total) Bilirubin	40 mg/dL

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:
Method comparisons to the predicate device were performed with whole blood, plasma (sodium heparin), and serum patient samples per CLSI EP9-A2 guideline. Some samples were spiked or diluted to fully span the claimed measuring ranges.

A total of 78 human serum samples were and used for the serum comparison study, among them eighteen samples were either spiked with $CaCl_2$ or diluted with deionized water to obtain samples spanning the entire measuring range of the ionized calcium assay. All serum samples were tested using the candidate device and predicate device.

A second method comparison study with a total of 42 volunteers that contributed to collection of whole blood and plasma (sodium heparin plasma) specimens. In addition to the native patient/donor samples eight (8) more samples were either spiked or diluted to obtain samples spanning the entire measuring range. Each sample was analyzed in triplicate on two candidate devices. The samples were also analyzed in triplicate on two

predicate devices. Only one singlet set of results from the candidate device was used to perform the linear regression analysis. The regression results are summarized below:

Total # samples	Sample range tested	Slope	Intercept	r
Serum				
78	0.18 – 5.61 mmol/L	0.963	0.075	0.998
Whole Blood				
50	0.54 – 5.23 mmol/L	0.917	0.076	1.000
Plasma (Sodium heparin)				
50	0.22 – 5.38 mmol/L	0.923	0.085	1.000

b. Matrix Comparison:

Assay performance in all claimed matrices is addressed in the method comparison studies described above.

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 sponsor has provided the following expected values in the Operator's Manual based on the literature:

Ionized Calcium: 1.15 - 1.33 mmol/L for whole blood, plasma, serum when sample is handled anaerobically or with pH correction.

References:

Tietz, N.W. (ed.) Fundamentals of Clinical Chemistry, 6th ed. (2008), p. 840.

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.