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

A. 510(k) Number:

k100829

B. Purpose for Submission:

Sodium, potassium, chloride: Addition of plasma and urine to the already cleared device (k070057 and k000926)

Carbon dioxide: Addition of plasma to the already cleared device (k080874)

C. Measurand:

Sodium, Potassium, Chloride, Carbon Dioxide

D. Type of Test:

Quantitative ion-selective electrode and colorimetric chemistry tests

E. Applicant:

Medica Corp

F. Proprietary and Established Names:

Easy RA Sodium Assay
Easy RA Potassium Assay
Easy RA Chloride Assay
Easy RA Carbon Dioxide reagent

G. Regulatory Information:

Measurand	Regulation Section	Classification	Product Code	Panel
Sodium	21CFR862.1665	II	JGS-Electrode, Ion Specific	(75) Clinical Chemistry
Potassium	21CFR862.1600	II	CEM – Electrode, Ion Specific	(75) Clinical Chemistry
Chloride	21CFR862.1170	II	CGZ-Electrode Ion Specific	(75) Clinical Chemistry
Carbon Dioxide	21CFR862.1160	II	KHS – Enzymatic	(75) Clinical Chemistry

H. Intended Use:

1. Intended use(s):

   See Indications for use below.

2. Indication(s) for use:

   The EasyRA sodium test is intended for the quantitative determination of sodium ions (Na+) in human serum, plasma, and urine using the MEDICA EasyRA Chemistry analyzer with the ISE module option in clinical laboratories. Sodium measurements are used in the diagnosis and treatment of aldosteronism, diabetes, insipidus, adrenal hypertension, Addison's disease, dehydration, inappropriate antidiuretic hormone secretion, or other diseases involving electrolyte imbalance. For *in vitro* diagnostic use only.

   The EasyRA potassium test is intended for the quantitative determination of potassium ions (K+) in human serum, plasma, and urine using the MEDICA EasyRA Chemistry analyzer with the ISE module option in clinical laboratories. Potassium measurements are used to monitor electrolyte balance in the diagnosis and treatment of disease conditions characterized by low or high blood potassium levels. For *in vitro* diagnostic use only.

   The EasyRA chloride test is intended for the quantitative determination of chloride ions (Cl-) in human serum, plasma, and urine using the MEDICA EasyRA Chemistry analyzer with the ISE module option in clinical laboratories. Chloride measurements are used in the diagnosis and treatment of electrolyte and metabolic disorders such as cystic fibrosis and diabetic acidosis. For *in vitro* diagnostic use only.

EasyRA carbon dioxide (CO_2) reagent is intended for the quantitative determination of bicarbonate/carbon dioxide (CO_2) in human serum and plasma, using MEDICA "Easy RA Chemistry Analyzer" in clinical laboratories. Bicarbonate/Carbon dioxide measurements are used in the diagnosis and treatment of numerous potentially serious disorders associated with changes in body acid-base balance. For *in vitro* diagnostic use only.

3. Special conditions for use statement(s):

   Prescription use only

4. Special instrument requirements:

   Easy RA Clinical Chemistry Analyzer

I. Device Description:

The Easy RA sodium (Na^+), potassium (K^+), and chloride (Cl^-) assays are designed for the ISE module option of the Easy RA clinical chemistry analyzer for measurement of these electrolytes in human serum, plasma, and urine. The Easy RA carbon dioxide (CO2) reagent is designed for the Easy RA analyzer without the ISE module option for measurement of bicarbonate/carbon dioxide in human serum and plasma. The Easy RA assays and reagents are in ready-for-use liquid form.

J. Substantial Equivalence Information:

1. Predicate Device Name(s):
   EasyRA Clinical Chemistry Analyzer
   EasyElectrolyte Analyzer and Rapidlyte Analyzer
   EasyRA CO2 Reagent

2. Predicate 510(k) number(s):
   k070057, k000926, k080874

3. Comparison with predicate:

Similarities and Differences for Na/K/Cl			
Item	Candidate Device EasyRA $Na^+/K^+/Cl^-$ Assay	Predicate Device 1 (k070057) EasyRA Clinical Chemistry Analyzer	Predicate Device 2 (k000926) EasyElectrolyte Analyzer and Rapidlyte Analyzer
Intended Use	EasyRA sodium (Na+), potassium (K+), and chloride (Cl-) assays are intended for the quantitative determination of sodium ions, potassium ions, and chloride ions, using the MEDICA EasyRA Chemistry analyzer with the ISE module option in clinical laboratories.	Same	Same
Specimen Type	Human serum, plasma, urine	Human serum	Human serum, plasma, whole blood, urine
Assay Type	Liquid reagent ready-for-use	Same	Same
Assay Principle	Ion Selective Electrode	Same	Same
Analytical Range	For Na+ 100-200 mmol/L and Cl- (50-150 mmol/L)- serum and plasma For K+ 1-10 mmol/L –serum and plasma For Urine: Na+: 10-300 mmol/L K+ : 5.0-200 mmol/L Cl-: 30.0 – 300 mmol/L	Same for serum	Same for urine

Similarities and Differences for CO2		
Item	Candidate Device EasyRA CO2 Assay	Predicate Device (k080874) EasyRA CO2 reagent
Intended Use	EasyRA carbon dioxide (CO2) reagent is intended for the quantitative determination of bicarbonate/carbon dioxide (CO2), using MEDICA "Easy RA Chemistry Analyzer" in clinical laboratories.	Same
Specimen Type	Human serum, plasma	Human serum
Assay Type	Liquid ready-for-use	Same
Assay Principle	Enzymatic method based on PEPC enzyme and colorimetric detection (monitoring 405 nm)	Same
Analytical Range	2.3-45.0 mmol/L	Same

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

- **CLSI Guideline, EP5-A2** *Evaluation of Precision Performance of Clinical Chemistry Devices – Second Edition*
- **CLSI Guideline, EP9-A2** *Method Comparison and Bias Estimation Using Patient Samples – Second Edition*
- **CLSI Guideline, EP6-A2** *Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline – Second Edition*
- **CLSI Guideline, EP7-A2** *Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition*
- **CLSI Guideline, EP17-A** *Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline*

L. Test Principle:

The Ion Selective Electrode (ISE) test principle for quantitative sodium, potassium, and chloride measurements uses a flow-through sodium electrode with a selective membrane specially formulated for sodium sensitivity. The potential of each

electrode is measured relative to a fixed voltage set by a double-junction silver/silver chloride reference electrode. The ISE develops a voltage that varies with electrolyte ion concentration. The relationship between the developed voltage and ion concentration is logarithmic and expressed by the Nernst Equation.

The test principle for quantitative measurement of carbon dioxide uses an enzymatic method based on the catalytic conversion of bicarbonate ion and phosoenolpyruvate to oxaloacetate and phosphate by the enzyme, phosphoenolpyruvate carboxylase (PEPC). PEPC distributes the equilibrium between carbon dioxide and bicarbonate towards conversion of all carbon dioxide to bicarbonate. In the presence of malate dehydrogenase and the reduced cofactor, NADH, the generated oxaloacetate is oxidized to malate. The decrease in concentration of reduced NADH is monitored at 405 nm and is proportional to the amount of carbon dioxide in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   Serum and Plasma-Precision studies were performed in conjunction with the matrix comparison study. Duplicate plasma and serum samples from the matrix studies 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.

Sodium

	Low	Medium	High
Analytical Range(mmol/L)	100 - 140.0	140.0 - 142.0	142.0 - 200.0
No. of Samples	18	22	18
No. of Replicates	2	2	2
Serum Mean	133.6	141.1	150.2
Serum SD	0.24	0.21	0.32
Serum % CV	0.18	0.15	0.21
Plasma Mean	133.5	140.9	150.0
Plasma SD	0.34	0.21	0.27
Plasma % CV	0.15	0.15	0.18

Potassium

	Low	Medium	High
Analytical Range(mmol/L)	1.0 – 4.0	4.0 – 4.4	4.4 – 10.0
No. of Samples	18	22	17
No. of Replicates	2	2	2
Serum Mean	3.4	4.2	5.2
Serum SD	0.0024	0.0021	0.0083
Serum %CV	0.18	0.15	0.16
Plasma Mean	3.3	3.9	4.9
Plasma SD	0.0034	0.0019	0.0058
Plasma %CV	0.25	0.13	0.12

Chloride

	Low	Medium	High
Analytical Range(mmol/L)	50.0 – 102.5	102.5 – 105.0	105.0 – 150.0
No. of Samples	22	20	16
No. of Replicates	2	2	2
Serum Mean	93.8	103.4	111.9
Serum SD	0.19	0.18	0.20
Serum %CV	0.21	0.17	0.18
Plasma Mean	93.6	103.4	112.2
Plasma SD	0.17	0.13	0.21
Plasma %CV	0.18%	0.12%	0.19%

Carbon Dioxide

	Low	Medium	High
Analytical Range(mmol/L)	2.3 – 25.5	25.5 – 28.0	28.0 – 45.0
No. of Samples	22	18	17
No. of Replicates	2	2	2
Serum Mean	21.1	27.0	29.4
Serum SD	0.16	0.30	0.34
Serum %CV	0.21	1.12	1.13
Plasma Mean	21.6	28.3	29.8

Plasma SD	0.17	0.22	0.34
Plasma %CV	0.78	0.77	0.12

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

	Mean (mmol/L)	SD (mmol/L)	%CV (mmol/L)
Na+	140.82	±0.43	0.31
K+	3.81	±0.01	0.29
Cl-	107.40	±0.33	0.31
CO2	20.37	±0.18	0.86

Urine - A precision study for urine samples was performed evaluating within run precision and total precision with quality control materials (Low, Medium, and High) following CLSI EP5-A2 guidelines. Quality control samples were analyzed twice a day, for 20 days. The data are summarized in the table below:

Urine-Na+

(mmol/L)	Low	Medium	High
Mean (Total and Within)	64.6	165.4	198.4
Within SD	0.83	0.47	0.40
Within %CV	1.29	0.29	0.20
Total SD	1.44	2.24	2.82
Total %CV	2.23	1.35	1.42

Urine-K+

(mmol/L)	Low	Medium	High
Mean (Total and Within)	33.2	60.4	104.3
Within SD	0.24	0.11	0.26
Within %CV	0.73	0.18	0.25
Total SD	0.60	0.79	1.42
Total %CV	1.80	1.30	1.36

Urine-Cl-

(mmol/L)	Low	Medium	High
Mean (Total and Within)	86.9	189.9	247.1
Within SD	0.87	0.97	0.52
Within %CV	1.00	0.51	0.21
Total SD	1.78	3.30	3.84
Total %CV	2.04	1.74	1.55

b. Linearity/assay reportable range:

Plasma - Linearity studies were not conducted in plasma. See previously cleared linearity data in k070057 (sodium, potassium, and chloride) and k080874 (carbon dioxide) for serum samples. The linear reportable ranges for each assay are summarized below.

	Na+	K+	Cl-	CO2
Linear Reportable Range	100-200 mmol/L	1-10 mmol/L	50-150 mmol/L	2.3-45.0 mmol/L

An extended linearity study was performed for carbon dioxide with the EasyRA analyzer to evaluate accuracy. The sponsor recommends a dilution of 1:2 when the patient carbon dioxide result in plasma falls outside the upper measuring range of 45 mmol/L. A dilution study was performed on 5 different patient plasma spiked with bicarbonate stock solution to increase the carbon dioxide level in the range of 45 to 90 mmol/L. Each sample was then diluted with saline at 1:2 dilution by the analyzer or manually. Each diluted sample was run in triplicate on two MEDICA EasyRA analyzers. The average percent recovery of the system was 97.96%. Extended linearity accuracy results for carbon dioxide are provided in the table below:

	Estimated Sample Value (mmol/L)	Test Results of Manually Diluted Samples (mmol/L)	True Value of Manually Diluted Samples (mmol/L)	EasyRA Value (mmol/L)	EasyRA Percent Recovery
High	75 - 80	38.77	77.53	73.98	95.42
	70 - 75	33.45	66.90	66.33	99.15
Medium	65 - 70	31.55	63.10	62.63	99.26

	60 -65	27.82	55.63	54.45	97.87
Low	50 - 55	26.48	52.97	51.95	98.08

In addition a within-run precision study was performed in the extended linearity range for carbon dioxide by analyzing a bicarbonate spiked plasma sample at three different concentration levels (low, medium, and high), 20 consecutive times. The within-run precision data is summarized in the table below:

Carbon Dioxide	Low	Medium	High
Mean (mmol/L)	49.5	60.0	64.6
SD	0.46	0.79	0.80
%CV	0.94	1.32	1.24

Urine – A linearity study was performed in conjunction with CLSI EP-6A guidelines using a total of (8) different concentrations tested in duplicate or a total of (9) different concentration samples tested in triplicate. All samples were prepared following the Appendix A of the aforementioned guidance. Linear regression correlations summaries and expected versus observed data for sodium, potassium, and chloride are as follows:

	Slope	Intercept	R^2	Standard Error	Range tested
Na+	1.0015	-5.7891	0.9944	7.37	5-305 mmol/L
K+	0.9767	1.3249	0.9983	2.71	5-205 mmol/L
Cl-	0.9786	1.8418	0.9985	3.89	25-300 mmol/L

The results of the study support the sponsor's claims that the urine Na is linear from 10-300 mmol/L, urine K is linear from 5-200 mmol/L, and urine Cl is linear from 25-300 mmol/L.

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

Calibrator materials were previously cleared under k070057 (sodium, potassium, and chloride) and k080874 (carbon dioxide).

d. *Detection limit:*

Detection limit studies were not conducted in plasma. See previously cleared

data in k070057 and k080874 for serum samples.

Urine- Detection limit studies were performed in conjunction with CLSI EP17-A for sodium, potassium, and chloride analytes. Each sample was analyzed in quadruplicate in five different runs over 2.5 days. Results form detection limit studies are summarized in the table below:

	LOB (mmol/L)	LOD (mmol/L)	LOQ (mmol/L)	Claimed measuring range
No. Samples tested	20	6	4	
Na+	2.45	3.07	7.00	10-300 mmol/L
K+	1.27	1.31	3.60	5-200 mmol/L
Cl-	16.4	17.1	24.0	25-300 mmol/L

e. Analytical specificity:

Plasma interference studies were not performed. See previously cleared interference data in k070057 and k080874 for serum samples.

Urine – Urine interference studies were performed in conjunction with CLSI EP7-A2 for sodium, potassium, and chloride analytes. The effect of pH (2.0 – 9.0), total protein (20 – 300 mg/dL), and hemoglobin (0 – 1,000 mg/dL) on analyte recovery was evaluated in these studies. Different concentrations of potential interference substances were spiked into pooled urine samples. The sponsor's definitions of no significant interference is <10% difference between the tested and the control samples. There was no significant interference for sodium, potassium, and chloride when these analytes and interferents were tested in the concentration ranges indicated in the table below:

	Sodium Test Concentrations (mmol/L)
pH (2.0 -9.0)	16.0 – 178.8
Total Protein (20- 300 mg/dL)	19.0 – 195.8
Hemoglobin (0-1000 mg/dL)	23.3 – 206.5

	Potassium Test Concentrations (mmol/L)
pH (2.0 -9.0)	13.1 – 178.8
Total Protein (20- 300 mg/dL)	15.0 – 142.9
Hemoglobin (0-300 mg/dL)	7.1 – 81.5

	Chloride Test Concentrations (mmol/L)
pH (2.0 -9.0)	25.4 – 263.0
Total Protein (20- 300 mg/dL)	28.6 – 288.8
Hemoglobin (0-600 mg/dL)	24.5 – 133.1

Hemoglobin concentrations greater than 300 mg/dL was found to significantly interfere with potassium concentrations of approximately 7.0 – 8.0 mmol/L. Hemoglobin concentrations greater than 600 mg/dL was found to significantly interfere with chloride concentrations of approximately 24.5 – 28.0 mmol/L. Therefore, the sponsor states the following in their labeling: "Do not use hemolyzed samples for Potassium and Chloride".

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

Plasma – See previously cleared method comparison data in k070057 and k080874 for serum samples. Plasma matrix comparison data is provided below in part (b) of this section.

Urine – A method comparison study was performed in conjunction with CLSI EP9-A2 guidelines. The study was completed with (44 (sodium) and 45 (potassium and chloride)) human urine samples spanning the linear range of the assay. Each sample was analyzed in duplicate using the MEDICA EasyRA chemistry analyzer (test method) vs. the predicates (k000926 and LabConco Digital Chloridometer). Comparison of a single set of individual test values versus mean reference values yielded the following results:

Analyte	Slope	Intercept	R^2	Conc. Range Tested (mmol/L)
Na+	0.9932	-1.0382	0.9989	20-300
K+	0.9859	0.0836	0.9997	7-200
Cl-	0.9872	2.0234	0.9981	25-250

b. Matrix comparison:

Plasma - A matrix comparison study was performed in conjunction with CLSI EP9-A2 guidelines. The study was completed with (58) human plasma/serum samples spanning the linear range of the assay. Each sample was analyzed in duplicate using ISE module – Reagent Pack Na/K/Cl/Li on the MEDICA EasyRA chemistry analyzer. Plasma samples were used as test samples, while serum samples were used as references. Comparison of a single set of individual test values (plasma and serum) yielded the following results:

Determined linear regression correlations are as follows:

Analyte	Slope	Intercept	R^2	Conc. Range Tested (mmol/L)
Na+	1.0166	-2.3950	0.9960	100-200
K+	0.9615	-0.0552	0.9880	1-10
Cl-	0.9967	0.1605	0.9985	50-150
CO2	1.0161	0.2934	0.9708	4-40

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:

   Reference ranges are provided in the labeling from literature as follows:

	Plasma (mmol/L)	Urine (24 hr) (mmol/L)
Sodium	136 – 146	40 – 220
Potassium	3.4 – 4.5	25 – 125
Chloride	98 – 107	110 – 250
Carbon Dioxide	23 - 34	----

Statland, B. Clinical Decision Levels for Lab Tests, 2nd ed., Oradell, NJ, Medical Economics Books, p. 22-209; 1987.

Tietz, N.W. Fundamentals of Clinical Chemistry, 5th ed., Philadelphia, PA, WB Saunders and Co., p. 961-1027; 2001.

N. Proposed Labeling:

The labeling is sufficient and does satisfy 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.