MEDICA

IVD CE

REF 5423-0041 1 X 520 mL / 190 mL

ISE MODULE – REAGENT PACK $NA^+/K^+/CL^-/LI^+$
Reagent pack includes a usable volume of 520 mL and 190 mL of each calibrant.

INTENDED USE
The EasyRA ISE Reagent is intended for the quantitative determination of Sodium, Potassium and Chloride in human serum, plasma and urine and Lithium in human serum only, using the MEDICA "EasyRA® Clinical Chemistry Analyzer." For *in vitro* diagnostic use only. For professional use only.

SUMMARY AND EXPLANATION
Electrolyte measurements in biological fluids were traditionally performed using flame photometry. The development of selective organic compounds for sodium, potassium, chloride, lithium, and other electrolytes has permitted the development of sensors capable of the direct measurement of biological fluids throughout the physiological range. These sensors are known as ion selective electrodes.

Sodium is the major cation in extracellular liquid and has a major effect on osmotic pressure and water distribution between cells, plasma, and interstitial fluid. Low sodium imbalance (Hyponatremia) is associated with diarrhea, severe polyuria, metabolic acidosis, Addison's disease and renal tubular disease. High sodium imbalance (Hypernatremia) is associated with hyperadrenalism, severe dehydration, brain injury, diabetic coma, and excess treatment with sodium salts.

Potassium is the major cation in intracellular liquid. Potassium imbalance has a direct effect on muscle irritability, myocardial function, and respiration. Some conditions that effect potassium levels in blood include hypoaldosternism, diarrhea, vomiting, and therapy with diuretics for hypertension or cardiac disease. Unlike sodium and chloride there is no mechanism to maintain a threshold potassium level in the body.

Chloride is the major extracellular anion and it has a direct effect on osmotic pressure, water distribution, and anion-cation balance. Low chloride levels are caused by chronic pyelonephritis, Addisonian crisis, metabolic acidosis, and prolonged vomiting. High chloride levels are observed in dehydration, congestive heart failure, hyperparathyroidism, and extensive treatment with or intake of chloride.

Lithium is not present in healthy people and it is not metabolized. However, it is administered in the form of a carbonate salt to control manic-depressive disorders. It is believed that lithium medications affect the central nervous system neurotransmitters, as well as the kidneys. Excessive levels of lithium may cause lithium toxicity.

PRINCIPLE OF THE PROCEDURE
The Medica ISE Module measures sodium, potassium, and chloride in human serum, plasma and urine and lithium in human serum only. using ion-selective electrode technology. The flow-through sodium electrode uses a selective membrane, specially formulated to be sensitive to sodium ions. The potassium, lithium, and chloride electrodes employ similar designs with appropriate selective membrane materials. The potential of each electrode is measured relative to a fixed, stable voltage established by the double-junction silver/silver chloride reference electrode. An ion-selective electrode develops a voltage that varies with the concentration of the ion to which it responds. The relationship between the voltage developed and the concentration of the sensed ion is logarithmic, as expressed by the Nernst equation:

$$E_x = E_s + \frac{RT}{nF} \log (\propto C)$$

where:
- E_x = The potential of the electrode in sample solution
- E_s = The potential developed under standard conditions
- RT/nF = A temperature dependent "constant", termed the slope(s)
- log = Base ten logarithm function
- $\propto$ = Activity coefficient of the measured ion in the solution
- C = Concentration of the measured ion in the solution

REAGENTS

520 mL, Calibrant A:
140.0 mmol/L Na+, 4.00 mmol/L K+, 125.0 mmol/L Cl-, 1.0 mmol/L Li+
Buffer
Preservative
Wetting agent

190 mL, Calibrant B:
70.0 mmol/L Na+, 8.00 mmol/L K+, 41.0 mmol/L Cl-, 0.4 mmol/L Li+
Buffer
Preservative
Wetting agent

PRECAUTIONS

1. Good laboratory safety practices should be followed when handling any laboratory reagent. (CLSI GP17-A2).
2. As with any diagnostic test procedure, results should be interpreted considering all other test results and the clinical status of the patient.

INSTRUCTIONS FOR REAGENT PACK HANDLING, STORAGE AND STABILITY

The reagent pack is ready to use as supplied. Unopened reagent is stable until the expiration date listed on the label if stored at 4 – 25°C. After installation, the reagent is stable on-board the EasyRA Analyzer until the expiration date listed on the label. DO NOT FREEZE.

SPECIMEN COLLECTION AND STORAGE / STABILITY

Serum

1. Collect the specimen by venipuncture into a serum collection tube. Fill the tube to at least 2/3 of the total volume. Note the time of collection.

2. Let blood stand for 20-30 minutes to allow clot formation.

3. Centrifuge the tube for 10-15 minutes and remove the serum to a clean specimen tube.

4. Prepared serum samples may be analyzed:
   - Immediately
   - Within 24 hours when stored at 4°C
   - Within one week when stored at -20°C

5. Samples must be brought to room temperature and mixed well before assaying. To obtain accurate results, samples should be free of any clots, fibrin or other debris that could obstruct sample flow and affect results. The use of a serum clearing agent is strongly recommended.

Plasma (Na/K/Cl only)

1. Collect the specimen by venipuncture into a lithium-heparin treated tube. Fill the tube to at least 2/3 of the total volume. Note the time of collection.

2. Mix the sample by gentle inversion for the number of times recommended by the manufacturer. Do not shake.

3. Centrifuge the specimen within one hour or less of collection. Carefully remove the plasma layer for analysis. Do not use hemolyzed samples.

4. For best results analyze the specimens within 4 hours of collection. Samples maybe stored at 2 – 8°C for 24 hours or frozen for one week. Centrifuge the plasma if a precipitate develops.

Urine (Na/K/Cl only)

1. Collect the specimen in a cup. Note the time of collection.

2. The urine must be diluted (1 part urine plus 9 parts Medica Urine Diluent).

3. Prepared urine samples may be analyzed:
   - Immediately
   - Within 24 hours when stored at 4°C
   - Within one week when stored at -20°C

4. Samples must be brought to room temperature and mixed well before assaying. To obtain accurate results, samples should be free of any clots, fibrin or other debris that could obstruct sample flow and affect results. The use of urine clearing agent is strongly recommended. For complete handling and storage information, the user should refer to the Clinical Chemistry Standard C27-A published by CLSI.

PROCEDURE

Materials Provided

Cat. No 5423-0041 ISE Reagent Pack
Cat. No 5408 (500 mL) or 5412 (125 mL) Urine Diluent

Additional materials required

Medica EasyQC® Bi-Level Kit, REF 2814 *or*
Medica EasyQC Tri-Level Kit, REF 2815 *or*
Medica EasyQC Chemistry/Electrolytes – Level A, REF 10793 *and*
Medica EasyQC Chemistry/Electrolytes – Level B, REF 10794
Medica Cleaner Wedge – Chemistry & ISE, REF 10660

Instructions for Use

The reagent is ready to use as supplied. To physically install the new reagent, place the reagent pack in the designated area on the EasyRA analyzer. Remove the red caps and red label and attach the reagent connector. For detailed instructions on proper removal and installation, refer to the EasyRA Operators Manual.

Calibration

All ISE Calibration materials are contained within the ISE Reagent Pack. Recalibration is required every 8 hours and/or whenever there is a change in reagent lot number or if a shift in quality control values occurs.

Quality Control

It is recommended that at least two levels of human serum based controls (normal and abnormal) be run with the assay daily whenever patient testing is performed and with each reagent lot change. Failure to obtain the proper range of values in the assay of control material may indicate reagent deterioration, instrument malfunction or procedural errors. Retain all quality control results to monitor ISE module performance. The laboratory should follow local, state and federal quality control guidelines when using quality control materials.

Results

After completion of the assay, the EasyRA Analyzer calculates Na+, K+, Cl-, and Li+ concentrations based on the Nernst equation.

Expected Values[1, 2]

The reference range for electrolytes is as follows:

Analyte	Serum (mmol/L)	Plasma (mmol/L)	Urine (mmol/L) (24 hour collection)
Sodium	136.0 – 146.0	136.0 – 146.0	40 – 220
Potassium	3.5 – 5.1	3.4 – 4.5	25 – 125
Chloride	98 – 106	98 – 107	110 – 250
Lithium (Therapeutic Range)	0.6 – 1.2	N/A	N/A

These values are guidelines. It is recommended that each laboratory establish its own range of expected values since differences exist among instruments, laboratories and local populations.

PERFORMANCE CHARACTERISTICS[3]

Reportable Range

The Medica EasyRA Chemistry Analyzer flags any result above the upper limit of the linear range as Linearity High “LH” and any result below the linear range as Linearity Low “LL”.

The reportable (linearity) ranges for electrolytes are as follows.

Analyte	Reportable Range Serum, Plasma	Reportable Range Urine
Sodium	100 – 200 mmol/L	10.0 – 300.0 mmol/L
Potassium	1.0 – 10.0 mmol/L	5.0 – 200.0 mmol/L
Chloride	50 – 150 mmol/L	30.0 – 300.0 mmol/L
Lithium	0.2 – 3.5 mmol/L	N/A

Inaccuracy / Correlation (CLSI, EP9-A2)

Serum Data:

The following table lists the data obtained in a comparison of the Medica ISE Reagent (y) on the EasyRA Analyzer to the performance of the Medica EasyElectrolytes™ Analyzer. The data shown below represents single determinations on the EasyRA Analyzer vs. the average of duplicate values obtained on the EasyElectrolytes Analyzer.

Sodium - Serum

Number of samples	40	Range of Samples	126.1 to 190.5 mmol/L
Slope	1.01	y Intercept	- 1.97
Correlation Coefficient	0.9974	Regression Equation:	Y = 1.01*X – 1.97

Potassium – Serum

Number of samples	42	Range of Samples	2.66 to 8.93 mmol/L
Slope	1.01	y Intercept	- 0.07
Correlation Coefficient	0.9989	Regression Equation:	Y = 1.01*X – 0.07

Chloride - Serum

Number of samples	41	Range of Samples	59 to 153 mmol/L
Slope	0.991	y Intercept	- 1.01
Correlation Coefficient	0.9954	Regression Equation:	Y = 0.991*X – 1.01

Lithium - Serum

Number of samples	40	Range of Samples	0.24 to 3.34 mmol/L
Slope	0.98	y Intercept	0.02
Correlation Coefficient	0.9995	Regression Equation:	Y = 0.98*X + 0.02

Plasma Data:

The following table lists the data obtained in a comparison of the Medica ISE Reagent (y) on the EasyRA Analyzer using plasma specimens to the performance of the ISE Reagent (x) on the EasyRA Analyzer using serum specimens. The data shown below represents single determinations of plasma on the EasyRA Analyzer vs. the average of duplicate serum values obtained on the EasyRA Analyzer.

Sodium - Plasma

Number of samples	58	Range of Samples	104.7 to 196.0 mmol/L
Slope	1.0166	y Intercept	- 2.3950
Correlation Coefficient	0.9960	Regression Equation:	Y = 1.0166*X – 2.3950

Potassium – Plasma

Number of samples	57	Range of Samples	1.27 to 9.77 mmol/L
Slope	0.9615	y Intercept	- 0.0552
Correlation Coefficient	0.9880	Regression Equation:	Y = 0.9615*X – 0.0552

Chloride - Plasma

Number of samples	58	Range of Samples	53.5 to 143.3 mmol/L
Slope	0.9967	y Intercept	0.1605
Correlation Coefficient	0.9985	Regression Equation:	Y = 0.9967*X + 0.1605

NOTE: Plasma K results may be about 0.1 to 0.7 mmol/L lower than serum K results[4]. Medica recommends that clinical laboratories establish their own reference ranges for the K test depending on sample type.

Urine Data:

The following table lists the data obtained in a comparison of the Medica ISE Reagent (y) on the EasyRA Analyzer using urine specimens to the performance of the Medica EasyElectrolytes™ Analyzer (Na & K) and Chloridometer (Cl) using urine specimens. The data shown below represents single determinations on the EasyRA Analyzer vs. the average of duplicate values obtained on the EasyElectrolytes Analyzer and Chloridometer.

Sodium - Urine

Number of samples	44	Range of Samples	20.7 to 298 mmol/L
Slope	1.01	y Intercept	- 0.07
Correlation Coefficient	0.9995	Regression Equation:	Y = 1.01*X – 0.07

Potassium – Urine

Number of samples	45	Range of Samples	6.2 to 200 mmol/L
Slope	0.99	y Intercept	0.08
Correlation Coefficient	0.9989	Regression Equation:	Y = 1.01*X + 0.08

Chloride - Urine

Number of samples	45	Range of Samples	23 to 242 mmol/L
Slope	0.99	y Intercept	2.02
Correlation Coefficient	0.999	Regression Equation:	Y = 0.99*X + 2.02

Imprecision (CLSI, EP5-A2)
Serum – Within run imprecision: Five replicates of two levels of QC material were tested over 5 days.

Sodium

QC Level mmol/L	Within Run SD mmol/L	Within Run CV %
144.6	0.61	0.42
161.8	0.71	0.44

Potassium

QC Level mmol/L	Within Run SD mmol/L	Within Run CV %
4.18	0.035	0.84
6.19	0.06	0.97

Chloride

QC Level mmol/L	Within Run SD mmol/L	Within Run CV %
99.4	0.55	0.55
117.4	0.49	0.41

Lithium

QC Level mmol/L	Within Run SD mmol/L	Within Run CV %
0.97	0.00	0.00
1.92	0.01	0.52

Serum – Total Imprecision: Two levels of QC material were tested twice a day for 20 days.

Sodium

QC Level mmol/L	Within Run SD mmol/L	Within Run CV %
143.50	2.02	1.41
159.98	1.51	0.95

Potassium

QC Level mmol/L	Within Run SD mmol/L	Within Run CV %
4.15	0.06	1.41
6.10	0.06	1.00

Chloride

QC Level mmol/L	Within Run SD mmol/L	Within Run CV %
99.0	1.00	1.01
117.1	1.02	0.87

Lithium

QC Level mmol/L	Within Run SD mmol/L	Within Run CV %
0.95	0.01	1.48
1.90	0.02	1.29

Urine – Within run imprecision: Five replicates of two levels of QC material were tested over 5 days.

Sodium

QC Level mmol/L	Within Run SD mmol/L	Within Run CV %
64.6	0.83	1.3
165.4	0.47	0.3
198.4	0.40	0.2

Potassium

QC Level mmol/L	Within Run SD mmol/L	Within Run CV %
33.2	0.24	0.73
60.4	0.11	0.18
104.3	0.26	0.25

Chloride

QC Level mmol/L	Within Run SD mmol/L	Within Run CV %
86.9	0.87	1.0
189.9	0.97	0.51
247.1	0.52	0.21

Urine – Total Imprecision: Two levels of QC material were tested twice a day for 20 days.

Sodium

QC Level mmol/L	Within Run SD mmol/L	Within Run CV %
64.6	1.44	2.23
165.4	2.24	1.35
198.4	2.82	1.55

Potassium

QC Level mmol/L	Within Run SD mmol/L	Within Run CV %
33.2	0.60	1.8
60.4	0.79	1.3
104.3	1.42	1.74

Chloride

QC Level mmol/L	Within Run SD mmol/L	Within Run CV %
86.9	1.78	2.04
189.9	3.3	1.74
247.1	3.84	1.55

Linearity (CLSI, EP6-A)
The linearity of the ISE sensors was determined using a series of NIST-traceable, third party assayed commercial bovine serum linearity standards. The results indicate the responses of all four analytes are linear over the entire reportable range.

NOTE: The Urine Linearity may be expanded to double the upper limit by performing a 1:20 dilution with Urine Diluent and down to half the lower limit by performing a 1:5 dilution with Urine Diluent. Sample results must be corrected by the user. Refer to the urine diluent insert sheet for more detail.

Interfering Substances (CLSI, EP7-A)

Serum
No significant interference was found in levels up to 500 mg/dL of hemoglobin for sodium, chloride and lithium.
Significant interference from hemoglobin was found for potassium. Avoid using hemolyzed samples.
No significant interference was found in levels up to 20 mg/dL of bilirubin for sodium, potassium, chloride and lithium.
No significant interference was found in levels up to 2000 mg/dL of triglycerides (using Intralipid*) for sodium, potassium, and chloride.
No significant interference was found in levels up to 800 mg/dL of triglycerides (using Intralipid*) for lithium.

**Intralipid is a registered trademark of Pharmacia AB, Clayton, NC.*

To test for drug-related interferences, serum was spiked with a potentially interfering substance to the test concentration shown in the following tables. The interference was calculated using the difference between the medians of the spiked and unspiked samples.
There was no interference with sodium, potassium, lithium and chloride sensors by the following chemicals at the corresponding levels

Chemical	Level tested (mg/dL)
Imipramine	0.1
Procainamide	10
Nortryptylene	0.15
Hydroxyramine	40
Chloropromazine	5
Erythromycin	5
Ethosuximide	20
Acetaminophen	20
Ampicillin	5
Potassium thiocynate	20
Salicylic acid	20
Acetylsalicylic acid	50
Ibuprofen	40

The following results are for substances found to significantly interfere with one or more sensors.

Chemical	Level tested (mg/dL)	Effect
Valproic Acid	50	Decrease in sodium by 5.7 mM
Benzalkonium Chloride	8	Increases by sodium by 14 mM and potassium by 1 mM

Urine
No significant pH interference was found for sodium, potassium and chloride in the pH range of 2 to 9 units,
There is no significant interference on sodium, potassium and chloride in urine samples with protein levels up to 300 mg/dL.
There is significant hemoglobin interference on the urine potassium assay above 300 mg/dL of hemoglobin.
There is significant hemoglobin interference on the urine chloride assay above 600 mg/dL of hemoglobin.
Do not use hemolyzed samples for measurement of potassium and chloride analytes.

For additional information on interferences on the sodium, potassium and chloride assays in serum and urine specimens, consult D.S. Young, "*Effects of Drugs on Clinical Laboratory Tests*", AAAC Press. This reference provides a list of drugs and other substances that interfere with clinical chemistry tests.[5]

References

1 Statland, B. *Clinical Decision Levels for Lab Tests*, 2nd ed., Oradell, NJ, Medical Economics Books, p. 22 – 209; 1987
2 Tietz, N.W. Fundamentals of Clinical Chemistry, 5th ed., Philadelphia, PA, WB Saunders and Co., p. 961 – 1027 (2001)
3 Data on file at Medica.
4 Tietz, N.W. Fundamentals of Clinical Chemistry, 3rd ed., Philadelphia, PA, WB Saunders and Co., p. 1058 – 1059 (1999)
5 Young DS. Young's Effects on-line. *Effects of Drugs, Physiology, Preanalytical variables and herbs on Clinical Laboratory Tests*. AACC www.fxol.org

EasyRA Assay Parameters (ISE) - $NA^+/K^+/CL^-/LI^+$

EasyRA Serum/Plasma Assay Parameters (ISE) – Na+/K+/Cl-/Li+		**EasyRA Urine Assay Parameters (ISE) – Na+/K+/Cl-/Li+**	
Reaction Type	Potentiometric	**Reaction Type**	Potentiometric
Analysis Time	33 seconds	**Analysis Time**	54 seconds
Sample Type	Serum/Plasma	**Sample Type**	Urine
Sample Volume (µL)	75	**Sample Volume (µL)**	350
Decimal Places (default)	1 – Na, K 2 – Cl, Li	**Decimal Places (default)**	1 – Na, K 2 – Cl, Li
Units (default)	mmol/L	**Units (default)**	mmol/L
Linearity Ranges (mmol/L)	Na: 100.0 – 200.0 K: 1.00 – 10.00 Cl: 50.0 – 150.0 Li: 0.20 – 3.50	**Linearity Ranges (mmol/L)**	Na: 10.0 – 300.0 K: 5.00 – 200.00 Cl: 30.0 – 300.0

Medica Corporation, 5 Oak Park Drive
Bedford, MA 01730-1413 USA

EC REP Emergo Europe, Prinsessegracht 20
2514 AP The Hague, The Netherlands