

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE ONLY TEMPLATE**

A. 510(k) Number: k040971

B. Purpose For Submission:

Premarket Notification 510(k) for GenChem, Inc. intentions to manufacture and market the GenChem ISE Electrolyte Reference Kit.

C. Analyte: Sodium, Potassium, Chloride and Total CO₂ in serum and plasma. Sodium, Potassium, and Chloride in urine. Chloride in cerebrospinal fluid and Calcium in serum, plasma and urine on appropriately configured SYNCHRON CX® Delta Systems.

D. Type of Test:

Quantitative for Sodium, Potassium, Chloride, CO₂ and Calcium as determined by the use of Ion Specific Electrodes.

E. Applicant: GenChem, Inc.

F. Proprietary and Established Names:

GenChem ISE Electrolyte Reference

G. Regulatory Information:

Regulation section:

1. Regulation section:

21 CFR §862.1665, Electrode, Ion Specific, Sodium
21 CFR §862.1600, Electrode, Ion Specific, Potassium
21 CFR §862.1170, Electrode, Ion Specific, Chloride
21 CFR §862.1160, pH Rate Measurement, Carbon Dioxide
21 CFR §862.1145, Electrode, Ion Specific, Calcium

2. Classification:

Class II

3. Product Code:

JGS (sodium)
CEM (potassium)

CGZ (chloride)
JFL (bicarbonate/ carbon dioxide)
JFP (calcium)

4. Panel:

75 (Chemistry)

H. Intended use(s):

1. Intended use(s)

GenChem ISE Electrolyte Reference, when used in conjunction with the GenChem ISE Electrolyte Buffer, GenChem CO₂ Acid Reagent, GenChem CO₂ Alkaline Buffer, GenChem Wash Concentrate, and appropriate Calibrators or Calibration Standards, is intended for the quantitative determination of sodium, potassium, chloride, and total CO₂ in serum and plasma, and sodium, potassium, and chloride in urine, and chloride in cerebrospinal fluid on the Beckman® CX® DELTA Systems. GenChem ISE Electrolyte Reference will also determine calcium in serum, plasma and urine.

Sodium results are for the diagnosis and treatment of aldosteronism (excessive secretion of the hormone aldosterone), diabetes insipidus (chronic excretion of large amounts of dilute urine, accompanied by extreme thirst), adrenal hypertension, Addison's disease (caused by the destruction of the adrenal glands), dehydration, inappropriate antidiuretic hormone secretion, or other diseases involving electrolyte imbalance. Potassium results are used to monitor electrolyte imbalance in the diagnosis and treatment of diseases and conditions characterized by low or high blood potassium levels. Chloride results are used in the treatment of electrolyte and metabolic disorders such as cystic fibrosis and diabetic acidosis. Carbon dioxide results are used in the diagnosis and treatment of numerous and potentially serious disorders associated with changes in the body's acid-base balance. Calcium results are used in the diagnosis and treatment of parathyroid diseases, chronic renal disease and tetany (intermittent muscular contractions or spasm).

2. Indication(s) for use:

GenChem ISE Electrolyte Reference, when used in conjunction with the GenChem ISE Electrolyte Buffer, GenChem CO₂ Acid Reagent, GenChem CO₂ Alkaline Buffer, GenChem Wash Concentrate, and appropriate Calibrators or Calibration Standards, is intended for the quantitative determination of sodium, potassium, chloride, and total CO₂ in serum and plasma, and sodium, potassium, and chloride in urine, and chloride in cerebrospinal fluid on the Beckman® CX® DELTA Systems. GenChem ISE Electrolyte Reference will also determine calcium in serum, plasma and urine.

Sodium results are for the diagnosis and treatment of aldosteronism (excessive secretion of the hormone aldosterone), diabetes insipidus (chronic excretion of large amounts of dilute urine, accompanied by extreme thirst), adrenal hypertension, Addison's disease

(caused by the destruction of the adrenal glands), dehydration, inappropriate antidiuretic hormone secretion, or other diseases involving electrolyte imbalance. Potassium results are used to monitor electrolyte imbalance in the diagnosis and treatment of diseases and conditions characterized by low or high blood potassium levels. Chloride results are used in the treatment of electrolyte and metabolic disorders such as cystic fibrosis and diabetic acidosis. Carbon dioxide results are used in the diagnosis and treatment of numerous and potentially serious disorders associated with changes in the body's acid-base balance. Calcium results are used in the diagnosis and treatment of parathyroid diseases, chronic renal disease and tetany (intermittent muscular contractions or spasm).

3. Special condition for use statement(s): For Prescription Use
4. Special instrument Requirements: Beckman® SYNCHRON CX3

I. Device Description:

The reagent kit consists of 1x2000mL solution containing sodium, potassium, chloride, total CO₂, calcium, surfactants, preservatives and other ingredients.

J. Substantial Equivalence Information:

1. Predicate device name(s):

GenChem claims substantial equivalence to the OEM Reagent marketed by Beckman, Hi Chem Diagnostics, Hi Chem Electrolyte Reagent.

2. Predicate K number(s): k925611
3. Comparison with Predicate:

Device Name	GenChem ISE Electrolyte Reference	Predicate Device Hi Chem Electrolyte Reference Reagent
510(k) Number	k040971	k925611
Chemical Principle	Measures electrolyte activity by use of ion specific electrode	Measures electrolyte activity by use of ion specific electrode
Intended Use	For the quantitative determination of Na, K, CL, CO ₂ and Calcium in serum, plasma or urine.	For the quantitative determination of Na, K, CL, CO ₂ and Calcium in serum, plasma or urine.
Format	Liquid ready to use	Liquid ready to use
Composition	Sodium 140 mmol/L Potassium 4 mmol/L Chloride 100 mmol/L CO ₂ 10 mmol/L Calcium 8 mg/dL	Sodium 140 mmol/L Potassium 4 mmol/L Chloride 100 mmol/L CO ₂ 10 mmol/L Calcium 8 mg/dL

Linearity	Sodium 0-200 mmol/L Potassium 0.9-15.2 mmol/L Chloride 0-150 mmol/L CO2 0-40 mmol/L Calcium 0.8-14.3 mg/dL	Sodium 0-200 mmol/L Potassium 0.9-15.2 mmol/L Chloride 0-150 mmol/L CO2 0-40 mmol/L Calcium 0.8-14.3 mg/dL
Storage	Room Temperature	Room Temperature

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

Within-Day and Day-to-Day precision was determined according to NCCLS EP5-A.
Linearity was performed according to NCCLS EP6-A Guideline.
Analytical specificity Determined according to NCCLS EP7-A.

L. Test Principle:

The sample is mixed with the high ionic strength ISE Electrolyte Buffer. This dilution minimizes the variation in the activity coefficients of the analytes to be measured. As the sample passes through the flow cell, a potential is generated at the surface of the ion selective electrodes. The calcium, chloride, potassium and sodium concentrations of the sample can then be determined from these potentials using the Nerst equation.

Before the sample leaves the flow cell, it is further diluted with the CO2 Acid Reagent. The acid in this reagent converts the bicarbonate in the sample to carbonic acid, which escapes the solution in the form of carbon dioxide. Some of this carbon dioxide transverses the silicone membrane of the CO2 electrode and lowers the pH of the CO2 Alkaline Buffer. The rate of this pH exchange is proportional to the amount of total CO2 in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Serum and CSF controls, and urine pools were each assayed for calcium, chloride, potassium, sodium, and total CO2 twice per day in triplicate on a SYNCHRON CX DELTA System. Data were collected on ten different days over a thirty day period.

Analyte Sample	n	mean	Within Run		Total	
			SD	%CV	SD	%CV
Calcium in mg/dL						
Serum 1	60	7.9	0.16	2.1	0.15	1.9
Serum 2	60	11.1	0.09	0.8	0.11	1.0
Serum 3	60	14.2	0.13	0.9	0.16	1.1
Urine 1	59	3.4	0.12	3.5	0.13	3.9
Urine 2	60	10.9	0.33	3.1	0.30	2.8

Chloride in mmol/L

Serum 1	60	84.5	1.16	1.4	1.21	1.4
Serum 2	60	103.2	0.60	0.6	1.04	1.0
Serum 3	60	122.6	1.01	0.8	1.34	1.1
Urine 1	59	64.1	1.16	1.8	1.21	1.9
Urine 2	60	235.6	2.33	1.0	5.67	2.4
CSF 1	58	117.5	1.37	1.2	1.65	1.4
CSF 2	58	99.1	1.00	1.0	1.45	1.5

Potassium in mmol/L

Serum 1	60	2.64	0.021	0.8	0.034	1.3
Serum 2	60	5.21	0.031	0.6	0.040	0.8
Serum 3	60	7.88	0.074	0.9	0.083	1.1
Urine 1	59	27.1	0.23	0.9	0.27	1.0
Urine 2	60	123.7	1.67	1.4	1.67	1.4

Sodium in mmol/L

Serum 1	60	114.7	1.71	1.5	1.51	1.3
Serum 2	60	144.4	0.87	0.6	0.94	0.7
Serum 3	60	173.3	1.54	0.9	1.59	0.9
Urine 1	59	45.7	2.02	4.4	1.78	3.9
Urine 2	60	159.9	2.19	1.4	1.98	1.2

Total CO2 in mmol/L

Serum 1	60	12.6	0.40	3.2	0.38	3.0
Serum 2	60	22.2	0.32	1.4	0.36	1.6
Serum 3	60	30.9	0.53	1.7	0.66	2.1

b. Linearity/assay reportable range:

Linearity was performed according to NCCLS Guideline EP6-A. Commercially available linearity standards were analyzed in triplicate on the Beckman CX3 and the results analyzed by the Least Squares method. The results are shown below. Specimens exceeding these limits should be diluted with normal saline and reanalyzed. Multiply the result by the appropriate dilution factor.

	Intercept	Slope	R ²	Se _y	Range
Calcium	0.34	0.911	1.000	0.35	0.8 – 14.3 mg/dL
Na	2.37	0.968	1.000	2.61	0 – 200 mmol/L
K	-0.09	1.017	1.000	0.03	0.9 – 15.2 mmol/L

CL	-0.71	0.999	1.000	0.99	0 – 197 mmol/L
CO ₂	0.15	1.000	1.000	0.41	0 – 40 mmol/L

The results show this method is linear as shown below:

Calcium	0.8 to 14.3 mg/dL
Chloride	0 to 150 mmol/L
Potassium	0.9 to 15.2 mmol/L
Sodium	0 to 200 mmol/L
Total CO ₂	0 to 40 mmol/L

c. Traceability (controls, calibrators, or method):

The use of ion selective electrodes in the potentiometric determination of sodium and potassium ions was described over seventy years ago.^{2,3} However, practical methods for their measurement were not reported until recently. A sodium electrode was developed with a selectivity over potassium of about 300 to 1.4 Simon and Proda described a valinomycin potassium electrode with a selectivity over sodium of about 1000 to 1.5 Recent advances in calcium electrode technology have made potentiometric calcium measurements both accurate and practical.⁶ Chloride electrodes have been routinely used for potentiometric titrations of chloride.⁷ However, recent improvements in selectivity and sensitivity have made possible the direct potentiometric analysis of chloride in biological specimens.⁸ Stow and Randall describe a procedure for the direct measurement of the partial pressure of CO₂ using a pCO₂ electrode in 1954.⁹ This electrode has since been made more sensitive.¹⁰

². Cremer. M. Z., *Biologi* 47: 562 (1977)

³. Haber, F., *Kleminscwics, Physik. Chem.* 67:385 (1909).

⁶. Bowers, G. N., et. Al., *Measurements of Ionized Calcium in Serum with ion-Selective Electrodes: A Mature Technology Than Can Meet the Daily Service Needs.* *Clin. Chem.* 32/8, 1437- 1447 (1986).

⁷. Sternberg, et. Al., *Ninth International Congress on Clinical Chemistry Procedures* (1970).

⁸. Bray, T. P., et. Al., *Clin. Chem. Acta.*, 77:69 (1977).

⁹. Stow, R.W., Randall, B.F., *Am. J. Physiol.* (1954)

¹⁰. Severinghaus, J.W., Bradley, A.F., *Appl. Physiol.* (1958).

d. Detection limit:

The sensitivity of this method was investigated by assaying serum first with a known concentration and then diluting the sample until the minimum result was obtained and then run in replicates of 10 on the SYNCHRON CX3® System. Under the conditions described the following limits of detection were established:

Analyte	Limit of Detection
Sodium	10 mmol/L
Potassium	1.0 mmol/L
Chloride	15 mmol/L

Total CO ₂	5.0 mmol/L
Calcium	1.5 mg/dL

e. Analytical specificity:

Determined according to NCCLS EP7-A, Hemoglobin levels up to 500 mg/dL, Bilirubin levels up to 20 mg/dL, and Lipemia levels up to 1800 mg/dL were tested and did not show any adverse effect on a stock sample with levels of sodium at 148 mmol/L, potassium at 5.2 mmol/L, chloride at 119 mmol/L, CO₂ at 19 mmol/L, and calcium at 9.4 mg/dL. Stock solutions of the substance to be tested were prepared at 20x concentrations and 0.5 ml of this stock was placed in a 10 ml volumetric flask and made up to volume with the base pool. The control stock was prepared similarly but with water as the diluent. Only Sodium Heparin, Lithium Heparin and Ammonium Heparin up to 45 Units/mL are acceptable anticoagulants.

f. Assay cut-off:

Not applicable for this type of device.

2. Comparison studies:

a. Method comparison with predicate device:

Serum, plasma, cerebrospinal fluid and urine specimens, collected from adult patients, were assayed for calcium, chloride, potassium, sodium, and total CO₂ on a Beckman SYNCHRON CX3 System using GenChem and Beckman flow cell reagents, wash solutions and calibrators. Results were compared by least squares linear regression where X = Beckman Results and Y = GenChem Results.

Analyte/Specimen	Regression Statistics			Summary Statistics		
	Unit	n	m	b	r	range
Calcium						
Serum	mg/dL	80	0.989	0.0	0.985	7.1 - 10.6
Plasma	mg/dL	80	0.990	0.0	0.995	7.1 - 10.7
Urine	mg/dL	74	1.007	-0.2	0.998	2.4 - 15.2
Chloride						
Serum	mmol/L	80	0.988	1.0	0.935	98 - 127
Plasma	mmol/L	80	0.998	0.8	0.985	98 - 127
Urine	mmol/L	78	1.049	-5.1	0.999	22 - 289
CSF	mmol/L	44	1.024	-3.4	0.985	113 - 152
Potassium						
Serum	mmol/L	80	0.969	0.13	1.000	3.2 - 10.8
Plasma	mmol/L	80	0.987	0.15	1.000	3.2 - 10.8
Urine	mmol/L	80	0.993	0.01	1.000	3.5 - 136

Sodium

Serum	mmol/L 80	0.930	9.1	0.938	132 - 159
Urine	mmol/L 78	1.000	-0.3	1.000	17 - 288

Total CO2

Serum	mmol/L 80	0.949	1.2	0.953	9.5 - 29
Plasma	mmol/L 80	0.965	0.9	0.960	9.5 - 29

b. Matrix Comparison

See above method comparison studies.

3. Clinical studies:*a. Clinical sensitivity:*

Clinical studies are not typically submitted for this device type.

b. Clinical specificity:

Clinical studies are not typically submitted for this device type.

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 expected values for calcium, chloride, potassium, sodium, and total CO2 are listed below. The applicant recommends that the user use these ranges only as guides and that each laboratory should establish its own reference ranges.

Reference Ranges¹

Analyte	Specimen	Conventional Units	SI Units
Calcium	Serum/Plasma	8.4 - 10.2 mg/dL	2.10 - 2.55 mmol/L
	Urine	100 - 300 mg/day	2.5 - 7.5 mmol/day
Chloride	Serum/Plasma	101 - 111 mmol/L	same
	Urine	110 - 250 mmol/day	same
	CSF	118 - 132 mmol/L	same
Potassium	Serum/Plasma	3.5 - 5.1 mmol/L	same
	Urine	25 - 125 mmol/day	same

Sodium	Serum/Plasma	136 - 145 mmol/L	same
	Urine	40 - 220 mmol/day	same
Total CO2	Serum/Plasma	22 - 28 mmol/L	same

¹ Burtis, C.A., Ashwood, E.R. (eds.) Tietz Textbook of Clinical Chemistry. W.B. Saunders Company. Philadelphia PA. (1994)

N. Conclusion:

The submitted material in this premarket notification is complete and supports a substantial equivalence decision.