

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE**

A. 510(k) Number:

k121140

B. Purpose for Submission:

Addition of Li⁺ ISE sensor to the PROLYTE Electrolyte Analyzer cleared under k102959

C. Measurand:

Sodium, Potassium, Chloride, Lithium

D. Type of Test:

Ion Selective Electrode

E. Applicant:

Diamond Diagnostics, Inc.

F. Proprietary and Established Names:

PROLYTE Electrolyte Analyzer Na⁺/K⁺/Cl⁻/Li⁺

G. Regulatory Information:

1. Regulation section:

21 CFR 862.1665 – Sodium Test System

21 CFR 862.1600 – Potassium Test System

21 CFR 862.1770 – Chloride Test System

21 CFR 862.3560 – Lithium Test System

2. Classification:

Class II

3. Product code:

JGS – Electrode, Ion Specific, Sodium

CEM – Electrode, Ion Specific, Potassium

CGZ – Electrode, Ion Specific, Chloride

JIH– Electrode, Ion Specific, Lithium

4. Panel:

75 - Chemistry

H. Intended Use:

1. Intended use(s):

See indications for use below.

2. Indication(s) for use:

The PROLYTE Electrolyte Analyzer $\text{Na}^+/\text{K}^+/\text{Cl}^-/\text{Li}^+$ is an automated, microprocessor-controlled analyzer which utilizes ion-selective electrodes for the measurement of sodium, potassium, chloride and lithium in whole blood, plasma, and serum. Sodium, potassium, and chloride can be measured in urine samples.

The PROLYTE Sodium Assay is intended to measure sodium in whole blood, plasma, serum, and urine on the PROLYTE Electrolyte Analyzer $\text{Na}^+/\text{K}^+/\text{Cl}^-/\text{Li}^+$. Measurements obtained by this device are used to monitor electrolyte balance in 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 destruction of the adrenal glands), dehydration, inappropriate antidiuretic hormone secretion, or other diseases involving electrolyte imbalance.

The PROLYTE Potassium Assay is intended to measure potassium in whole blood, plasma, serum, and urine on the PROLYTE Electrolyte Analyzer $\text{Na}^+/\text{K}^+/\text{Cl}^-/\text{Li}^+$. Measurements obtained by this device are used to monitor electrolyte balance in the diagnosis and treatment of disease conditions characterized by low or high blood potassium levels.

The PROLYTE Chloride Assay is intended to measure the level of chloride in whole blood, plasma, serum, and urine on the PROLYTE Electrolyte Analyzer $\text{Na}^+/\text{K}^+/\text{Cl}^-/\text{Li}^+$.

Chloride measurements are used in the diagnosis and treatment of electrolyte and metabolic disorders such as cystic fibrosis and diabetic acidosis.

The PROLYTE Lithium test system is intended to measure lithium (from the drug lithium carbonate) in whole blood, plasma, or serum on the PROLYTE Electrolyte Analyzer $\text{Na}^+/\text{K}^+/\text{Cl}^-/\text{Li}^+$. Measurements of lithium are used to assure that the proper drug dose is administered in the treatment of patients with mental disturbances, such as manic-depressive illness (bipolar disorder).

For In Vitro Diagnostic Use

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

PROLYTE Electrolyte Analyzer $\text{Na}^+/\text{K}^+/\text{Cl}^-/\text{Li}^+$

I. Device Description:

The PROLYTE Electrolyte Analyzer $\text{Na}^+/\text{K}^+/\text{Cl}^-/\text{Li}^+$ has all the features of the PROLYTE Electrolyte Analyzer ($\text{Na}^+/\text{K}^+/\text{Cl}^-$)(k102959), with the added feature that the Cl^- ISE sensor may be replaced by a Li^+ ISE sensor by the end user. The instrument software was upgraded to accommodate the addition of the Li^+ assay.

The PROLYTE Electrolyte Analyzer $\text{Na}^+/\text{K}^+/\text{Cl}^-/\text{Li}^+$ uses the previously cleared Diamond Diagnostic Fluid Pack (k031159) which contains the two levels of calibrants (Standard A 800 mL, Standard B 180 mL) required for calibration for each ion in a sealed package with a flush solution (80 mL) and a waste container. The analyzer can be programmed to self-calibrate at set intervals or on request. Mission Controls (k033063) are the recommended quality control material to be used daily.

J. Substantial Equivalence Information:

1. Predicate device name(s):

GemLyte Electrolyte Analyzer

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

k082462

3. Comparison with predicate:

| Item | Proposed Device PROLYTE Lithium Test System | Predicate GemLyte Lithium Test System (k082462) |
|-----------------------------------------------|---------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| Similarities | | |
| Intended use /Indication for use | Same | The Lithium Test System is intended to measure lithium (from the drug lithium carbonate) in whole blood, plasma, or serum. |
| Measurement Method | Same | Ion selective electrode |
| Calibration | Same | Automatic and on demand |
| Matrix | Same | Whole Blood, Serum, Plasma |
| Reagent composition | Same | Fluid Pack |
| Differences | | |
| Instrument | PROLYTE | GemLyte |
| Measuring Range Whole Blood, Serum, Plasma | 0.15-5.0 mEq/L | 0.2-5.5 mEq/L |
| Reagent Pack Volume | 800 mL | 350 mL |

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

CLSI EP07-A2, Interference Testing in Clinical Chemistry

L. Test Principle:

The principles of measurement used in the PROLYTE Electrolyte Analyzer $\text{Na}^+/\text{K}^+/\text{Cl}^-/\text{Li}^+$ are identical to those principles existing in the Predicate GemLyte Electrolyte Analyzer ($\text{Na}^+/\text{K}^+/\text{Cl}^-/\text{Ca}^{2+}/\text{Li}^+$).

The PROLYTE Electrolyte Analyzer measures sodium, potassium, chloride in whole blood, serum, plasma, and urine, and lithium in whole blood, serum and plasma using ion selective electrode technology. The sodium electrode contains a glass tube, specially formulated to be sensitive to sodium ions. The potassium and lithium electrodes incorporate a neutral carrier ionophore membrane. The chloride contains an ionophore covalently bound to a substrate which is sensitive to negatively charged ions. The potential of each electrode is measured relative to a fixed, stable reference established by a silver/silver chloride electrode in concentrated salt solution. The measured potential varies with the concentration of the ion sensed by the electrode.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

The analytical performance of Na⁺/K⁺/Cl⁻ in whole blood, serum, plasma, and urine was evaluated in the previously cleared 510(k) (k102959). Analytical performance of Li⁺ is presented below. Sodium Heparin was the anticoagulant used in the preparation of plasma and whole blood samples.

a. Precision/Reproducibility:

Five whole blood, serum, and plasma samples were analyzed with Li⁺ concentrations at the low, near mid point, and high end of the reference ranges, and at the low and high end of the reporting limits.

Within run precision was calculated with results from 30 replicates of each sample without calibration between measurements. The replicates were run consecutively in one day. Total precision was evaluated by measuring the same set of samples in duplicate twice a day for ten consecutive days resulting in 40 replicates. Whole blood total precision was conducted with calibrations after each 10 replicates on a single day due to instability of the whole blood samples. The results are summarized below.

Whole Blood, mEq/L

| Within Run | V Low | Low | Mid | High | V High |
|-------------|-------|-------|-------|-------|--------|
| Mean | 0.216 | 0.607 | 1.035 | 1.727 | 4.153 |
| %CV | 4.76 | 1.24 | 0.82 | 0.57 | 0.72 |
| n | 30 | 30 | 30 | 30 | 30 |

| Total | V Low | Low | Mid | High | V High |
|-------------|-------|-------|-------|-------|--------|
| Mean | 0.227 | 0.607 | 1.031 | 1.740 | 4.171 |
| %CV | 6.31 | 1.56 | 0.95 | 0.52 | 0.85 |
| n | 40 | 40 | 40 | 40 | 40 |

Plasma, mEq/L

| Within Run | V Low | Low | Mid | High | V High |
|-------------|-------|-------|-------|-------|--------|
| Mean | 0.321 | 0.620 | 1.093 | 2.296 | 4.415 |
| %CV | 1.65 | 0.78 | 0.28 | 0.58 | 1.43 |
| n | 30 | 30 | 30 | 30 | 30 |

| Total | V Low | Low | Mid | High | V High |
|-------------|-------|-------|-------|-------|--------|
| Mean | 0.327 | 0.628 | 1.095 | 2.285 | 4.379 |
| %CV | 4.47 | 1.09 | 0.61 | 1.07 | 1.52 |
| n | 40 | 40 | 40 | 40 | 40 |

Serum, mEq/L

| Within Run | V Low | Low | Mid | High | V High |
|-------------|-------|-------|-------|-------|--------|
| Mean | 0.256 | 0.594 | 1.058 | 1.999 | 4.308 |
| %CV | 3.30 | 1.09 | 0.42 | 0.58 | 0.98 |
| n | 30 | 30 | 30 | 30 | 30 |

| Total | V Low | Low | Mid | High | V High |
|-------------|-------|-------|-------|-------|--------|
| Mean | 0.293 | 0.596 | 1.061 | 2.007 | 4.356 |
| %CV | 9.56 | 2.76 | 0.70 | 2.12 | 1.89 |
| n | 40 | 40 | 40 | 40 | 40 |

b. *Linearity/assay reportable range:*

Linearity was evaluated by preparing stock solutions with high concentrations of Li⁺ in whole blood, plasma, and serum. These stock solutions were diluted serially (20%) to obtain concentrations across the measuring range for each matrix. Linear regression was performed and the results are shown below to support the claimed reportable range of 0.15-5.0 mEq/L.

| Matrix | Slope | Intercept | R2 | Conc. Tested (mEq/L) |
|---------------|--------------|------------------|-----------|-----------------------------|
| Whole Blood | 0.9854 | 0.0285 | 0.9979 | 0.15-5.5 |
| Plasma | 0.9985 | -0.0315 | 0.9997 | 0.1-5.9 |
| Serum | 1.0068 | 0.019 | 0.9998 | 0.1-5.7 |

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

The calibrators intended to be used with this device were previously cleared under k031159.

d. *Detection limit:*

Reportable ranges were determined based on the linearity studies (see above).

e. *Analytical specificity:*

Plasma samples were prepared with high and low concentrations of Lithium (0.4 and 1.3 mEq/L). Clinically significant interferences were spiked into the lithium samples at the indicated concentrations shown in the below table. Each spiked sample and the control were measured in 20 replicates and the mean results were compared. The below table shows the change in sample results (spiked versus control) in mEq/L when the interferent is tested at the indicated concentrations. The change in sample results (spiked versus control) for all tested interferences was 5 % or less.

| Effect of interferent on Li ⁺ test result, mEq/L | | | | | | | |
|-------------------------------------------------------------|------|------|-----------------|-----------------------------------------|------|------|-----------------|
| Li ⁺ concentration 0.4 mEq/L | | | | Li ⁺ concentration 1.3 mEq/L | | | |
| Alb | Bili | Trig | Na ⁺ | Alb | Bili | Trig | Na ⁺ |
| 12g/dL | 29 | 2650 | 160 | 12g/dL | 29 | 2650 | 160 |

| | | | | | | | | |
|-----------------------------------------|-------|-------|-------|--|-----------------------------------------|--------|-------|-------|
| | mg/dL | mg/dL | mEq/L | | | mg/dL | mg/dL | mEq/L |
| 0.021 | 0.000 | 0.003 | 0.016 | | -0.021 | -0.009 | 0.004 | 0.002 |
| Li ⁺ concentration 0.3 mEq/L | | | | | Li ⁺ concentration 1.5 mEq/L | | | |
| Hb | | | | | Hb | | | |
| 500 mg/dL | | | | | 500 mg/dL | | | |
| 0.003 | | | | | 0.002 | | | |

In the labeling, the sponsor stated that:

The following compounds did not interfere with the results: Bilirubin at 29 mg/dL (500 uM), Triglycerides at 2650 mg/dL (30 mM), Albumin at 12g/dL, Sodium at 160 mEq/L and hemoglobin at 500 mg/dL did not have a significant effect on Lithium result.

f. *Assay cut-off:*

Not applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

Method comparisons to predicate device GemLyte Li⁺ (k082462) were performed with whole blood, plasma, and serum patient samples using Na heparin as the anti-coagulant for whole blood and plasma. A small number of samples were spiked or diluted (<10%) to fully span the claimed measuring ranges. The results are summarized below:

| | Slope | Intercept | R² | N | Conc. Tested (mEq/L) |
|--------------------|--------------|------------------|----------------------|----------|-----------------------------|
| Whole Blood | 1.0096 | 0.0719 | 0.9947 | 94 | 0.15-5.0 |
| Plasma | 0.9806 | 0.1292 | 0.9971 | 100 | 0.16-5.0 |
| Serum | 0.9977 | 0.0133 | 0.9881 | 91 | 0.17-4.7 |

b. *Matrix comparison:*

Assay performance in all claimed matrices (serum, sodium heparin plasma, whole blood) is addressed in the method comparison studies described above. Na heparin is the only indicated anticoagulant for whole blood and plasma. The sponsor states in the labeling that lithium heparin tubes should not be used for lithium measurements.

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 recommends in the labeling that the values given in the tables below are intended to be used only as a guide. Each laboratory or testing site should establish its own range of normal values, taking into account factors such as age, sex, diet, and other determinants of electrolyte levels.

Whole Blood, Serum, Plasma (mmol/L or mEq/L)

Sodium (Na⁺) 135 to 148

Potassium (K⁺) 3.5 to 5.3

Chloride (Cl⁻) 98 to 107

Lithium (Li⁺) therapeutic range 0.6-1.2

Urine (mmol/L or mEq/L) spot

Sodium (Na⁺) 40 to 220

Potassium (K⁺) 25 to 120

Chloride (Cl⁻) 110 to 250

Reference:

1 Burtis, C; Ashwood, E. (eds.) Tietz Fundamentals of Clinical Chemistry, 5th ed., 2001

2 Geige Scientific Tables, Vol. 3, 8th edition

N. Instrument Name:

PROLYTE Electrolyte Analyzer Na⁺/K⁺/Cl⁻/Li⁺

O. System Descriptions:

1. Modes of Operation:

Fully automated with 'Yes' or 'No' commands for menu navigation.

2. Software:

FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

Yes X or No _____

3. Specimen Identification:

Manual

4. Specimen Sampling and Handling:

Samples are manually placed on the instrument one at a time, tested, and removed.

5. Calibration:

One point automated on board calibration performed every four hours or upon request. The slope is calculated during calibration and stored for sample measurement.

6. Quality Control:

Controls are run manually and recommended daily. Results can be stored in instrument memory for future use.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The “Performance Characteristics” Section above:

None

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

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