

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

A. 510(k) Number:

k112995

B. Purpose for Submission:

Modification of a cleared device (k061974 and k093623) -Potassium sensor change

C. Measurand:

Potassium

D. Type of Test:

Quantitative, potentiometric method

E. Applicant:

Instrumentation Laboratory Co.

F. Proprietary and Established Names:

GEM Premier 4000 with iQM (Intelligent Quality Management)
GEM CVP 1 and 2 (Calibration Valuation Product) with CO-Ox
GEM CVP 3 and 4 (Calibration Valuation Product) Hematocrit
GEM CVP 5 (Calibration Valuation Product) tBili

G. Regulatory Information:

- GEM Premier 4000 with iQM (Intelligent Quality Management):

Description	CFR Section	Device Class	Product Code
Blood gases and blood pH	862.1120	Class II	CHL
Sodium test system	862.1665	Class II	JGS
Potassium test system	862.1600	Class II	CEM
Calcium test system	862.1145	Class II	JFP

Chloride test system	862.1170	Class II	CGZ
Glucose test system	862.1345	Class II	CGA
Lactic acid test system	862.1450	Class I, meets limitations of exemptions per 21 CFR 862.9 (c)(9)	KHP
Automated hematocrit instrument	864.5600	Class II	GKF
Carboxyhemoglobin assay	864.7425	Class II	GHS
Automated hemoglobin system	864.5620	Class II	GKR
Whole blood hemoglobin assays	864.7500	Class II	GLY
Bilirubin (Total or Direct) Test System	862.1110	Class II	CIG
(Total and Unbound) in the Neonate Test System	862.1113	Class I, Reserved	MQM

- GEM CVP 1 and 2 (Calibration Valuation Product) *with* CO-Ox:
- GEM CVP 5 (Calibration Valuation Product) tBili:

Description	CFR Section	Device Class	Product Code
Quality Control Material	862.1660	Class I, reserved	JJY

- GEM CVP 3 and 4 (Calibration Valuation Product) Hematocrit:

Description	CFR Section	Device Class	Product Code
Hematocrit Control	864.8625	Class II	GLK

H. Intended Use:

1. Intended use(s):

Refer to indications for use below.

2. Indication(s) for use:

The GEM Premier 4000 is a portable critical care system for use by health care professionals to rapidly analyze whole blood samples at the point of health care delivery in a clinical setting and in a central laboratory. The instrument provides quantitative measurements of pH, $p\text{CO}_2$, $p\text{O}_2$, sodium, potassium, chloride, ionized calcium, glucose, lactate, hematocrit, total bilirubin and CO-Oximetry (tHb, O_2Hb , COHb, MetHb, HHb)

parameters. Total bilirubin can also be quantitated from heparinized plasma samples when analyzed in the tBili/CO-Ox mode. These parameters, along with derived parameters, aid in the diagnosis of a patient's acid/base status, electrolyte and metabolite balance and oxygen delivery capacity. Total bilirubin measurements are used in the diagnosis and management of biliary tract obstructions, liver disease and various hemolytic diseases and disorders involving the metabolism of bilirubin. In neonates, the level of total bilirubin is used to aid in assessing the risk of kernicterus.

Intelligent Quality Management (iQM) is used as the quality control and assessment system for the GEM Premier 4000 system. iQM is an active quality process control program designed to provide continuous monitoring of the analytical process with real-time, automatic error detection, automatic correction of the system and automatic documentation of all corrective actions, replacing the use of traditional external quality controls. Facilities should follow local, state and federal regulatory guidelines to ensure that a total quality management system is followed.

As part of this program, GEM CVP (Calibration Valuation Product) *with* CO-Ox, GEM CVP tBili and GEM CVP Hematocrit are external solutions intended to complete the calibration process and final accuracy assessment of the iQM cartridge calibration following warm-up. The reported values for GEM CVP (two levels for pH, blood gases, electrolytes, metabolites, total bilirubin, CO-Oximetry and hematocrit) must meet IL's specifications before the iQM cartridge can be used for patient sample measurements. Once the cartridge calibration is verified, the internal iQM program monitors the status of the system during the cartridge use life.

3. Special conditions for use statement(s):

For prescription use only

At point-of-care or central laboratory settings.

4. Special instrument requirements:

GEM Premier 4000 Analyzer

I. Device Description:

The GEM Premier 4000 analyzer utilizes an ion-selective electrode for the measurement of potassium. The potassium (K⁺) electrode has a sensor membrane on the surface of the electrode. The GEM Premier 4000 K sensor membrane is being modified to lower the Valinomycin concentration, along with a proportional decrease in the amount of counterion. This modification is to the Potassium sensor for the K⁺ assay on the GEM Premier 4000. There are no changes to other analyte measurements and device components.

J. Substantial Equivalence Information:

1. Predicate device name:

GEM Premier 4000 with iQM and CVP

2. Predicate 510(k) number:

k061974

3. Comparison with predicate:

Comparison Table: Potassium		
Item	New Device (k112995)	Predicate (k061974)
Intended Use	Quantitative measurement of potassium	Same
Test Principle	Potentiometric ion-selective electrode	Same
Specimen Type	Whole blood	Same
Assay Range	0.2 to 19.0 mmol/L	Same
Membrane Formulation	Modified	Unmodified

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

1. CLSI EP5-A2. Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline Second edition
2. CLSI EP6-A. Evaluation of the Linearity of Quantitative Analytical Methods; Approved Guideline
3. CLSI EP7-A2. Interference Testing in Clinical Chemistry; Approved Guideline- Second edition
4. CLSI EP9-A2. Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline Second edition
5. CLSI EP17-A. Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline.
6. CLSI C29-A2. Standardization of Sodium and Potassium Ion-selective electrode systems to the flame photometric reference method; Approved Guideline, Second Edition

L. Test Principle:

The GEM Premier 4000 potassium sensor technology is based on ion selective electrode methodology. Valinomycin is an ionophore that functions as the potassium recognition component in the sensor. When the sensor is exposed to solutions containing potassium, an electrical signal response (change in electrode potential in millivolts) proportional to the concentration of potassium in the sample is measured. The measured response is converted into potassium concentration based on the slope from the sensor calibration.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Precision studies were performed to evaluate the performance of the modified K⁺ sensor using three levels of whole blood samples under the syringe mode (150 µL), the full capillary mode (150 µL) and the micro capillary (65 µL) mode. Due to the instability of whole blood, fresh levels of whole blood were prepared (using 0.1M KCL as the spiking solution) for each run, each day, with a target concentration of 3.0, 4.0 and 7.0 mmol/L of potassium. Testing was completed in replicates of 8 per run, twice a day for 5 days on 2 GEM Premier 4000 instruments. The mean, standard deviation (SD), and coefficients of variation (CV) were determined for each level and each mode as summarized below:

Precision Data Summary						
Whole Blood- Syringe Mode						
Sample	N	Within Run			Total	
		Mean (mmol/L)	SD (mmol/L)	CV (%)	SD (mmol/L)	CV (%)
1	160	2.90	0.04	1.51	0.04	1.51
2	160	3.88	0.05	1.32	0.05	1.32
3	160	7.41	0.06	0.86	0.06	0.86
Whole Blood- Full Capillary Mode						
Sample	N	Within Run			Total	
		Mean (mmol/L)	SD (mmol/L)	CV (%)	SD (mmol/L)	CV (%)
1	160	3.06	0.11	3.55	0.11	3.55
2	160	4.06	0.11	2.71	0.11	2.71
3	160	7.44	0.12	1.58	0.16	2.16
Whole Blood- Micro Capillary Mode						
Sample	N	Within Run			Total	
		Mean (mmol/L)	SD (mmol/L)	CV (%)	SD (mmol/L)	CV (%)
1	160	3.34	0.11	3.31	0.11	3.31
2	158	4.25	0.11	2.66	0.11	2.66
3	160	7.83	0.10	1.27	0.10	1.27

b. *Linearity/assay reportable range:*

A linearity study was performed using whole blood samples according to the CLSI EP6-A guideline. 7 different concentrations of potassium were measured in triplicate on 3 different GEM Premier 4000 analyzers using 3 different sample modes. The measured values were plotted against the expected values measured by the reference method (Flame Photometer). The linear regressions analysis is summarized in the table below:

Linearity Data Summary			
Testing Mode	Linear regression equation	R ²	Sample range tested
Syringe mode	Y= 1.0144X – 0.0612	0.9999	0.18-24.17 mmol/L
Full capillary	Y= 1.0115X + 0.0251	0.9997	0.13-24.57 mmol/L
Micro capillary	Y= 1.0791X – 0.2189	0.9998	0.17-26.14 mmol/L

The results of the study support the sponsor’s claim that the assay is linear from 0.2 to 19.0 mmol/L

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

Traceability:

Potassium is traceable to a reference material (NIST standard). See k061974

GEM CVP 1 and 2 (Calibration Valuation Product) with CO-Ox, GEM CVP 3 and 4 (Calibration Valuation Product) Hematocrit, and GEM CVP 5 (Calibration Valuation Product) tBili are part of the iQM quality control and assessment system for the GEM Premier 4000 system. They have been previously cleared in k061974 and k093623.

Potassium sensor stability:

The shelf life stability study was performed on three lots of sensors and the in-use (cartridge use life) stability study was performed on six lots of sensors. Real-time stability study is still on-going. Based on the results, the sponsor claims that the K sensor has a shelf life stability of 2 months at 15 to 25 °C and an in-use stability of at least 600 samples. The stability study protocol and acceptance criteria were found to be adequate.

d. *Detection limit:*

See linearity study in section M.1.b above.

e. *Analytical specificity:*

An interference study was performed based on the CLSI EP7-A guideline. A comprehensive interference screen was conducted, followed by a dose-response evaluation to characterize the interference according to the CLSI EP7-A. Two levels of human whole blood pooled samples (K approximately 3.0 and 5.0 mmol/L) were spiked with various potential interference substances (48 drugs and endogenous compounds). All samples were analyzed in triplicates on the GEM Premier 4000 and the reference method (flame photometer). The sponsor defines non-significant interference as difference within ± 0.1 mmol/L when compared to the reference method. Results are summarized in the table below for non-significant interference when tested at the concentrations listed:

Potential Interfering Substances and the Concentrations Tested

Substance	“Worst Case” Test Concentration	Substance	“Worst Case” Test Concentration
Acetaminophen	20 mg/dL	Hydroxyurea	0.8 mg/dL
Acetoacetate	2 mmol/L	Ibuprofen	2.425 mmol/L
Ammonium	107 μ mol/L	Icodextrin	20 mg/dL
Aprotinin	50 mg/L	Iodide	3 mmol/L
Ascorbic acid	6 mg/dL	Isoniazide	4 mg/dL
Atracurium	50 mg/L	Lactate	6.6 mmol/L
Benzalkonium	5 mg/L	Lithium	3.2 mmol/L
Bromide	37.5 mmol/L	Ionized Magnesium	15 mmol/L
Ionized Calcium	2.5 mmol/L	Maltose	0.2 mg/dL
Chlorpromazine	0.0063 mmol/L	Mannose	20 mg/dL
Creatinine	5 mg/dL	Oxalate	500 mg/dL
Dobutamine	2 mg/dL	Perchlorate	20 mg/dL
Dopamine	0.1 mg/dL	pH	6.80
Ethanol	400 mg/dL	Pralidoxime iodide	40 μ g/mL
Etomidate	50 mg/L	Pyruvate	0.309 mmol/L
Flaxedil	5 mg/dL	Salicylate	4.34 mmol/L
Fluoride	0.4 mg/dL	Sodium	180 mmol/L
Fructose	18 mg/dL	Thiocyanate	56 mg/dL
Galactose	15 mg/dL	Thiopental	66 mg/L

Substance	“Worst Case” Test Concentration	Substance	“Worst Case” Test Concentration
Glucose	1000 mg/dL	Triglycerides	3250 mg/dL
Glycolic acid	1 mmol/L	Urea	42.9 mmol/L
Heparin	300 IU/mL	Uric acid	23.5 mg/dL
β-hydroxybutyrate	2 mmol/L	Xylose	20 mg/dL

Because hemolysis and sodium citrate have shown significant interference, the sponsor stated the following limitations in the labeling:

“Hemolyzed samples may result in falsely elevated potassium levels.”

“Blood collection tubes containing sodium citrate as an additive will produce clinically significant interference on Potassium and should not be used.”

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison study was performed for potassium according to the CLSI EP9-A guideline. Six GEM Premier 400 analyzers were tested with two in each sample mode, over a period of 18 days, against the results performed with a commercially available blood gases analyzer. A total of 109 samples were tested. Approximately 10% to 14% of the samples were altered in order to cover the hard-to-find sample range. The linear regressions analysis is summarized in below:

Test mode	N	Slope (95%CI)	Intercept (95% CI)	R ²	Sample range tested (mmol/L)
Syringe	109	1.002 (0.994-1.011)	0.052 (0.012-0.1092)	0.998	0.2-18.6
Full capillary	109	1.001 (0.992-1.011)	0.092 (0.047-0.137)	0.997	0.2-18.2
Micro capillary	109	1.016 (1.006-1.027)	0.148 (0.095-0.200)	0.997	0.2-18.2

b. Matrix comparison:

Not applicable

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:

K: 3.4 to 4.5 mmol/L

The reference range for potassium was taken from the literature.

References: Wu, A., Tietz Clinical Guide to Laboratory Tests, W.B. Saunders Co., St. Louis MO, 4th, 2006.

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.