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

## A. 510(k) Number:

k160225

## B. Purpose for Submission:

New device

## C. Measurand:

Sodium (Na+), Potassium (K+), Chloride (Cl-), ionized Calcium (Ca++)

## D. Type of Test:

Quantitative, potentiometric, ion selective multisensors for electrolytes

## E. Applicant:

Instrumentation Laboratory Inc.

## F. Proprietary and Established Names:

GEM Premier 5000 (Measured Parameters: Sodium, Potassium, Chloride, Ionized Calcium)
GEM System Evaluator
GEM Hematocrit Evaluator
GEM CVP 5 tBili

## G. Regulatory Information:

| Product Code | Classification | Regulation Section | Panel |
|---|---|---|---|
| JGS | Class II | 21 CFR 862.1665 Sodium Test System | Clinical Chemistry (75) |
| CEM | | 21 CFR 862.1600 Potassium Test System | |
| CGZ | | 21 CFR 862.1170 Chloride Test System | |
| JFP | | 21 CFR 862.1145 Calcium Test System | |
| JJY | Class I, reserved | 21 CFR 862.1660 Quality Control Material (assayed and unassayed) | |
| JJE | Class I, exempt | 21 CFR 862.2160 Discrete Photometric Analyzer Chemistry For Clinical Use | |
| GLK | Class II | 21 CFR 864.8625 Hematocrit Control | Hematology (81) |

## H. Intended Use:

1. Intended use(s):

   See Indications for use below

2. Indication(s) for use:

   The GEM Premier 5000 is a portable critical care system for use by health care professionals to rapidly analyze heparinized 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 sodium and ionized calcium from venous, arterial and capillary heparinized whole blood, as well as quantitative measurements of potassium and chloride from venous and arterial heparinized whole blood. These parameters, along with derived parameters, aid in the diagnosis of electrolyte balance.

   Sodium (Na+) measurements are used in the diagnosis and treatment of aldosteronism, diabetes insipidus, adrenal hypertension, Addison's disease, dehydration, inappropriate antidiuretic secretion, or other diseases involving electrolyte imbalance.

   Potassium (K+) measurements are used to monitor electrolyte balance in the diagnosis and treatment of disease conditions characterized by low or high blood potassium levels.

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

   Ionized calcium (Ca++) measurements are used in the diagnosis and treatment of parathyroid disease, a variety of bone diseases, chronic renal disease and tetany.

   GEM System Evaluator is a three-level assayed quality control material for evaluating performance characteristics of pH, pCO2, pO2, Electrolytes, Metabolites, Total Bilirubin (tBili) and CO-Oximetry on the GEM Premier 4000 and GEM Premier 5000 analyzers.

   GEM Hematocrit Evaluator is a three-level assayed quality control material intended for evaluating performance characteristics of hematocrit on the GEM Premier 4000 andGEM Premier 5000 analyzers.

   GEM CVP 5 tBili is an external Calibration Valuation Product used to complete the calibration process of the GEM Premier 4000 and GEM Premier 5000 analyzers prior to use with patient samples for total bilirubin (tBili) testing.

3. Special conditions for use statement(s):

   For prescription use only at point-of-care and central laboratory settings

4. Special instrument requirements:

   GEM Premier 5000 analyzer

## I. Device Description:

The GEM Premier 5000 system contains two key components: the GEM Premier 5000 analyzer and the GEM Premier 5000 PAK (cartridge). The GEM Premier 5000 PAK contains reagents, sensors, optical cell for Co-Ox and total bilirubin, sampler and waste bag. It enables analysis of 75 to 600 samples per cartridge. There are five process control solutions (A, B, C, D and E), one reference electrode solution and one lysing solution in each GEM Premier 5000 PAK. The five process control solutions are utilized each day at different frequencies to confirm sensor, CO-Ox and PAK performance.

The target values of the Process Control Solutions are stated in the following table:

| Analyte | Units | A | B | C | D | E |
|---|---|---|---|---|---|---|
| Na+ | mmol/L | 105 | 155 | N/A | 166 | 129 |
| K+ | mmol/L | 7.1 | 1.9 | N/A | 7.2 | 4.5 |
| Cl- | mmol/L | 49 | 88 | N/A | 141 | 101 |
| Ca++ | mmol/L | 1.77 | 0.79 | N/A | 1.18 | 0.59 |

Intelligent Quality Management 2 (iQM2) is used as the quality control and assessment system for the GEM Premier 5000 system. It is a statistical process control system with well-defined performance characteristics that maximizes probability of error detection, minimizes time to error detection, while minimizing probability of false rejection. It provides continuous monitoring of the analytical process before, during and after sample measurement with real-time, automatic error detection, automatic correction of the system and automatic documentation of all corrective actions.

GEM CVP 5 tBili is an external Calibration Valuation Product used to complete the calibration process of the GEM Premier 4000 and GEM Premier 5000 analyzers prior to use with patient samples for total bilirubin (tBili) testing. GEM CVP 5 tBili comes in a liquid, ready to use sealed ampoule, contains 1.8 mL of solution. Solution contains purified human hemoglobin, stabilizers and biocide in a physiologically buffered matrix. This product has been previously cleared in k112995.

GEM System Evaluator is a three-level assayed quality control material for evaluating performance characteristics of pH, pCO2, pO2, Electrolytes, Metabolites, Total Bilirubin (tBili) and CO-Oximetry on the GEM Premier 4000 and GEM Premier 5000 analyzers. GEM System Evaluator is buffered bicarbonate solution, containing inorganic salts and organic metabolites, dye and biocides; equilibrated with carbon dioxide and oxygen. Each ampoule contains 1.8 mL of solution. This product has been previously cleared in k093623.

GEM Hematocrit Evaluator is a three-level assayed quality control material intended for evaluating performance characteristics of hematocrit on the GEM Premier 4000 and GEM Premier 5000 analyzers. GEM Hematocrit Evaluator is buffered bicarbonate solution containing inorganic salts and biocides; equilibrated with carbon dioxide and oxygen. Each ampoule contains 1.8 mL of solution. This product has been previously cleared in k093623.

Each donation of human blood or blood component used in preparation of QC materials was tested by FDA approved methods and found non-reactive for the presence of the antibody to Human Immunodeficiency Virus 1 and 2 (HIV 1/2), the Hepatitis B surface antigen (HBsAg), and the antibody to Hepatitis C (HCV).

## J. Substantial Equivalence Information:

1. Predicate device name(s):

   GEM Premier 4000,
   CVP 5 tBili,
   GEM System Evaluator,
   GEM Hematocrit Evaluator

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

   k133407 (for GEM Premier 4000),
   k112995 (for CVP 5 tBili),
   k093623 (for GEM System Evaluator and GEM Hematocrit Evaluator)

3. Comparison with predicate:

Similarities and Differences of the instrument with electrolytes:

| Item | GEM Premier 5000 for measurement of Na, K, Cl, and Ca (Candidate Device k160225) | GEM Premier 4000 for measurement of Na, K, Cl, and Ca (Predicate Device k133407) |
|---|---|---|
| Similarities | | |
| Intended Use | 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 sodium, potassium, chloride, ionized calcium. | Same |
| Intended User | Central Laboratory and Point-of-Care sites | Same |
| Types of Measurements | Quantitative, photometric, ion selective multisensors for electrolytes | Same |
| Sampling Modes and Sample Volumes | Normal Mode 150 µL<br>Micro Mode 65 µL<br>tBili/CO-Ox Mode 100 µL | Same |

| Item | GEM Premier 5000 for measurement of Na, K, Cl, and Ca (Candidate Device k160225) | GEM Premier 4000 for measurement of Na, K, Cl, and Ca (Predicate Device k133407) |
|---|---|---|
| Differences | | |
| Sample Type | Na+ and Ca++: Arterial, venous or capillary heparinized whole blood.<br>K+ and Cl-: Arterial or venous heparinized whole blood | Heparinized whole blood |
| Measuring Range | Na+: 100 to 180 mmol/L<br>K+: 1.0 to 19.0 mmol/L<br>Cl-: 40 to 158 mmol/L<br>Ca++: 0.11 to 4.25 mmol/L | Na+: 100 to 180 mmol/L<br>K+: 0.2 to 19.0 mmol/L<br>Cl-: 40 to 158 mmol/L<br>Ca++: 0.10 to 4.25 mmol/L |
| Instrument Dimensions | GEM Premier 5000 Instrument:<br>• Height: 18.6 inches<br>• Width: 13.0 inches<br>• Depth: 16.4 inches<br>• Weight: 45.4 pounds | GEM Premier 4000 Instrument:<br>• Height: 18 inches<br>• Width: 12 inches<br>• Depth: 15 inches<br>• Weight: 44 pounds |
| Intelligent Quality Management Name | iQM2 | iQM |
| Error Detection Scheme in Intelligent Quality Management | Multi-level checks for detecting cartridge errors, including<br>1. System checks<br>2. Sensor/CO-Ox checks<br>3. IntraSpect checks<br>4. Pattern Recognition checks<br>5. Process Stability checks | Same except without IntraSpect checks |
| Calibration solutions | Two internal Process Control Solutions (PCS D and E) in the GEM Premier 5000 PAK are intended to complete the calibration process and final accuracy assessment of GEM Premier 5000 iQM2 process prior to use with patient samples. | Four external solutions (CVP 1,2,3,and 4) are intended to complete the calibration process and final accuracy assessment of the GEM Premier 4000 iQM process prior to use with patient samples. |
| Process Control Solutions (PCS) in GEM PAK (cartridge) | 5 PCSs (A,B,C,D,E) | 4 PCSs (A,B,C,D)<br><br>Same formulation for PCSs A, B, and C |
| External QC material | CVP 5 tBili<br>GEM System Evaluator 1, 2 and 3<br>GEM Hematocrit Evaluator 1, 2 and 3. No more CVP 1,2,3,and 4 (replaced by internal PCSs D and E) | CVP 1,2,3,4 and 5<br>GEM System Evaluator 1, 2 and 3<br>GEM Hematocrit Evaluator 1, 2 and 3 |

| Item | GEM Premier 5000 for measurement of Na, K, Cl, and Ca (Candidate Device k160225) | GEM Premier 4000 for measurement of Na, K, Cl, and Ca (Predicate Device k133407) |
|---|---|---|
| | | Same formulation for CVP 5 tBili, GEM System Evaluator 1, 2 and 3, GEM Hematocrit Evaluator 1, 2 and 3. |

Similarities and differences of the CVP 5 tBili:

| Item | Candidate Device k160225 | Predicate Device k112995 |
|---|---|---|
| Trade Names | CVP 5 tBili | Same |
| Intended Use | GEM CVP 5 tBili is an external Calibration Valuation Product used to complete the calibration process of the GEM Premier analyzer prior to use with patient samples for total bilirubin (tBili) testing. | Same |
| Value Assigned | GEM Premier 4000 and GEM Premier 5000 | GEM Premier 4000 |
| Formulation | Purified human hemoglobin, stabilizers and biocide in a physiologically buffered solution. | Same |
| Storage | 2-8°C until expiration | Same |

Similarities and differences of the GEM System Evaluator

| Item | Candidate Device k160225 | Predicate Device k093623 |
|---|---|---|
| Trade Names | GEM System Evaluator | Same |
| Intended Use | Intended for evaluating performance characteristics of pH, pCO2, pO2, Electrolytes, Metabolites, Total Bilirubin (tBili) and CO-Oximetry on the GEM Premier analyzer. | Same |
| Value Assigned | GEM Premier 4000 and GEM Premier 5000 | GEM Premier 4000 |
| Formulation | Aqueous buffered bicarbonate solution | Same |
| Storage | 2-8°C until expiration<br>15-25°C for 4 months | Same |

Similarities and differences of the GEM Hematocrit Evaluator

| Item | Candidate Device k160225 | Predicate Device k093623 |
|---|---|---|
| Trade Names | GEM Hematocrit Evaluator | Same |
| Intended Use | Intended for evaluating performance characteristics of hematocrit on the GEM Premier analyzer. | Same |
| Value Assigned | GEM Premier 4000 and GEM Premier 5000 | GEM Premier 4000 |
| Formulation | Aqueous buffered bicarbonate solution | Same |
| Storage | 15-25°C until expiration | Same |

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

CLSI - EP05-A3 Evaluation of Precision of Quantitative Measurement Procedures
CLSI - EP06-A Evaluation of Linearity of Quantitative Measurement Procedures
CLSI - EP07-A2. Interference Testing in Clinical Chemistry
CLSI - EP09-A3 Measurement Procedure Comparison and Bias Estimation Using Patient Samples
CLSI - EP17-A2 Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures
CLSI - EP25-A Evaluation of Stability of In Vitro Diagnostic Reagents

**L. Test Principle:**

The electrolyte sensors (Na+, K+, Cl- and Ca++) are polyvinyl chloride (PVC) based ion selective electrodes consisting of an internal Ag/AgCl reference electrode and an internal electrolyte layer. Their potentials are measured against the card reference electrode (Ag/Ag+). The electrolyte sensors are based on the principle of ion selective electrodes; in which electrical potential can be established across a membrane resulting from chemical selectivity of the membrane to a specific ion. The electrical potential is proportional to the logarithm of the analyte activity in the sample, and the concentration of the desired ions is calculated using Nernst equation.

**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:

   a. *Precision/Reproducibility:*
   Both Internal and External Precision studies were performed in accordance with CLSI EP05-A3 guidance.

Internal Precision Studies:

1) An internal 20-day precision study was performed on the GEM Premier 5000 with GEM System Evaluator 1, 2 and 3. Each of the control levels was run on 3 GEM Premier 5000 analyzers for 20 days, with 2 runs per day and 1 replicate measured per run per level. Results are summarized below:

| Analyte | System Evaluator Level | N | Mean mmol/L | Within Run SD | Within Run %CV | Total SD | Total CV% |
|---|---|---|---|---|---|---|---|
| Na+ | 1 | 120 | 124 | 0.7 | 0.6% | 0.8 | 0.6% |
| | 2 | 120 | 141 | 0.5 | 0.4% | 0.5 | 0.4% |
| | 3 | 120 | 156 | 0.7 | 0.5% | 0.7 | 0.5% |
| K+ | 1 | 120 | 2.4 | 0.02 | 0.7% | 0.02 | 0.7% |
| | 2 | 120 | 4.7 | 0.04 | 0.9% | 0.05 | 1.1% |
| | 3 | 120 | 7.7 | 0.04 | 0.5% | 0.05 | 0.6% |
| Cl- | 1 | 120 | 85 | 0.6 | 0.7% | 0.6 | 0.7% |
| | 2 | 120 | 108 | 0.5 | 0.4% | 0.6 | 0.6% |
| | 3 | 120 | 141 | 1.0 | 0.7% | 1.3 | 1.0% |
| Ca++ | 1 | 120 | 1.56 | 0.013 | 0.8% | 0.015 | 1.0% |
| | 2 | 120 | 1.16 | 0.006 | 0.5% | 0.006 | 0.6% |
| | 3 | 120 | 0.64 | 0.006 | 1.0% | 0.007 | 1.1% |

2) In addition, an internal precision study was performed using five levels of lithium heparin whole blood samples under normal mode (150 µL) for all 4 electrolytes, and micro capillary (65 µL) mode for Na and Ca. Due to the instability of whole blood, fresh whole blood samples were prepared each day. Testing was completed in 8 replicates per run for each level and 1 run per day for 5 days on 3 GEM Premier 5000 instruments. Results are summarized below:

| Analyte | Mode | Level | Mean mmol/L | N | Within Run SD | Within Run %CV | Total SD* | Total CV%* |
|---|---|---|---|---|---|---|---|---|
| Na+ | Normal Mode | 1 | 104 | 120 | 0.5 | 0.5% | 0.6 | 0.6% |
| | | 2 | 114 | 120 | 0.4 | 0.4% | 0.4 | 0.4% |
| | | 3 | 132 | 120 | 0.4 | 0.3% | 0.5 | 0.4% |
| | | 4 | 148 | 120 | 0.6 | 0.4% | 0.7 | 0.4% |
| | | 5 | 187 | 120 | 1.1 | 0.6% | 1.4 | 0.8% |
| | Micro Mode | 1 | 104 | 120 | 0.4 | 0.3% | 0.5 | 0.5% |
| | | 2 | 114 | 120 | 0.3 | 0.3% | 0.5 | 0.4% |
| | | 3 | 131 | 120 | 0.3 | 0.2% | 0.4 | 0.3% |
| | | 4 | 147 | 120 | 0.4 | 0.3% | 0.5 | 0.3% |
| | | 5 | 186 | 120 | 0.6 | 0.3% | 1.2 | 0.6% |

| Analyte | | | | | Run SD | Run %CV | SD* | CV%* |
|---|---|---|---|---|---|---|---|---|
| K+** | Normal Mode | 1 | 1.6 | 120 | 0.04 | 2.5% | 0.04 | 2.8% |
| | | 2 | 2.9 | 120 | 0.05 | 1.7% | 0.06 | 2.0% |
| | | 3 | 5.5 | 120 | 0.05 | 0.9% | 0.09 | 1.7% |
| | | 4 | 7.5 | 120 | 0.14 | 1.9% | 0.18 | 2.5% |
| | | 5 | 17 | 120 | 0.32 | 1.9% | 0.51 | 3.0% |
| Cl-** | Normal Mode | 1 | 52 | 120 | 0.4 | 0.8% | 0.6 | 1.1% |
| | | 2 | 71 | 120 | 0.3 | 0.5% | 0.4 | 0.6% |
| | | 3 | 90 | 120 | 0.4 | 0.4% | 0.4 | 0.4% |
| | | 4 | 115 | 120 | 0.7 | 0.6% | 1 | 0.9% |
| | | 5 | 167 | 120 | 1.4 | 0.9% | 2.3 | 1.4% |
| Ca++ | Normal Mode | 1 | 0.23 | 120 | 0.009 | 3.9% | 0.012 | 5.2% |
| | | 2 | 0.37 | 120 | 0.006 | 1.7% | 0.009 | 2.3% |
| | | 3 | 0.86 | 120 | 0.005 | 0.6% | 0.006 | 0.7% |
| | | 4 | 1.54 | 120 | 0.02 | 1.3% | 0.022 | 1.4% |
| | | 5 | 4.26 | 120 | 0.074 | 1.7% | 0.084 | 2.0% |
| | Micro Mode | 1 | 0.22 | 120 | 0.005 | 2.4% | 0.006 | 2.8% |
| | | 2 | 0.35 | 120 | 0.004 | 1.1% | 0.005 | 1.4% |
| | | 3 | 0.83 | 120 | 0.004 | 0.5% | 0.005 | 0.6% |
| | | 4 | 1.51 | 120 | 0.015 | 1.0% | 0.015 | 1.0% |
| | | 5 | 4.2 | 120 | 0.057 | 1.3% | 0.069 | 1.6% |

* The day-to-day contribution was excluded in total precision evaluation for whole blood samples since different whole blood samples were prepared each day.

** The candidate device is not intended for the measurement of K and Cl in capillary samples; therefore, only data from syringe samples tested under normal mode for K and Cl are shown in the table.

External Precision Studies:

3) A reproducibility study was performed at 3 external clinical point-of-care (POC) sites in hospital settings. The studies were run by a total of 9 different operators (perfusionists and respiratory therapists) on 3 different GEM Premier 5000 instruments using a single lot of GEM Premier 5000 PAK (cartridge). Each site used the same lots of GEM System Evaluator (GSE) 1, 2 and 3, running each control level in triplicate, twice a day for 5 days, for a total of 30 replicates per level per site. The pooled repeatability and reproducibility results for these 3 POC sites are summarized below:

| Analyte | Level | N | Mean mmol/L | Repeatability | | Reproducibility | |
|---|---|---|---|---|---|---|---|
| | | | | SD | %CV | SD | %CV |
| Na+ | GSE 1 | 90 | 125 | 0.4 | 0.3% | 0.5 | 0.4% |
| | GSE 2 | 90 | 141 | 0.3 | 0.2% | 0.5 | 0.4% |
| | GSE 3 | 90 | 155 | 0.3 | 0.2% | 0.4 | 0.2% |
| K+ | GSE 1 | 90 | 2.4 | 0.0 | 0.0% | 0.0 | 0.0% |
| | GSE 2 | 90 | 4.7 | 0.03 | 0.6% | 0.04 | 0.8% |
| | GSE 3 | 90 | 7.7 | 0.02 | 0.3% | 0.03 | 0.4% |
| Cl- | GSE 1 | 90 | 85 | 0.3 | 0.4% | 0.4 | 0.4% |
| | GSE 2 | 90 | 108 | 0.2 | 0.2% | 0.3 | 0.3% |
| | GSE 3 | 90 | 142 | 0.4 | 0.3% | 0.6 | 0.4% |
| Ca++ | GSE 1 | 90 | 1.58 | 0.007 | 0.4% | 0.009 | 0.6% |
| | GSE 2 | 90 | 1.16 | 0.005 | 0.4% | 0.007 | 0.6% |
| | GSE 3 | 90 | 0.64 | 0.003 | 0.5% | 0.005 | 0.8% |

4) To evaluate whole blood imprecision on the new GEM Premier 5000 system in the central laboratory and point-of-care (POC) sites in hospital settings, whole blood patient samples were tested at 2 external central laboratories and 1 internal Customer Simulation Laboratory, as well as at 3 external POC locations. For the central laboratory setting, the studies were performed by 3 operators on 3 GEM Premier 5000 instruments using a single lot of GEM Premier 5000 PAK (cartridge). For the POC Setting, the studies were performed by 11 operators on 3 GEM Premier 5000 instruments, using a single lot of GEM Premier 5000 PAK (cartridge). At least two whole blood specimens were analyzed in triplicate daily for 5 days in both normal mode (150 µL) for all 4 electrolytes, and micro capillary (65 µL) mode for Na and Ca. Due to the use of unique whole blood samples at each clinical site, only repeatability can be evaluated. Reproducibility was not assessed for the whole blood samples. At the internal Customer Simulation Laboratory (CSL), contrived whole blood specimens were analyzed in addition to native specimens in order to cover the low and high medical decision levels of each analyte.

   The precision results are summarized below:

| Analyte | Mode | Site | N | mean | Within sample SD or CV% |
|---|---|---|---|---|---|
| Na+ (mmol/L) | Normal Mode | POC1 | 54 | 138 | 0.5 |
| | | POC2 | 42 | 139 | 0.6 |
| | | POC3 | 30 | 138 | 0.5 |
| | | POC All | 126 | 138 | 0.5 |
| | | CSL | 33 | 140 | 0.6 |
| | | Lab1 | 30 | 141 | 0.5 |
| | | Lab2 | 30 | 137 | 0.5 |
| | | Lab All | 93 | 139 | 0.5 |

| Analyte | Mode | Site | N | mean | Within sample SD or CV% |
|---|---|---|---|---|---|
| Na+ (mmol/L) | Micro Mode | POC1 | 30 | 136 | 0.6 |
| | | POC2 | 36 | 137 | 0.4 |
| | | POC3 | 36 | 138 | 0.4 |
| | | POC All | 102 | 137 | 0.5 |
| | | CSL | 33 | 140 | 0.3 |
| | | Lab1 | 30 | 142 | 0.6 |
| | | Lab2 | 30 | 136 | 0.5 |
| | | Lab All | 93 | 139 | 0.5 |
| K+* (mmol/L) | Normal Mode | POC1 | 54 | 4.2 | 0.05 |
| | | POC2 | 42 | 4.3 | 0.03 |
| | | POC3 | 30 | 4.1 | 0.05 |
| | | POC All | 126 | 4.2 | 0.04 |
| | | CSL | 33 | 4.0 | 0.07 |
| | | Lab1 | 30 | 4.2 | 0.04 |
| | | Lab2 | 30 | 4.2 | 0.05 |
| | | Lab All | 93 | 4.1 | 0.06 |
| Cl-* (mmol/L) | Normal Mode | POC1 | 54 | 105 | 0.2% |
| | | POC2 | 42 | 107 | 0.2% |
| | | POC3 | 30 | 104 | 0.3% |
| | | POC All | 126 | 106 | 0.2% |
| | | CSL | 36 | 105 | 0.3% |
| | | Lab1 | 30 | 110 | 0.3% |
| | | Lab2 | 30 | 104 | 0.4% |
| | | Lab All | 96 | 106 | 0.3% |
| Ca++ (mmol/L) | Normal Mode | POC1 | 54 | 1.17 | 0.6% |
| | | POC2 | 36 | 1.15 | 0.4% |
| | | POC3 | 27 | 1.12 | 0.6% |
| | | POC All | 117 | 1.15 | 0.6% |
| | | CSL | 33 | 1.23 | 0.6% |
| | | Lab1 | 27 | 1.16 | 0.3% |
| | | Lab2 | 27 | 1.20 | 0.9% |
| | | Lab All | 87 | 1.20 | 0.6% |
| | Micro Mode | POC1 | 27 | 1.15 | 0.8% |
| | | POC2 | 27 | 1.17 | 0.5% |
| | | POC3 | 30 | 1.13 | 0.6% |
| | | POC All | 84 | 1.15 | 0.6% |
| | | CSL | 33 | 1.20 | 0.6% |
| | | Lab1 | 30 | 1.15 | 0.6% |
| | | Lab2 | 30 | 1.12 | 0.6% |
| | | Lab All | 93 | 1.16 | 0.6% |

*The candidate device is not intended for the measurement of K and Cl in capillary samples; therefore, only data from syringe samples tested under normal mode for K and Cl are shown in the table.

b. *Linearity/assay reportable range:*
The linearity studies were performed followed the CLSI EP06-A guidance. For the electrolytes, nine to ten equally spaced samples covering the measurement range were prepared by diluting high concentration lithium heparin whole blood samples. Three replicates were measured on three (3) GEM Premier 5000 analyzers for each sample. The mean of these replicates was compared to those obtained on the reference analyzers. The linear regression results support the claimed measuring ranges, as summarized in the table below:

| Analyte | Claimed Measuring Range (mmol/L) | Sample Range Tested (mmol/L) | Slope | Intercept | $\gamma^2$ |
|---|---|---|---|---|---|
| Na+ | 100 to 180 | 85 to 214 | 0.972 | 5.377 | 0.999 |
| K+ | 1.0 to 19.0 | 0.7 to 21.9 | 0.993 | -0.072 | 0.999 |
| Cl- | 40 to 158 | 35 to 189 | 0.964 | 2.805 | 1.000 |
| Ca++ | 0.11 to 4.25 | 0.10 to 5.05 | 0.999 | 0.011 | 0.999 |

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

Traceability

The GEM Premier 5000 Na+ measurement is traceable to a flame emission spectrophotometry reference method, which uses secondary standards prepared from NaCl, NIST #919.

The GEM Premier 5000 K+ measurement is traceable to a flame emission spectrophotometry reference method, which uses secondary standards prepared from KCl, NIST #918.

The GEM Premier 5000 Cl- measurement is traceable to a coulometric-amperometric titration with silver ion using secondary standards prepared from NaCl, NIST #919.

The GEM Premier 5000 Ca++ measurement is traceable to a direct potentiometry using secondary standards prepared from calcium carbonate, NIST #915.

Stability

Since there is no change in the formulation for CVP 5 tBili, GEM System Evaluator (1, 2, 3) or GEM Hematocrit Evaluator (1, 2, 3), the shelf-life and stability data from their original 510(k) filings (k112995 and k093623) are still valid.

Shelf life stability studies were performed with GEM Premier 5000 PAKs (cartridges)

and demonstrated that they are stable for 180 days when stored in the claimed range of 15-25°C. The GEM Premier 5000 PAKs are stable for 31 days or for 600-sample use on board. The protocols for stability and acceptance criteria were reviewed and found to be adequate.

Value assignment

The value assignment procedures for GEM System Evaluator, GEM Hematocrit Evaluator and GEM CVP 5 tBili are the same as those in original 510(k) filings (k112995 and k093623) except adding in GEM Premier 5000.

*d. Detection limit:*

The Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantification (LoQ) were evaluated in accordance with CLSI EP17-A2 Guideline.

Samples tested were all lithium heparin whole blood samples. LoB was determined by running three blank samples in 60 replicates per day over 3 days using 3 lots of GEM Premier 5000 PAKs (cartridges) on 3 different GEM Premier 5000 instruments.

LoD and LoQ were determined by running low level samples in 60 replicates per day over 3 days using 3 lots of GEM Premier 5000 PAKs (cartridges) on 3 different GEM Premier 5000 instruments. LoD is calculated based on LoB (mean) + 1.65 SD (low sample). LoQ was defined as the lowest concentration at which measured total error is less than the pre-defined total error. The results are summarized in the table below:

| Analyte | LoB (mmol/L) | LoD (mmol/L) | LoQ (mmol/L) |
|---|---|---|---|
| Na+ | 11 | 13 | 97 |
| K+ | 0.0 | 0.1 | 0.9 |
| Cl- | 5 | 7 | 38 |
| Ca++ | 0.00 | 0.02 | 0.08 |

The claimed measuring range of the assays is summarized in the tables below:

| Analyte | Claimed Measuring Range (mmol/L) |
|---|---|
| Na+ | 100 to 180 |
| K+ | 1.0 to 19.0 |
| Cl- | 40 to 158 |
| Ca++ | 0.11 to 4.25 |

*e. Analytical specificity:*

Interference studies were performed according to CLSI EP-7A guidance to determine the effects from potential interferents on the electrolyte assays. Various concentrations of interferents were spiked into two levels (low and high) of each analyte. Testing was performed in singlet per level using 3 GEM Premier 5000 analyzers. The sponsor ‘s definition of a non-significant interference for each analyte

was as follow:

±4 mmol/L for Na, ±7% for K, ±5% for Cl, and ±10% for Ca.

The highest concentration tested that shows non-significant interference are summarized below:

| Substance | Concentration | Tested analytes with no observed interference |
|---|---|---|
| Ammonium (Chloride) | 107 µmol/L | Sodium, Potassium, Calcium |
| Benzalkonium (Chloride) | 5 mg/L | Sodium, Potassium, Calcium |
| (Sodium) Bromide | 37.5 mmol/L | Potassium, Calcium |
| Calcium (Chloride) | 2.5 mmol/L | Sodium, Potassium |
| (Sodium) Citrate | 12 mmol/L | Potassium, Calcium, |
| Ethanol | 86.8 mmol/L | Sodium, Potassium, Calcium, Chloride |
| (Sodium) Fluoride | 105 µmol/L | Potassium, Calcium, Chloride |
| Heparin | 100,000 U/L | Sodium, Potassium, Calcium, Chloride |
| Ibuprofen | 2425 µmol/L | Sodium, Potassium, Calcium, Chloride |
| (Sodium) Iodide | 3 mmol/L | Potassium, Calcium |
| Ipratropium bromide | 0.08 mg/L | Sodium, Potassium, Calcium, Chloride |
| Lithium (Chloride) | 3.2 mmol/L | Sodium, Potassium, Calcium |
| Magnesium (Chloride) | 15 mmol/L | Sodium, Potassium |
| (Sodium) Oxalate | 500 mg/dL | Potassium, Calcium, Chloride |
| (Sodium) Perchlorate | 20 mg/dL | Potassium, Chloride, Calcium |
| pH (with HCl) | 6.8 | Sodium, Potassium, Calcium |
| (Sodium) Salicylate | 4.34 mmol/L | Potassium, Calcium, Chloride |
| Sodium (Chloride) | 180 mmol/L | Potassium, Calcium |
| (Sodium) Thiocyanate | 6880 µmol/L | Potassium, Calcium |
| Thiopental | 248 µmol/L | Sodium, Potassium, Calcium, Chloride |

| Substance | Concentration | Tested analytes with no observed interference |
|---|---|---|
| (Sodium) Thiosulfate | 20 mmol/L | Potassium, Calcium, Chloride |
| Triglycerides (as intralipids) | 4012 mg/dL | Sodium, Calcium, Chloride |

The sponsor lists the following substances that demonstrated interference with electrolyte results based on the initial screening test. Additional dose response study was performed to evaluate the concentration at which the interference substances started to cause significant interference. Results are summarized in the table below.

| Interfering Substance | Affected Analyte | Analyte Concentration | Interfering Concentration Tested | Bias Observed (Mean) | Lowest Interfering Concentration with Analyte Impact | Bias Observed at the Lowest Concentration |
|---|---|---|---|---|---|---|
| Bromide (Sodium) | Chloride | 90 mmol/L | 9.375 mmol/L | +31% | 1.346 mmol/L | +5% |
| | | 108 mmol/L | 9.375 mmol/L | +25% | 1.880 mmol/L | +5% |
| Citrate (Sodium) | Chloride | 88 mmol/L | 6.000 mmol/L | - 7% | 4.083 mmol/L | -5% |
| | | 111 mmol/L | 6.000 mmol/L | -5% | 5.344 mmol/L | -5% |
| Iodide (Sodium) | Chloride | 88 mmol/L | 0.750 mmol/L | +6% | 0.700 mmol/L | +5% |
| | | 106 mmol/L | 1.500 mmol/L | +9% | 0.810 mmol/L | +5% |
| Ionized Magnesium (Chloride) | Calcium | 1.02 mmol/L | 3.938 mmol/L | +13% | 3.128 mmol/L | +10% |
| | | 2.00 mmol/L | 7.875 mmo/L | +11% | 6.862 mmol/L | +10% |
| Thiocyanate (Sodium) | Chloride | 87 mmol/L | 1720 µmol/L | +31% | 388.3 µmol/L | +5% |
| | | 109 mmol/L | 1720 µmol/L | +27% | 407.5 µmol/L | +5% |
| Triglycerides (Intralipids) | Potassium | 3.2 mmol/L | 1003 mg/dL | +14% | 522 mg/dL | +7% |
| | | 5.1 mmol/L | 1003 mg/dL | +11% | 662 mg/dL | +7% |

The sponsor also listed the following limitations in their labeling:

| Condition | Result |
|---|---|
| Under-Heparinized Sample Due to Using Non-Heparinized Sampling Devices or Inadequate Mixing with Heparinized Devices. | Blood clot can form in the sensor chamber causing various sensor failures if sample is not properly heparinized. |
| Hemolysis | Hemolyzed samples may result in falsely elevated potassium levels. |
| Over-Heparinized Sample Due to under filling Heparinized Sampling Device or Transferring Heparinized Sample to a Second Heparinized Sampling Device | Over Heparinization can cause bias in Na+, iCa and Hct results. |

*f. Assay cut-off:*

Not Applicable

2. Comparison studies:

*a. Method comparison with predicate device:*

Method comparison studies were performed following CLSI EP9-A3 at three external representative point-of-care (POC) settings using <15% spiked samples to cover the claimed measuring ranges. The regression results for syringe samples from both arterial and venous blood samples are presented below:

| Syringe samples | | | | | |
|---|---|---|---|---|---|
| Analyte | N | Slope | Intercept | r | Sample Range |
| Na+ | 486 | 0.991 | 1.184 | 0.991 | 103 to 180 (mmol/L) |
| K+ | 491 | 1.000 | 0.100 | 0.998 | 1.0 to 15.7 (mmol/L) |
| Cl- | 485 | 1.000 | 1.000 | 0.990 | 40 to 157 (mmol/L) |
| Ca++ | 491 | 1.01 | 0.008 | 0.998 | 0.14 to 4.21 (mmol/L) |

Another method comparison study for capillary whole blood was performed at an external POC site in a hospital and an internal laboratory. Capillary whole blood specimens were collected via capillary puncture into 2 capillary tubes containing lithium heparin, and tested immediately on GEM4000 (predicate) and GEM5000 (new device). In addition, <20% of altered capillary samples were tested internally to cover the claimed measuring ranges. The study results are summarized below:

| Capillary Samples | | | | | |
|---|---|---|---|---|---|
| Analyte | N | Slope | Intercept | r | Sample Range |
| Na+ | 201 | 1.015 | -1.750 | 0.981 | 103-180 mmol/L |
| Ca++ | 205 | 1.050 | -0.016 | 0.998 | 0.14-4.25 mmol/L |

Results based on native capillary samples at Medical Decision Level (MDL) are shown below:

| Analyte | N | Range Min | Range Max | MDL | Bias at MDL | 95% CI of Bias at MDL |
|---|---|---|---|---|---|---|
| Na+ (mmol/L) | 171 | 124 | 143 | 115 | -3.6 | -7.2 to -0.0 |
| | | | | 135 | 0.4 | 0.0 to 0.8 |
| | | | | 150 | 3.4 | 0.8 to 5.9 |
| K+ (mmol/L) | 171 | 3.5 | 7.2 | 3.0 | 0.20 | 0.00 to 0.27 |
| | | | | 5.8 | 0.20 | -0.03 to 0.44 |
| | | | | 7.5 | 2.7% | -2.8% to 9.1% |

| Analyte | | Min | Max | | MDL | MDL |
|---|---|---|---|---|---|---|
| Cl- (mmol/L) | 171 | 91 | 117 | 90 | -3.3% | -8.0 to -2.2% |
| | | | | 112 | -2.7% | -2.9% to -1.8% |
| Ca++ (mmol/L) | 171 | 1.03 | 1.38 | 0.37 | -0.127 | -0.234 to 0.040 |
| | | | | 0.82 | -0.027 | -0.071 to 0.040 |
| | | | | 1.58 | 9.0% | 3.2% to 12.7% |

*b. Matrix comparison:*

Not applicable. Sponsor stated that only lithium heparin anticoagulant whole blood is the acceptable sample type to be used for their device.

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 of Na, K, Cl and Ca are cited from literature:
Sodium: 136 – 145 mmol/L
Potassium: 3.5 – 5.1 mmol/L
Chloride: 98 – 107 mmol/L
Calcium: 1.16 – 1.32 mmol/L (venous)

Burtis, Carl and David Bruns, Tietz Textbook of Clinical Chemistry and Molecular Diagnostics, Elsevier Saunders, 7th edition, 2015, pp 952-982

**N. Instrument Name:**

GEM Premier 5000

## O. System Descriptions:

1. Modes of Operation:

   Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

   Yes ___ X _____ or No _____

   Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?

   Yes _____ or No ___X_____

2. Software:

   The software for the GEM Premier 5000 is determined to have a moderate level of concern.

   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 entry or barcode identification

4. Specimen Sampling and Handling:

   The following types of sampling devices are acceptable to GEM Premier 5000:

   • syringe (lithium heparin only) for arterial, venous, and mixed-venous
   • capillary tube (lithium heparin only)
   • opened ampoules
   • uncapped collection tubes using the syringe or ampoule sampling position

5. Calibration:

   The iQM2 technology in GEM Premier 5000 provides active process control that monitors and maintains the stability of calibration during GEM PAK use-life. The iQM2 technology monitors and controls the GEM PAK using 5 PC Solutions analyzed at different intervals and after every patient sample. Difference between the observed values for PC Solutions and the target values are compared to control limits (drift limits).

   - When the observed PC Solution A, B and C values are within established control

limits, the active process control technology re-establishes the target value for PC Solutions A, B or C to maintain the stability of the measurement process.
- Any PC Solution A, B and C value that exceeds the established statistical control limits for an analyte leads to further assessment via PR (Pattern Recognition) software which may include corrective actions based upon pattern detection algorithms.
- iQM2 control mechanism is predicated on the stability of the PC Solutions, which are monitored via the iQM2 PC Stability Check.

6. Quality Control:

The sponsor states on their labeling that "Intelligent Quality Management 2 (iQM2) is used as the quality control and assessment system for the GEM Premier 5000 system. iQM2 is an active quality process control program designed to provide continuous monitoring of the analytical process before, during, and after sample measurement 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 (QC). Facilities should follow local, state and federal regulatory guidelines to ensure that a total quality management system is followed."

**P. Other Supportive Instrument Performance Characteristics Data Not Covered In the "Performance Characteristics" Section above:**

Not Applicable

**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.