DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

December 14, 2016

INSTRUMENTATION LABORATORY CO.
CAROL MARBLE
REGULATORY AFFAIRS DIRECTOR
180 HARTWELL ROAD
BEDFORD MA 01730

Re: K160225
Trade/Device Name: GEM Premier 5000 (Measured Parameters: Sodium, Potassium, Chloride, Ionized Calcium), GEM System Evaluator, GEM Hematocrit Evaluator, GEM CVP 5 tBili
Regulation Number: 21 CFR 862.1665
Regulation Name: Sodium Test System
Regulatory Class: II
Product Code: JGS, CEM, CGZ, JFP, JJY, JJE, GLK
Dated: December 6, 2016
Received: December 7, 2016

Dear Ms. Marble:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the

electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Courtney H. Lias -S

Courtney H. Lias, PhD
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K160225

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

Indications for Use *(Describe)*

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 and GEM 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.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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Instrumentation Laboratory
A Werfen Company

K160225

510(k) Summary

This 510(k) Summary of Safety and Effectiveness is being submitted in accordance with the requirements of the Safe Medical Device Act of 1990 and 21 CFR 807.92.

Submitter's Information	Instrumentation Laboratory (IL) Co. 180 Hartwell Road Bedford, MA 01730, USA

Contact Person	Carol Marble, Regulatory Affairs Director Phone: 781-861-4467 Fax: 781-861-4207 Email: cmarble@ilww.com

Preparation Date	December 6, 2016

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

Predicate Devices	GEM Premier 4000	K133407
	GEM CVP 5 tBili	K112995
	GEM System Evaluator	K093623
	GEM Hematocrit Evaluator	K093623

Regulatory Information					
System	**Regulation Section**	**Regulatory Description**	**Class**	**Product Code**	**Panel**
Instrument	862.2160	Discrete photometric chemistry analyzer for clinical use	I	JJE	75
Sodium	862.1665	Sodium test system	II	JGS	75
Potassium	862.1600	Potassium test system	II	CEM	
Chloride	862.1170	Chloride test system	II	CGZ	
Ionized Calcium	862.1145	Calcium test system	II	JFP	
Controls (Internal PCS D and E)	862.1660	Quality control material (assayed and unassayed)	I (Reserved)	JJY	75
	864.8625	Hematocrit Control	II	GLK	81

GEM CVP 5 tBili				
Regulation Section	**Regulatory Description**	**Class**	**Product Code**	**Panel**
862.1660	Quality control material (assayed and unassayed)	I (Reserved)	JJY	75

GEM System Evaluator				
Regulation Section	**Regulatory Description**	**Class**	**Product Code**	**Panel**
862.1660	Quality control material (assayed and unassayed)	I (Reserved)	JJY	75

GEM Hematocrit Evaluator				
Regulation Section	**Regulatory Description**	**Class**	**Product Code**	**Panel**
864.8625	Hematocrit Control	II	GLK	81

Device Description	
The GEM Premier 5000 system provides health care professionals in central laboratory or point-of-care clinical settings with fast, accurate, 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.	
Key Components	**Description**
Analyzer	Employs a unique color touch screen and a simple set of menus and buttons for user interaction. The analyzer guides operators through the sampling process with simple, clear messages and prompts.
GEM Premier 5000 PAK (disposable, multi-use GEM PAK)	Houses all required components necessary to operate the instrument once the cartridge is validated. These components include the sensors, CO-Ox/tBili optical cell, Process Control (PC) Solutions, sampler, pump tubing, distribution valve and waste bag. The GEM PAK has flexible menus and test volume options to assist facilities in maximizing efficiency. NOTE: The EEPROM on the GEM PAK includes all solution values and controls the analyte menu and number of tests. Step 1: After inserting the GEM PAK, the instrument will perform an automated PAK warm-up during which the sensors are hydrated and a variety of checks occur, all of which take about 40 minutes. During warm-up, the instrument requires no user intervention**.** Step 2: After GEM PAK warmup, Auto PAK Validation (APV) process is automatically completed: two completely independent solutions (PC Solution D and E) that are traceable to NIST standards, CLSI procedures or internal standards, containing two levels of concentration for each analyte, are run by the analyzer to validate the integrity of the PC Solutions and the overall performance of the analytical system. NOTE: For total bilirubin, CVP 5 tBili (Calibration Valuation Product) must be run prior to performing tBili samples. Step 3: After successful performance of APV, iQM2 manages the quality control process, replacing external quality controls.
Intelligent Quality Management 2 (iQM2)	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. iQM2 is a statistical process control system that performs 5 types of continuous, quality checks to monitor the performance of the GEM PAK, sensors, CO-Ox, and reagents. These checks include System, Sensor, IntraSpect, Pattern Recognition and Stability Checks.

Indications for Use / Intended Use	
GEM Premier 5000 *with* Intelligent Quality Management 2 (iQM2)	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 CVP 5 tBili	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 System Evaluator	GEM System Evaluator is a three-level assayed quality control material for evaluating performance characteristics of pH, pCO_2, pO_2, Electrolytes, Metabolites, Total Bilirubin (tBili) and CO-Oximetry on the GEM Premier 4000 and GEM Premier 5000 analyzers.
GEM Hematocrit Evaluator	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.

Special Conditions for Use Statement

- For prescription use only.
- For clinical laboratory and point-of-care use.

Substantial Equivalency		
The GEM Premier 5000 system is substantially equivalent in function and intended use to the following predicate device for Na^+, K^+, Cl^- and Ca^{++}:		
Item	**Predicate Device**	**New Device**
Trade Name	GEM Premier 4000	GEM Premier 5000
510(k) No.	K133407	K160225
Manufacturer	Instrumentation Laboratory Co.	Instrumentation Laboratory Co.
Indications 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, pCO_2, pO_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.	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.

Substantial Equivalency (Cont.)				
Item	**Predicate Device**		**New Device**	
Trade Names	GEM Premier 4000	K133407	GEM Premier 5000	K160225
Intended User	Central Laboratory and Point-of-Care		Same	
Sample Type	Heparinized whole blood		Na^+, Ca^{++}	Arterial, venous or capillary heparinized whole blood
			K^+, Cl^-	Arterial or venous heparinized whole blood
Electrolyte Measurement	Potentiometry		Same	
Sample Introduction	Aspiration		Same	
PAK Shelf-Life Stability	Up to 180 days		Same	
PAK Storage Temperature	15-25°C		Same	
System Operating Temperature	12-32°C		Same	
Operating System Software	Linux-based		Same	
Calibration	2-point calibration		Same	
QC Material	CVP 1 and 2		PC Solution D and E (PAK Internal)	
	CVP 3 and 4		PC Solution D and E (PAK Internal)	
	CVP 5 tBili		Same; No Formulation Change GEM Premier 5000 claims added	
	GEM System Evaluator			
	GEM Hematocrit Evaluator			

<table>
<tr><th colspan="5">Substantial Equivalency (Cont.)</th></tr>
<tr><th>Item</th><th colspan="2">Predicate Device</th><th colspan="2">New Device</th></tr>
<tr><td>Trade Name</td><td colspan="2">GEM Premier 4000 K133407</td><td colspan="2">GEM Premier 5000 K160225</td></tr>
<tr><td>Instrument Dimensions</td><td colspan="2">GEM Premier 4000 Instrument:
• Height: 18 inches
• Width: 12 inches
• Depth: 15 inches
• Weight: 44 pounds</td><td colspan="2">GEM Premier 5000 Instrument:
• Height: 18.6 inches
• Width: 13.0 inches
• Depth: 16.4 inches
• Weight: 45.4 pounds</td></tr>
<tr><td>Cartridge (PAK) Dimensions</td><td colspan="2">GEM Premier 4000 Cartridge (PAK):
• Height: 6.75 inches
• Width: 10 inches
• Depth: 8 inches
• Weight: 8 pounds</td><td colspan="2">GEM Premier 5000 Cartridge (PAK):
• Height: 6.75 inches
• Width: 10 inches
• Depth: 8 inches
• Weight: 8.1 pounds</td></tr>
<tr><td rowspan="5">Reportable Range</td><td>Analyte</td><td>GEM Premier 4000</td><td colspan="2">GEM Premier 5000</td></tr>
<tr><td>Na^+</td><td>100 to 180 mmol/L</td><td colspan="2">100 to 180 mmol/L</td></tr>
<tr><td>K^+</td><td>0.2 to 19.0 mmol/L</td><td colspan="2">1.0 to 19.0 mmol/L</td></tr>
<tr><td>Cl^-</td><td>40 to 158 mmol/L</td><td colspan="2">40 to 158 mmol/L</td></tr>
<tr><td>Ca^{++}</td><td>0.10 to 4.25 mmol/L</td><td colspan="2">0.11 to 4.25 mmol/L</td></tr>
</table>

Substantial Equivalency (Cont.)		
NOTE: The following table compares iQM on the GEM Premier 4000 to iQM2 on the GEM Premier 5000.		
Item	**Predicate Device**	**New Device**
Trade Names	iQM (Intelligent Quality Management)	iQM2 (Intelligent Quality Management 2)
Instrument	GEM Premier 4000	GEM Premier 5000
510(k) No.	K133407	K160225
Quality Control Principle	Active quality process control program using five levels of external Calibration Valuation Product (CVP), four internal Process Control Solutions (PCSs) and Pattern Recognition (PR) software, all of which are designed to provide immediate error detection and automatic remedial action, replacing the use of traditional external quality controls.	Active quality process control program using a combination of internal Auto PAK Validation (APV) and one level of external Calibration Valuation Product (CVP 5), five internal Process Control Solutions (PCSs) Pattern Recognition (PR) software and IntraSpect sample integrity quality checks, all of which are designed to provide immediate error detection and automatic remedial action, replacing the use of traditional external quality controls.
Error Detection Scheme	Multi-level checks for detecting cartridge errors. • System checks • Sensor/CO-Ox checks • Pattern Recognition (PR checks) • Process Control Solution (PCS) Stability	Same except addition of IntraSpect. IntraSpect provides continuous sample integrity quality checks that detect abnormal sensor response slope or absorbance residual error during the measurement process.
Error Mitigation	Automatic error handling: • Performing special rinse cycle after detecting micro-clots and verifying the cartridge function after clot removal. • Permanently disabling failed sensor if its functionality could not be recovered. • Rejecting cartridge for process stability failure. • Alerting the user if interferences are detected in a sample. • Automatically documenting the failure and action taken.	Same except addition of IntraSpect, which flags results if an abnormal sensor response slope or absorbance residual error is detected.
Documentation	Automatic documentation: • Process Control Solutions delta charts. • Error reporting and corrective action report. • GEM CVP report.	Same; no change

Substantial Equivalency (Cont.)		
NOTE: The following table compares internal Process Control (PC) Solutions in the GEM Premier 4000 PAK (cartridge) to internal Process Control (PC) Solutions in the GEM Premier 5000 PAK (cartridge).		
Item	**Predicate Device**	**New Device**
Trade Names	Process Control (PC) Solutions	Process Control (PC) Solutions
Instrument	GEM Premier 4000	GEM Premier 5000
510(k) No.	K133407	K160225
PC Solutions	• **PC Solution B** is the primary Process Control Solution measured at a minimum of every half hour or after every sample. Furthermore, Solution B is monitored every 30 seconds while residing in the sensor card between measurements. Further, PC Solution B is used as a reference blank for CO-Oximetry. • **PC Solution A** is measured at a minimum of every 4 hours. All sensor slope values are also measured and checked. Slope, which is an indicator of sensor sensitivity and drift, must be within allowable limits. PC Solution A also contains dyes that are used for checking functionality of the optical cell and the CO-Oximetry. • **PC Solution C** is measured at a minimum of once every 24 hours. PC Solution C is primarily used for measuring low-level oxygen; however, PC Solution C is also used to provide an additional measurement of pH, pCO_2 and K^+ sensor functionality. • **PC Solution D** is measured every 12 hours. PC Solution D provides additional measurement for all analytes including CO-Oximetry. Reference values for analytes in PC Solution D are established within the first 3 days after cartridge insertion by averaging multiple measurements of the D solution. The D sensor check starts once the reference values are established. • **<u>No</u> PC Solution E** on the GEM Premier 4000.	• **PC Solution B** – Same • **PC Solution A** – Same • **PC Solution C** – Same • **PC Solution D** – is measured every 12 hours. PC Solution D provides additional measurement for all analytes including CO-Oximetry. Reference values for analytes in PC Solution D are assigned at time of manufacturing. The D sensor check starts after the successful completion of Auto PAK Validation (APV). • ***New* PC Solution E** - is measured every 12 hours. PC Solution E provides additional measurement for all analytes including CO-Oximetry. Reference values for analytes in PC Solution E are assigned at time of manufacturing. The E sensor check starts after the successful completion of Auto PAK Validation (APV). **NOTE:** The GEM Premier 5000 PAKs include a new PC Solution E. The new system uses PC Solution D and PC Solution E to replace the necessity to run CVP 1, 2, 3 and 4 after cartridge (PAK) warm-up. Only CVP 5 tBili is required if running total bilirubin. See the comparison of PC Solution D and PC Solution E to CVP 1-4 on the next page.

Substantial Equivalency (Cont.)		
Item	**Predicate**	**New Device**
Trade Names	CVP 5 tBili	Same
Value Assigned	GEM Premier 4000	GEM Premier 4000 and GEM Premier 5000
510(k) No.	K112995	K160225
Indications for Use ***Differences in bold/italic***	GEM CVP 5 tBili is an external Calibration Valuation Product used to complete the calibration process of the GEM Premier 4000 analyzer prior to use with patient samples for total bilirubin (tBili) testing.	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.
Formulation	Purified human hemoglobin, stabilizers and biocide in a physiologically buffered solution.	Same
Storage	Store at 2-8°C	Same

Item	**Predicate**	**New Device**
Trade Names	GEM System Evaluator	Same
Value Assigned	GEM Premier 4000	GEM Premier 4000 and GEM Premier 5000
510(k) No.	K093623	K160225
Manufacturer	Instrumentation Laboratory Co.	Same
Indications for Use ***Differences in bold/italic***	GEM System Evaluator is a three-level assayed quality control material for evaluating performance characteristics of pH, pCO_2, pO_2, Electrolytes, Metabolites, Total Bilirubin (tBili) and CO-Oximetry on the GEM Premier 4000 analyzer.	GEM System Evaluator is a three-level assayed quality control material for evaluating performance characteristics of pH, pCO_2, pO_2, Electrolytes, Metabolites, Total Bilirubin (tBili) and CO-Oximetry on the GEM Premier 4000 ***and GEM Premier 5000 analyzers.***
Formulation	Aqueous buffered bicarbonate solution.	Same
Storage	• 2-8°C until expiration • 15-25°C for 4 months	Same

Item	**Predicate**	**New Device**
Trade Names	GEM Hematocrit Evaluator	Same
Value Assigned	GEM Premier 4000	GEM Premier 4000 and GEM Premier 5000
510(k) No.	K093623	Pending
Manufacturer	Instrumentation Laboratory Co.	Same
Indications for Use ***Differences in bold/italic***	GEM Hematocrit Evaluator is a three-level assayed quality control material intended for evaluating performance characteristics of hematocrit on the GEM Premier 4000 analyzer.	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.***
Formulation	Aqueous buffered bicarbonate solution.	Same
Storage	15-25°C until expiration	Same

Performance Summary

Internal Precision Study – Aqueous Controls

In accordance with CLSI EP05-A3, an internal 20-day precision study was performed on the GEM Premier 5000, with GEM System Evaluator. Each of the control levels was run on three (3) GEM Premier 5000 analyzers for twenty (20) days, with two (2) runs per day and one (1) replicate measured per run per level (n=120). All results were within specification.

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

Performance Summary (Cont.)

Internal Precision Study – GEM PAK (Cartridge) Process Control Solutions D and E

In accordance with CLSI EP05-A3, an internal 20-day precision study was performed with the GEM PAK (cartridge) Process Control Solutions (PCS) D and E run on three (3) GEM Premier 5000 analyzers for twenty (20) days, with two (2) runs per day and one (1) replicate measured per run per level (N=120 per analyte/per level). All results were within specification.

Material	Analyte	Mean	N	Within Analyzer SD	Within Analyzer %CV
PCS D	Na^+ (mmol/L)	167	120	0.4	0.3%
PCS E		128	120	0.2	0.2%
PCS D	K^+ (mmol/L)	7.3	120	0.02	0.2%
PCS E		4.5	120	0.01	0.3%
PCS D	Cl^- (mmol/L)	144	120	0.7	0.5%
PCS E		102	120	0.3	0.3%
PCS D	Ca^{++} (mmol/L)	1.21	120	0.004	0.3%
PCS E		0.56	120	0.007	1.3%

Performance Summary (Cont.)

Internal Precision Study – Whole Blood

In accordance with CLSI EP05-A3, an internal precision study was performed using five (5) different concentrations of whole blood per analyte, each run on three (3) GEM Premier 5000 analyzers per sample mode for five (5) days, with one (1) run per day and eight (8) replicates measured per run per level (N=120 per analyte/per sample mode). All results were within specification.

Sample Modes and Volumes:

- Normal Mode 150 µL
- Micro Mode 65 µL

NOTE: Capillary not claimed for K^+ or Cl^- on the GEM Premier 5000.

Analyte	Mode	Level	Mean	N	Within Run SD	Within Run %CV	Total SD	Total %CV
Na^+ (mmol/L)	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%
K^+ (mmol/L)	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	17.0	120	0.32	1.9%	0.51	3.0%

Performance Summary (Cont.)

Internal Precision Study – Whole Blood (Cont.)

Analyte	Mode	Level	Mean	N	Within Run SD	Within Run %CV	Total SD	Total %CV
Cl^- (mmol/L)	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	0.9%
		5	167	120	1.4	0.9%	2.3	1.4%
Ca^{++} (mmol/L)	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	0.020	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	4.20	120	0.057	1.3%	0.069	1.6%

Performance Summary (Cont.)

Reproducibility Study with Aqueous Controls – Point-of-Care (POC) Setting

In accordance with CLSI EP05-A3, a reproducibility study was performed at three (3) external clinical point-of-care (POC) sites. The studies were run by a total of nine (9) different operators on three (3) different GEM Premier 5000 instruments, using a single lot of GEM Premier 5000 PAKs (cartridges). Each site used the same lots of GEM System Evaluator (GSE), running each control level in triplicate, twice a day for 5 days, for a total of 30 replicates per level (N=90 pooled). All results at all sites were within specification.

Pooled Multi-Site POC Data																
Analyte	**Material/ Level**	**N**	**Insert Range**	**Target**	**SD/CV Spec**	**Mean**	**Repeatability**		**Between-Run**		**Between-Day**		**Between-Site**		**Reproducibility**	
							SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Na^+ (mmol/L)	GSE 1	90	119-129	124	2	125	0.4	0.3%	0.0	0.0%	0.2	0.2%	0.2	0.1%	0.5	0.4%
	GSE 2	90	136-146	141	2	141	0.3	0.2%	0.1	0.1%	0.3	0.2%	0.3	0.2%	0.5	0.4%
	GSE 3	90	149-161	155	2	155	0.3	0.2%	0.0	0.0%	0.2	0.1%	0.1	0.1%	0.4	0.2%
K^+ (mmol/L)	GSE 1	90	2.1-2.7	2.4	0.25	2.4	0.00	0.0%	0.00	0.0%	0.00	0.0%	0.00	0.0%	0.00	0.0%
	GSE 2	90	4.2-5.0	4.6	0.25	4.7	0.03	0.6%	0.02	0.5%	0.00	0.0%	0.02	0.4%	0.04	0.8%
	GSE 3	90	7.0-8.0	7.5	3.5%	7.7	0.02	0.3%	0.01	0.2%	0.01	0.1%	0.01	0.1%	0.03	0.4%
Cl^- (mmol/L)	GSE 1	90	80-90	85	2.5%	85	0.3	0.4%	0.1	0.1%	0.2	0.2%	0.1	0.1%	0.4	0.4%
	GSE 2	90	102-112	107	2.5%	108	0.2	0.2%	0.0	0.0%	0.2	0.2%	0.0	0.0%	0.3	0.3%
	GSE 3	90	136-146	141	2.5%	142	0.4	0.3%	0.3	0.2%	0.1	0.1%	0.2	0.2%	0.6	0.4%
Ca^{++} (mmol/L)	GSE 1	90	1.45-1.65	1.55	5%	1.58	0.007	0.4%	0.004	0.3%	0.002	0.1%	0.002	0.1%	0.009	0.6%
	GSE 2	90	1.06-1.24	1.15	5%	1.16	0.005	0.4%	0.001	0.1%	0.003	0.3%	0.003	0.3%	0.007	0.6%
	GSE 3	90	0.56-0.72	0.64	0.05	0.64	0.003	0.5%	0.000	0.0%	0.003	0.5%	0.003	0.5%	0.005	0.8%

Performance Summary (Cont.)

External Precision – Whole Blood

To evaluate whole blood precision on the GEM Premier 5000 system in the central laboratory and point-of-care (POC) settings, whole blood patient samples were tested at 2 external central laboratories and 1 internal Customer Simulation Laboratory (CSL), 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^{++}. 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:

NOTE: Capillary not claimed for K^+ or Cl^- on the GEM Premier 5000.

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
	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

Performance Summary (Cont.)

External Precision – Whole Blood (Cont.)

Analyte	Mode	Site	N	Mean	Within Sample SD or CV%
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%

Performance Summary (Cont.)

LoB, LoD and LoQ

In accordance with CLSI EP17-A2, LoB, LoD and LoQ were established for Na^+, K^+, Ca^{++} and Cl^-, using three (3) lots of GEM Premier 5000 PAKs (cartridges).

Following are the combined data results for LoB, LoD and LoQ:

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

Linearity

In accordance with CLSI EP06-A, nine (9) or ten (10) levels per analyte were prepared by spiking or diluting whole blood to challenge the claimed reportable range for each parameter. Each blood level was analyzed in triplicate on three (3) GEM Premier 5000 test analyzers and results compared to reference analyzers.

Combined data from limit of quantitation (LOQ) and linearity were used to support the lower limits of the claimed reportable ranges.

Analyte	# of Levels	N per Level	Slope	Intercept	R^2	Tested Range	Reportable Range
Na^+ (mmol/L)	9	9	0.972	5.377	0.999	85 to 214	100 to 180
K^+ (mmol/L)	9	9	0.993	-0.072	0.999	0.7 to 21.9	1.0 to 19.0
Cl^- (mmol/L)	9	9	0.964	2.805	1.000	35 to 189	40 to 158
Ca^{++} (mmol/L)	10	9	0.999	0.011	0.999	0.10 to 5.05	0.11 to 4.25

Performance Summary (Cont.)

Analytical Specificity

In accordance with EP07-A2, an interference study was conducted on the GEM Premier 5000.

The table below lists substances that were screen tested with no observed interference on electrolyte results:

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
(Sodium) Thiosulfate	20 mmol/L	Potassium, Calcium, Chloride
Triglycerides (Intralipids)	2% or 4012 mg/dL	Sodium, Calcium, Chloride

Performance Summary (Cont.)

Analytical Specificity (Cont.)

The table below lists substances that demonstrated interference with electrolyte results and the concentration of the interfering substance, as well as the bias observed and its direction (positive / negative):

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%

Performance Summary (Cont.)

Internal Method Comparison

In accordance with EP09-A3, an internal method comparison study was conducted using clinical samples to compare the performance of the GEM Premier 5000 versus the GEM Premier 4000:

Samples were altered as needed to cover the medical decision levels. All parameter levels passed specification.

NOTE: Capillary not claimed for K^+ or Cl^- on the GEM Premier 5000.

Analyte	N	Slope	Intercept	R^2	Medical Decision Level	Bias at Medical Decision Level
Na^+ (mmol/L)	373	1.021	-2.577	0.995	115	-0.2
					135	0.2
					150	0.5
K^+ (mmol/L)	373	1.034	-0.066	0.999	3.0	0.04
					5.8	0.13
					7.5	2.5%
Cl^- (mmol/L)	373	1.000	0.500	0.998	90	0.6%
					112	0.4%
Ca^{++} (mmol/L)	373	1.031	-0.033	0.999	0.37	-0.021
					0.82	-0.007
					1.58	1.0%

Performance Summary (Cont.)

Whole Blood Performance at Medical Decision Levels

The data from the internal method comparison and precision studies were combined to assess the performance at medical decision levels.

Total Error was computed based on the following equation and the results were compared to the GEM Premier 5000 Total Error Specifications:

Total Error Observed = Bias + 2 * SD (or %CV)

Note: Previously shown bias and precision data were used in Total Error computations below.

Analyte	Medical Decision Level	Absolute Value of Bias at Medical Decision Level	2*(SD or %CV)	Total Error Observed Bias + 2*(SD or %CV)
Na^+ (mmol/L)	115	0.2	0.8	1.0
	135	0.2	0.7	0.9
	150	0.5	1.1	1.6
K^+ (mmol/L)	3.0	0.04	0.10	0.14
	5.8	0.13	0.10	0.23
	7.5	2.5%	3.7%	6.2%
Cl^- (mmol/L)	90	0.6%	0.8%	1.4%
	112	0.4%	1.2%	1.6%
Ca^{++} (mmol/L)	0.37	0.021	0.012	0.033
	0.82	0.007	0.010	0.017
	1.58	1.0%	2.6%	3.6%

Performance Summary (Cont.)

Reference Ranges

Analyte	Reference Range	Unit
Na^+	136 to 145	mmol/L
Na^+	136 to 145	mEq/L
K^+	3.5 to 5.1	mmol/L
K^+	3.5 to 5.1	mEq/L
Ca^{++}	1.15 to 1.33	mmol/L
Ca^{++}	2.30 to 2.66	mEq/L
Ca^{++}	4.60 to 5.32	mg/dL
Ca^{++}	1.16 to 1.32 (venous)	mmol/L
Ca^{++}	4.64 to 5.28 (venous)	mEq/L
Cl^-	98 to 107	mmol/L
Cl^-	98 to 107	mEq/L
Anion Gap	10 to 20 $(Na^+ + K^+) - (Cl^- + HCO_3^-)$ 10 to 20 $(Na^+ + K^+) - (Cl^- + HCO_3^-)$	mEq/L mmol/L

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

Performance Summary (Cont.)

Clinical Testing

In accordance with EP09-A3, a method comparison study was conducted on the GEM Premier 5000 compared to the predicate device, the GEM Premier 4000, in the point-of-care (POC) setting using heparinized whole blood patient samples from the intended use population.

- Study Design:
  - Three (3) external point-of-care (POC) sites.
  - One (1) internal Customer Simulation Laboratory (CSL) at IL, where three (3) intended POC users were brought on site to run the samples, allowing spiking to cover the reportable ranges.

The pooled results from the POC sites and the IL internal Customer Simulation Laboratory (CSL) for the Normal Mode (with samples collected in syringes) are presented below.

Pooled Point-of-Care Site and CSL Data - Normal Mode (with Syringe Samples)					
Analyte	**N**	**Slope**	**Intercept**	**r**	**Sample Range**
Na^+ (mmol/L)	486	0.991	1.184	0.991	103 to 180
K^+ (mmol/L)	491	1.000	0.100	0.998	1.0 to 15.7
Cl^- (mmol/L)	485	1.000	1.000	0.990	40 to 157
Ca^{++} (mmol/L)	491	1.010	0.008	0.998	0.14 to 4.21

To support capillary claims, finger-stick samples were collected at an external POC site (N=65 native samples) and the IL internal Customer Simulation Laboratory (CSL) (N=106 native samples) with POC operators. The observed total error at the medical decision levels is shown below:

NOTE: Capillary not claimed for K^+ or Cl^- on the GEM Premier 5000.

Pooled Point-of-Care Site and CSL Data with Native Capillary Samples Only							
Analyte	**N**	**Range Min**	**Range Max**	**MDL**	**Bias at MDL**	**95% CI of Bias at MDL**	**TEa**
Na^+ (mmol/L)	171	124	143	115.0	-3.6	-7.2 to -0.0	± 4.0
				135	0.4	0.0 to 0.8	± 5.0
				150	3.4	0.8 to 5.9	± 5.0
Ca^{++} (mmol/L)	171	1.03	1.38	0.37	-0.127	-0.234 to 0.040	± 0.10
				0.82	-0.027	-0.071 to 0.040	± 0.10
				1.58	9.0%	3.2% to 12.7%	± 10%

Performance Summary (Cont.)

Clinical Testing (Cont.)

In addition, the data from the native capillary samples (finger-stick samples) previously presented were pooled with contrived capillary samples prepared internally. The regression analysis is shown below:

NOTE: Capillary not claimed for K^+ or Cl^- on the GEM Premier 5000.

Pooled Point-of-Care Site and CSL Data with Additional Contrived Capillary Results					
Analyte	**N**	**Slope**	**Intercept**	**r**	**Sample Range**
Na^+ (mmol/L)	201	1.015	-1.750	0.981	103 to 180
Ca^{++} (mmol/L)	205	1.050	-0.016	0.998	0.14 to 4.25

Conclusion	The technological and functional characteristics of the new GEM Premier 5000 as described above are substantially equivalent to that of the predicate device (GEM Premier 4000) for sodium, potassium, chloride and ionized calcium. The analytical and clinical study results demonstrate that the GEM Premier 5000 is safe and effective for its intended purpose and equivalent in performance to the predicate device.