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: K160402
Trade/Device Name: GEM Premier 5000 (Measured Parameters: Glucose, Lactate and Total Bilirubin)
Regulation Number: 21 CFR 862.1345
Regulation Name: Glucose test system
Regulatory Class: II
Product Code: CGA, MQM, KHP
Dated: December 8, 2016
Received: December 9, 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, Ph.D.
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)*
K160402

Device Name
GEM Premier 5000 (Measured Parameters: Glucose, Lactate, Total Bilirubin)

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 glucose, lactate and total bilirubin from venous, arterial and capillary heparinized whole blood. These parameters aid in the diagnosis of a patient's metabolite balance.

Glucose (Glu) measurement is used in the diagnosis, monitoring and treatment of carbohydrate metabolism disturbances including diabetes mellitus, neonatal hypoglycemia, idiopathic hypoglycemia, and pancreatic islet cell carcinoma.

Lactate (Lac) measurement is used:
• to evaluate the acid-base status of patients suspected of having lactic acidosis;
• to monitor tissue hypoxia and strenuous physical exertion;
• in the diagnosis of hyperlactatemia.

Total bilirubin measurement is used to aid in assessing the risk of kernicterus and hyperbilirubinemia in neonates.

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

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 8, 2016

Device Trade Name	GEM Premier 5000 (Measured Parameters: Glucose, Lactate, Total Bilirubin)

Predicate Devices	GEM Premier 4000	K133407	Glucose and Lactate
	ABL 837	K142898	Total Bilirubin

Regulatory Information					
GEM Premier 5000					
Analyte	**Regulation Section**	**Regulatory Description**	**Class**	**Product Code**	**Panel**
Glucose	862.1345	Glucose test system	II	CGA	75
Lactate	862.1450	Lactic acid test system	I*	KHP	
Total Bilirubin	862.1113	Bilirubin (total and unbound) in the neonate test system	I (Reserved)	MQM	

* Meets limitations of exemptions per 21 CFR 862.9(c)(9)

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 glucose, lactate and total bilirubin from venous, arterial and capillary 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	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 glucose, lactate and total bilirubin from venous, arterial and capillary heparinized whole blood. These parameters aid in the diagnosis of a patient's metabolite balance. Glucose (Glu) measurement is used in the diagnosis, monitoring and treatment of carbohydrate metabolism disturbances including diabetes mellitus, neonatal hypoglycemia, idiopathic hypoglycemia, and pancreatic islet cell carcinoma. Lactate (Lac) measurement is used: • to evaluate the acid-base status of patients suspected of having lactic acidosis; • to monitor tissue hypoxia and strenuous physical exertion; • in the diagnosis of hyperlactatemia. Total bilirubin measurement is used to aid in assessing the risk of kernicterus and hyperbilirubinemia in neonates.

Special Conditions for Use Statement

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

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<table>
<tr><th colspan="4">Substantial Equivalency</th></tr>
<tr><td colspan="4">The GEM Premier 5000 system is substantially equivalent in function and intended use to the following predicate devices:
• Predicate Device No. 1: GEM Premier 4000 for glucose and lactate.
• Predicate Device No. 2: ABL 837 for total bilirubin.</td></tr>
<tr><th>Item</th><th colspan="2">Predicate Devices</th><th colspan="2">New Device</th></tr>
<tr><td rowspan="2">Trade Names</td><td>GEM Premier 4000</td><td>K133407</td><td rowspan="2">GEM Premier 5000</td><td rowspan="2">K160402</td></tr>
<tr><td>ABL 837</td><td>K142898</td></tr>
<tr><td rowspan="2">Manufacturers</td><td>GEM Premier 4000</td><td>Instrumentation Laboratory Co.</td><td colspan="2" rowspan="2">Instrumentation Laboratory Co.</td></tr>
<tr><td>ABL 837</td><td>Radiometer Medical ApS</td></tr>
<tr><td>Indications for Use</td><td colspan="2">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.</td><td colspan="2">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 glucose, lactate and total bilirubin from venous, arterial and capillary heparinized whole blood. These parameters aid in the diagnosis of a patient’s metabolite balance.
Glucose (Glu) measurement is used in the diagnosis, monitoring and treatment of carbohydrate metabolism disturbances including diabetes mellitus, neonatal hypoglycemia, idiopathic hypoglycemia, and pancreatic islet cell carcinoma.
Lactate (Lac) measurement is used:
• to evaluate the acid-base status of patients suspected of having lactic acidosis;
• to monitor tissue hypoxia and strenuous physical exertion;
• in the diagnosis of hyperlactatemia.
Total bilirubin measurement is used to aid in assessing the risk of kernicterus and hyperbilirubinemia in neonates.</td></tr>
</table>

Substantial Equivalency (Cont.)				
NOTE: The comparison on this page is to the predicate device, the GEM Premier 4000, ***except*** where noted to the predicate device for Total Bilirubin (tBili), ABL 837.				
Item	**Predicate Devices**		**New Device**	
Trade Names	GEM Premier 4000 (All Analytes ***except*** tBili)	K133407	GEM Premier 5000	K160402
	ABL 837 Total Bilirubin (tBili)	K142898		
Intended User	Central Laboratory and Point-of-Care		Same	
Sample Type ***(Glucose and Lactate)***	Heparinized whole blood		Venous, arterial and capillary heparinized whole blood	
Sample Type ***(tBili on ABL 837)***	Heparinized whole blood		Venous, arterial and capillary heparinized whole blood	
	Heparinized plasma			
Intended Population ***(tBili on ABL 837)***	Total Bilirubin for adults and neonates		Total Bilirubin for neonates only.	
Metabolite Measurement	Amperometry: Glucose and Lactate		Same	
Total Bilirubin ***(vs. ABL 837)***	Spectrophotometry		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	
External 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 System Evaluator		GEM Premier 5000 claims added	

<table>
<tr><th colspan="5">Substantial Equivalency (Cont.)</th></tr>
<tr><td colspan="5">NOTE: The comparison on this page is to the predicate device, the GEM Premier 4000, except where noted to the predicate device for Total Bilirubin (tBili), ABL 837.</td></tr>
<tr><th>Item</th><th colspan="2">Predicate Devices</th><th colspan="2">New Device</th></tr>
<tr><td rowspan="2">Trade Names</td><td>GEM Premier 4000
(All Analytes except tBili)</td><td>K133407</td><td rowspan="2">GEM Premier 5000</td><td rowspan="2">K160402</td></tr>
<tr><td>ABL 837
Total Bilirubin (tBili)</td><td>K142898</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="4">Reportable Range</td><td>Analyte</td><td>Predicate Devices</td><td colspan="2">GEM Premier 5000</td></tr>
<tr><td>Glucose</td><td>4 to 685 mg/dL</td><td colspan="2">4 to 685 mg/dL</td></tr>
<tr><td>Lactate</td><td>0.3 to 17.0 mmol/L</td><td colspan="2">0.3 to 17.0 mmol/L</td></tr>
<tr><td>tBili</td><td>0.0 to 58.5 mg/dL</td><td colspan="2">2.0 to 40.0 mg/dL</td></tr>
</table>

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 and CVP 5 tBili. 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	Glucose (mg/dL)	Level 1	378	120	10.9	2.9%	11.2	3.0%
		Level 2	104	120	1.6	1.6%	1.6	1.6%
		Level 3	46	120	1.3	2.7%	1.3	2.7%
	Lactate (mmol/L)	Level 1	7.3	120	0.06	0.9%	0.07	0.9%
		Level 2	0.8	120	0.03	3.7%	0.03	3.7%
		Level 3	2.5	120	0.04	1.8%	0.04	1.8%
	tBili (mg/dL)	Level 1	33.8	120	0.14	0.4%	0.16	0.5%
		Level 2	17.7	120	0.13	0.8%	0.18	1.0%
		Level 3	3.3	120	0.13	4.0%	0.16	4.9%
CVP 5 tBili	tBili (mg/dL)	NA	4.8	120	0.13	2.6%	0.18	3.7%

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	Glucose (mg/dL)	347	120	1.7	0.5%
PCS E		71	120	0.6	0.8%
PCS D	Lactate (mmol/L)	8.0	120	0.11	1.3%
PCS E		1.6	120	0.02	1.3%
PCS D	tBili (mg/dL)	10.4	120	0.05	0.4%
PCS E		20.0	120	0.04	0.2%

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
- tBili / CO-Ox Mode 100 µL

Analyte	Mode	Level	Mean	N	Within Run SD	Within Run %CV	Total SD	Total %CV
Glucose (mg/dL)	Normal Mode	1	24	120	0.8	3.3%	0.8	3.5%
		2	42	120	0.8	2.0%	1.1	2.7%
		3	120	120	1.7	1.4%	2.5	2.1%
		4	179	120	3.1	1.7%	4.0	2.2%
		5	729	120	13.1	1.8%	13.4	1.8%
	Micro Mode	1	26	120	0.7	2.8%	0.8	3.0%
		2	44	120	0.8	1.8%	1.2	2.7%
		3	118	120	2.5	2.1%	3.0	2.6%
		4	176	120	2.9	1.7%	4.1	2.3%
		5	761	120	11.6	1.5%	24.9	3.3%
Lactate (mmol/L)	Normal Mode	1	0.5	120	0.05	9.4%	0.05	9.4%
		2	1.8	120	0.06	3.3%	0.07	3.7%
		3	4.9	120	0.09	1.7%	0.10	2.0%
		4	7.8	120	0.17	2.1%	0.18	2.3%
		5	17.9	120	0.40	2.2%	0.45	2.5%
	Micro Mode	1	0.5	120	0.04	7.5%	0.04	7.6%
		2	1.9	120	0.05	2.9%	0.06	3.1%
		3	4.9	120	0.14	2.9%	0.15	3.1%
		4	7.8	120	0.13	1.6%	0.16	2.0%

Analyte	Mode	Level	Mean	N	Within Run SD	Within Run %CV	Total SD	Total %CV
		5	18.2	120	0.31	1.7%	0.37	2.0%

Performance Summary (Cont.)

Internal Precision Study – Whole Blood (Cont.)

Analyte	Mode	Level	Mean	N	Within Run SD	Within Run %CV	Total SD	Total %CV
tBili (mg/dL)	Normal Mode	1	3.3	120	0.12	3.5%	0.24	7.3%
		2	6.2	120	0.12	1.8%	0.29	4.6%
		3	14.1	120	0.13	0.9%	0.41	2.9%
		4	19.7	120	0.17	0.9%	0.50	2.5%
		5	29.6	120	0.18	0.6%	0.75	2.5%
	tBili/CO-Ox Mode	1	3.3	120	0.10	2.9%	0.12	3.7%
		2	6.3	120	0.13	2.0%	0.19	3.0%
		3	14.0	120	0.14	1.0%	0.27	1.9%
		4	19.6	120	0.17	0.9%	0.36	1.8%
		5	29.4	120	0.16	0.5%	0.51	1.7%

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) and CVP 5 tBili, 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 (Cont.)																	
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**
Glu (mg/dL)	GSE 1	90	347-411	379	5%	381	2.1	0.5%	1.1	0.3%	2.8	0.7%	2.9	0.8%	4.7	1.2%
	GSE 2	90	93-117	105	5%	102	0.5	0.5%	0.3	0.3%	0.5	0.5%	0.2	0.2%	0.8	0.8%
	GSE 3	90	38-56	47	3	45	0.5	1.2%	0.0	0.0%	0.3	0.7%	0.1	0.2%	0.6	1.4%
Lac (mmol/L)	GSE 1	90	6.5-8.1	7.3	7.5%	7.2	0.06	0.8%	0.06	0.8%	0.05	0.7%	0.00	0.0%	0.09	1.3%
	GSE 2	90	0.5-1.1	0.8	0.2	0.8	0.02	2.3%	0.00	0.0%	0.01	1.1%	0.00	0.0%	0.02	2.5%
	GSE 3	90	2.0-3.0	2.5	0.2	2.4	0.02	0.7%	0.03	1.2%	0.04	1.8%	0.00	0.0%	0.06	2.3%
tBili (mg/dL)	GSE 1	90	32.5-34.9	33.7	10%	33.7	0.14	0.4%	0.00	0.0%	0.05	0.1%	0.07	0.2%	0.16	0.5%
	GSE 2	90	16.9-18.5	17.7	10%	17.6	0.10	0.5%	0.00	0.0%	0.05	0.3%	0.07	0.4%	0.13	0.7%
	GSE 3	90	2.5-3.9	3.2	0.4	3.2	0.10	3.0%	0.02	0.8%	0.03	0.8%	0.01	0.3%	0.10	3.3%
	CVP-5	90	4.0-6.0	5.0	10%	4.9	0.11	2.2%	0.00	0.0%	0.05	1.0%	0.12	2.5%	0.17	3.5%

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) and micro capillary (65 µL) mode. 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 %CV or SD
Glu (mg/dL)	Normal Mode	POC1	51	140	1.1%
		POC2	39	142	1.0%
		POC3	27	137	1.2%
		POC-All	117	140	1.1%
		CSL	33	113	1.7%
		Lab1	30	163	1.0%
		Lab2	30	132	1.0%
		Lab-All	93	135	1.2%
	Micro Mode	POC1	30	155	1.0%
		POC2	36	146	1.0%
		POC3	30	122	0.8%
		POC-All	96	141	0.9%
		CSL	33	110	0.8%
		Lab1	30	166	1.2%
		Lab2	30	136	1.4%
		Lab-All	93	136	1.1%

Performance Summary (Cont.)

External Precision – Whole Blood (Cont.)

Analyte	Mode	Site	N	Mean	Within Sample %CV or SD
Lactate (mmol/L)	Normal Mode	POC1	33	1.7	0.07
		POC2	12	1.8	0.03
		POC3	21	2.0	0.06
		POC-All	66	1.9	0.06
		CSL	30	1.7	0.03
		Lab1	21	2.0	0.07
		Lab2	15	2.0	0.06
		Lab-All	66	1.9	0.06
	Micro Mode	POC1	27	1.9	0.06
		POC2	33	1.6	0.05
		POC3	18	1.6	0.06
		POC-All	78	1.7	0.05
		CSL	30	1.9	0.04
		Lab1	30	1.8	0.08
		Lab2	12	1.9	0.06
		Lab-All	72	1.8	0.06

Performance Summary (Cont.)

External Precision – Whole Blood (Cont.)

Note: No Lab 2 results presented for Total Bilirubin.

Analyte	Mode	Site	N	Mean	Within Sample %CV or SD
tBili (mg/dL)	Normal Mode	POC1	24	18.7	0.8%
		POC2	24	16.8	2.0%
		POC3	27	11.5	1.9%
		POC-All	75	15.5	1.6%
		CSL	15	18.5	0.6%
		Lab1	6	4.9	7.5%
		Lab-All	21	14.6	2.5%
	tBili/ CO-Ox Mode	POC1	33	22.1	1.2%
		POC2	27	11.6	1.6%
		POC3	30	11.8	1.3%
		POC-All	90	15.5	1.4%
		CSL	15	18.3	0.7%
		Lab1	3	8.3	2.5%
		Lab-All	18	16.7	1.0%

Performance Summary (Cont.)

LoB, LoD and LoQ

In accordance with CLSI EP17-A2, LoB, LoD and LoQ were established for glucose, lactate and total bilirubin, 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
Glucose (mg/dL)	0	2	2
Lactose (mmol/L)	0.0	0.0	0.2
Total Bilirubin (mg/dL)	0.1	0.3	1.4

Linearity

In accordance with CLSI EP06-A, nine (9) 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
Glucose (mg/dL)	9	9	0.982	-12.489	0.995	1 to 777	4 to 685
Lactate (mmol/L)	9	9	1.037	-0.131	0.998	0.2 to 25.5	0.3 to 17.0
tBili (mg/dL)	9	9	1.040	0.227	0.998	1.4 to 43.7	2.0 to 40.0

Performance Summary (Cont.)

Analytical Specificity

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

The table below and on the next page lists substances that were screen tested with no observed interference on glucose, lactate and/or total bilirubin (tBili) results:

Substance	Concentration	Tested analytes with no observed interference
Acetaminophen	1324 µmol/L	Glucose, Lactate, tBili
Acetoacetate	2 mmol/L	Glucose, Lactate
N-acetylcysteine	10.2 mmol/L	Glucose, Lactate
Amoxicillin	206 µmol/L	tBili
Ascorbic acid	342 µmol/L	Glucose, Lactate, tBili
Benzalkonium (Chloride)	5 mg/L	tBili
Bilirubin	20 mg/dL	tBili
Biliverdin	4 mg/dL	tBili
Ceftriaxone	1460 µmol/L	tBili
Chlorpromazine	6.3 µmol/L	Glucose, Lactate
Ciprofloxin	30.2 µmol/L	tBili
(Sodium) Citrate	12 mmol/L	Glucose, Lactate
Creatinine	5 mg/dL	Glucose, Lactate
Diazepam	18 µmol/L	tBili
Dobutamine	2 mg/dL	Glucose, Lactate
Dopamine	5.87 µmol/L	Glucose, Lactate
Epinephrine	0.5 µmol/L	tBili
Ethanol	86.8 mmol/L	Glucose, Lactate
Evans Blue	10 mg/L	tBili
Fetal Hemoglobin	75%	tBili
Flaxedil (Gallamine triethiodide)	5 mg/dL	Glucose, Lactate
(Sodium) Fluoride	105 µmol/L	Glucose, Lactate
Fructose	1 mmol/L	Glucose, Lactate
Galactose	0.84 mmol/L	Glucose, Lactate
Gentamycin	21 µmol/L	tBili
Glucose	1000 mg/dL	Lactate
Glycolic acid	1 mmol/L	Glucose

Performance Summary (Cont.)

Analytical Specificity (Cont.)

Substance	Concentration	Tested analytes with no observed interference
Hematocrit	25%	Glucose
	75%	Glucose
Hemoglobin	20 g/dL	tBili
Heparin	100,000 U/L	Glucose, Lactate
β-hydroxybutyrate	2 mmol/L	Glucose, Lactate
Ibuprofen	2425 µmol/L	Glucose, Lactate
Icodextrin	20 mg/dL	Glucose, Lactate
Indocyanine Green	10 mg/L	tBili
Isoniazide	292 µmol/L	Glucose, Lactate
Lactate	6.6 mmol/L	Glucose
Lithium (Chloride)	3.2 mmol/L	tBili
Maltose	200 mg/dL	Glucose, Lactate
Mannose	20 mg/dL	Glucose, Lactate
Methadone	6.46 µmol/L	tBili
Morphine	1.75 µmol/L	tBili
Omeprazole	17.4 µmol/L	tBili
(Sodium) Oxalate	500 mg/dL	Glucose, Lactate
pO_2	30 mmHg	Glucose, Lactate
Pralidoxime iodide	40 µg/mL	Glucose, Lactate
Propofol	0.05 mg/mL	tBili
Pyruvate	309 µmol/L	Glucose, Lactate
Sulfhemoglobin	10%	tBili
Suxamethonium	68 µmol/L	tBili
(Sodium) Thiocyanate	6880 µmol/L	Glucose, Lactate
Thiopental	248 µmol/L	tBili
Thyroxine	1.29 µmol/L	tBili
Urea	42.9 mmol/L	Glucose, Lactate
Uric acid	1.4 mmol/L	Glucose, Lactate
Xylose	20 mg/dL	Glucose, Lactate

Performance Summary (Cont.)

Analytical Specificity (Cont.)

The table below lists substances that demonstrated interference with glucose, lactate or total bilirubin (tBili) results and the concentration of the interfering substance, as well as the bias 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
Cyanocobalamin	tBili	4.8 mg/dL	0.18 g/L	-11%	0.16 g/L	-10%
		13.3 mg/dL	0.53 g/L	- 10%	0.47 g/L	-10%
Cyanomethemoglobin	tBili	5.2 mg/dL	1.0%	+18%	0.5%	+10%
		15.1 mg/dL	3.0%	+15%	2.1%	+10%
Glycolic Acid	Lactate	1.0 mmol/L	0.250 mmol/L	+0.4 mmol/L	0.237 mmol/L	+0.4 mmol/L
		2.9 mmol/L	0.250 mmol/L	+0.4 mmol/L	0.241 mmol/L	+0.4 mmol/L
Hydroxocobalamin	tBili	5.0 mg/dL	0.18 g/L	-14%	0.12 g/L	-10%
		14.7 mg/dL	0.35 g/L	-13%	0.27 g/L	-10%

Performance Summary (Cont.)

Analytical Specificity (Cont.)

Interfering Substance	Affected Analyte	Analyte Concentration	Interfering Concentration Tested	Bias Observed (Mean)	Lowest Interfering Concentration with Analyte Impact	Bias Observed at the Lowest Concentration
Hydroxyurea	Glucose	86 mg/dL	0.60 mg/dL	+15%	0.41 mg/dL	+10%
		115 mg/dL	0.60 mg/dL	+11%	0.57 mg/dL	+10%
Hydroxyurea	Lactate	1.0 mmol/L	0.40 mg/dL	0.4 mmol/L	0.37 mg/dL	+0.4 mmol/L
		2.8 mmol/L	0.40 mg/dL	0.5 mmol/L	0.35 mg/dL	+0.4 mmol/L
Methylene Blue	tBili	5.0 mg/dL	10 mg/L	-25%	4.6 mg/L	-10%
		14.2 mg/dL	15 mg/L	-11%	12.9 mg/L	-10%
Turbidity (Intralipid)	tBili	4.8 mg/dL	1505 mg/dL	-11%	1143 mg/dL	-10%
		14.0 mg/dL	2006 mg/dL	No Interference Observed		

Performance Summary (Cont.)

Internal Method Comparison

In accordance with EP09-A3, an internal method comparison study was conducted using clinical samples to compare the GEM Premier 5000 to the following predicate devices:

- GEM Premier 4000: Glucose and Lactate
- ABL 837: Total Bilirubin

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

Analyte	N	Slope	Intercept	R^2	Medical Decision Level	Bias at Medical Decision Level
Glucose (mg/dL)	373	0.985	3.746	0.997	45	3.1
					120	1.6%
					180	0.6%
					350	-0.4%
Lactate (mmol/L)	373	1.000	-0.050	0.998	2.0	-0.05
					5.0	-1.0%
tBili (mg/dL)	163	0.977	0.384	0.998	3.0	0.31
					6.0	4.1%
					14.0	0.4%
					20.0	-0.4%

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)
Glucose (mg/dL)	45	3.1	1.7	4.8
	120	1.6%	2.9%	4.5%
	180	0.6%	3.5%	4.1%
	350	0.4%	3.6%	4.0%
Lactate (mmol/L)	2.0	0.05	0.12	0.017
	5.0	1.0%	3.5%	4.5%
tBili (mg/dL)	3.0	0.31	0.24	0.55
	6.0	4.1%	3.7%	7.8%
	14.0	0.4%	1.8%	2.2%
	20.0	0.4%	1.7%	2.1%

Performance Summary (Cont.)

Reference Ranges

Analyte	Reference Range	Unit
Glu[1,2]	65 to 95	mg/dL
Glu[1,2]	3.6 to 5.3	mmol/L
Lac[1]	0.36 to 0.75 (at rest)	mmol/L
Lac[1]	2.24 to 6.76 (at rest)	mg/dL
Lac[1]	0.56 to 1.39 (venous)	mmol/L
Lac[1]	2.0 to 12.5 (venous)	mg/dL

Analyte	Age	Reference Range	Unit
tBili[2]	Premature Infant 0 – 1 day	<8.0	mg/dL
	Premature Infant 0 – 1 day	<137	µmol/L
	Premature Infant 1 – 2 days	<12.0	mg/dL
	Premature Infant 1 – 2 days	<205	µmol/L
	Premature Infant 3 – 5 days	<16.0	mg/dL
	Premature Infant 3 – 5 days	<274	µmol/L
	Full-term Infant 0 – 1 day	1.4 – 8.7	mg/dL
	Full-term Infant 0 – 1 day	24 – 149	µmol/L
	Full-term Infant 1 – 2 days	3.4 – 11.5	mg/dL
	Full-term Infant 1 – 2 days	58 – 197	µmol/L
	Full-term Infant 3 – 5 days	1.5 – 12.0	mg/dL
	Full-term Infant 3 – 5 days	26 – 105	µmol/L
	>5 days to < 60 years	0.3 – 1.2	mg/dL
	>5 days to < 60 years	5 – 21	µmol/L

1. Burtis, Carl and David Bruns, Tietz Textbook of Clinical Chemistry and Molecular Diagnostics, Elsevier Saunders, 7th edition, 2015.
2. Wu, A., Tietz Clinical Guide to Laboratory Tests, W.B. Saunders Co., St. Louis MO, 4th Edition, 2006.

Performance Summary (Cont.)

Clinical Testing

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

- Study Design:
  - Point-of-Care for glucose and lactate: Sites included three (3) external point-of-care (POC) sites and 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 claimed measuring ranges.
  - Point-of-Care for tBili: Sites included three (3) external point-of care settings with neonate samples, using adult samples and spiked samples to cover the claimed measuring range.

In each setting, the performance of the GEM Premier 5000 was compared to the GEM Premier 4000, ***except tBili***, which used the commercially available whole blood or chemistry analyzer in use at each facility.

For glucose and lactate, 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**
Glucose (mg/dL)	489	0.973	3.622	0.998	12 to 619
Lactate (mmol/L)	488	1.000	0.000	0.996	0.5 to 15.0

To support capillary claims for glucose and lactate, 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:

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**
Glucose (mg/dL)	171	68	280	45	3.9	1.0 to 6.2	± 6.0
				120	1.8%	-0.1% to 2.9%	± 10%
				180	-0.5%	-2.0% to 2.1%	± 10%
				350	-0.9%	-4.0% to 1.1%	± 10%
Lactate (mmol/L)	171	0.4	3.7	2.0	0.00	0.00 to 0.11	± 0.4
				5.0	0.0%	0.00% to 10.3%	± 15%

Performance Summary (Cont.)

Clinical Testing (Cont.)

In addition for glucose and lactate, 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:

Pooled Point-of-Care Site and CSL Data with Additional Contrived Capillary Results					
Analyte	**N**	**Slope**	**Intercept**	**r**	**Sample Range**
Glucose (mg/dL)	197	0.966	4.775	0.997	12 to 637
Lactate (mmol/L)	201	1.000	0.000	0.995	0.4 to 16.4

For Total Bilirubin (tBili), the pooled results from the POC sites, with a combination of heel-stick samples (capillary Blood) and syringe (arterial/venous), are presented below for the different instrument modes:

Normal Mode					
Predicate	**N**	**Slope**	**Intercept**	**r**	**Sample Range**
tBili (mg/dL) vs. Roche Cobas 6000*	53	1.062	0.630	0.996	3.1 to 39.7
tBili (mg/dL) vs. Ortho Clinical Diagnostics Vitros 5600**	76	1.076	-0.099	0.996	2.0 to 39.7
Capillary Mode					
Predicate	**N**	**Slope**	**Intercept**	**r**	**Sample Range**
tBili (mg/dL) vs. Roche Cobas 6000*	58	1.051	0.533	0.996	3.9 to 39.9
tBili (mg/dL) vs. Ortho Clinical Diagnostics Vitros 5600**	77	1.072	-0.255	0.996	2.1 to 39.4
tBili/CO-Ox Mode					
Predicate	**N**	**Slope**	**Intercept**	**r**	**Sample Range**
tBili (mg/dL) vs. Roche Cobas 6000*	53	1.068	0.404	0.996	2.0 to 39.7
tBili (mg/dL) vs. Ortho Clinical Diagnostics Vitros 5600**	77	1.076	-0.163	0.995	2.0 to 39.2

*tBili data against Roche Cobas 6000 were from one (1) POC site.
**tBili data against Ortho Clinical Diagnostics Vitros 5600 were from two (2) POC sites.

Conclusion	The technological and functional characteristics of the new GEM Premier 5000 as described above are substantially equivalent to that of the predicate devices: GEM Premier 4000 for glucose and lactate, and ABL 837 for total bilirubin. 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 devices.