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

A. 510(k) Number:
k061974

B. Purpose for Submission:
Clearance of a new device.

C. Measurand:
Blood gases, blood pH, sodium, potassium, calcium, chloride, glucose, lactic acid, hematocrit, carboxyhemoglobin, hemoglobin

D. Type of Test:
Potentiometric for pH, pCO2, Na+, K+, Cl-, Ca++
Amperometric for pO2, Glucose, Lactate
Conductivity for Hematocrit
Spectrophotometry for CO-Oximeter parameters

E. Applicant:
Instrumentation Laboratory Co.

F. Proprietary and Established Names:
GEM® Premier 4000 with iQM® (Intelligent Quality Management)
GEM CVP 1 and 2 (Calibration Valuation Product) with CO-Ox
GEM CVP 3 and 4 (Calibration Valuation Product) Hematocrit

G. Regulatory Information:

1. Regulation section:
GEM Premier 4000 with iQM (Intelligent Quality Management)

Description	CFR Section
Blood gases and blood pH	862.1120
Sodium test system	862.1665
Potassium test system	862.1600
Calcium test system	862.1145
Chloride test system	862.1170
Glucose test system	862.1345
Lactic acid test system	862.1450
Automated hematocrit instrument	864.5600
Carboxyhemoglobin assay	864.7425
Automated hemoglobin system	864.5620
Oximeter to measure hemoglobin	864.7500
Quality Control Material	862.1660

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

Description	CFR Section
Quality Control Material	862.1660

GEM CVP 3 and 4 (Calibration Valuation Product) Hematocrit

Description	CFR Section
Hematocrit Control	864.8625

2. Classification:

GEM Premier 4000 with iQM (Intelligent Quality Management)

Description	Class
Blood gases and blood pH	Class II
Sodium test system	Class II
Potassium test system	Class II
Calcium test system	Class II
Chloride test system	Class II
Glucose test system	Class II
Lactic acid test system	Class I
Automated hematocrit instrument	Class II
Carboxyhemoglobin assay	Class II
Automated hemoglobin system	Class II
Oximeter to measure hemoglobin	Class II
Quality Control Material	Class I

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

Description	Class
Quality Control Material	Class I

GEM CVP 3 and 4 (Calibration Valuation Product) Hematocrit

Description	Class
Hematocrit Control	Class II

3. Product code:
GEM Premier 4000 with iQM (Intelligent Quality Management)

Description	Product Code
Blood gases and blood pH	CHL
Sodium test system	JGS
Potassium test system	CEM
Calcium test system	JFP
Chloride test system	CGZ
Glucose test system	CGA
Lactic acid test system	KHP
Automated hematocrit instrument	GKF
Carboxyhemoglobin assay	GHS
Automated hemoglobin system	GKR
Oximeter to measure hemoglobin	GLY
Quality Control Material	JJY

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

Description	Product Code
Quality Control Material	JJY

GEM CVP 3 and 4 (Calibration Valuation Product) Hematocrit

Description	Product Code
Hematocrit Control	GLK

4. Panel:
75 (Clinical Chemistry), 81 (Hematology)

H. Intended Use:

1. Intended use(s):
See Indications for use.

2. Indication(s) for use:
The GEM Premier 4000 is a portable critical care system for use by health care professionals to rapidly analyze whole blood samples at the point of health care delivery in a clinical setting and in a central laboratory. The instrument provides quantitative measurements of pH, pCO2, pO2, Na+, K+, Cl-, Ca++, glucose, lactate, hematocrit and

CO-Oximetry (tHb, O2Hb, COHb, MetHb, HHb) parameters. 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.

Intelligent Quality Management (iQM) is used as the quality control and assessment system for the GEM Premier 4000 system. iQM is an active quality process control program designed to provide continuous monitoring of the analytical process with real-time, automatic error detection, automatic correction of the system and automatic documentation of all corrective actions, replacing the use of traditional external quality controls.

As part of this program, GEM CVP 1 and 2 (Calibration Valuation Product) with CO-Ox and GEM CVP 3 and 4 Hematocrit are external solutions intended to complete the calibration process and final accuracy assessment of the iQM cartridge calibration after initial warm-up. The reported values for the four levels of GEM CVP (two levels for pH, blood gases, electrolytes, metabolites and CO-Oximetry; two levels for hematocrit) must meet specifications before the iQM cartridge can be used for patient sample measurements. Once the cartridge calibration is verified, the internal iQM program monitors the status of the system during the cartridge use life.

3. Special conditions for use statement(s):
   For prescription use.
4. Special instrument requirements:
   GEM Premier 4000 with iQM and GEM CVP

I. Device Description:

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, pCO2, pO2, Na+, K+, Cl-, Ca++, glucose, lactate, hematocrit and CO-Oximetry (tHb, O2Hb, COHb, MetHb, HHb) parameters. 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.

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the cartridge calibration is verified, the internal iQM program monitors the status of the system during the cartridge use life.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   IL Synthesis, GEM Premier 3000, and IL 682 CO-Oximeter
2. Predicate 510(k) number(s):
   k963800, k052121, and k945677 respectively.
3. Comparison with predicate:

Similarities		
Item	**GEM Premier 4000 with iQM and GEM CVP**	**Predicate Devices**
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, blood gases, Na^+, K^+, Cl^-, Ca^{++}, glucose, lactate, hematocrit and CO-Oximetry (tHb, O2Hb, COHb, MetHb, HHb) parameters. 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.	The GEM Premier 3000 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. The instrument provides quantitative measurements of pH, pCO_2, pO_2, Na^+, K^+, Ca^{++}, glucose, lactate and hematocrit. These parameters, along with derived parameters, aid in the diagnosis of a patient's acid/base status, oxygen delivery capacity, and electrolyte and metabolite balance. NOTE: The GEM Premier 4000 introduces additional measured parameters for chloride and CO-Oximetry.
Operating Principle	• Electrochemical: potentiometric ion-selective electrode • Electrochemical: amperometric enzyme biosensor • Electrochemical: Conductometric measurement of red cell volume • Optical measurement of hemoglobin and fractional derivatives of hemoglobin in lysed blood	Same
Sample Type	Whole blood samples	Same

Differences		
Item	**GEM Premier 4000 with iQM and GEM CVP**	**Predicate Devices**
Quality Control Principle	Active quality process control program using external Calibration Valuation Product (CVP), four internal Process Control Solutions (PCSs) and Failure Pattern Recognition (FPR) software designed to provide immediate error detection and automatic remedial action, replacing the use of traditional external quality controls.	GEM Premier 3000 with iQM: • Same as GEM Premier 4000 IL Synthesis (Chloride) and IL CO-Oximeter 682: • Use of multi-level external quality control solutions on a regular basis for error detection.
Detection Frequency	GEM Premier 4000 Internal Process Control Solutions (PCSs): • **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. Solution D provides additional	GEM Premier 3000 Internal Process Control Solutions (PCSs): • **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. • **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 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 and pCO2 sensor functionality. IL Synthesis (Chloride) and IL CO-Oximeter 682: • Use of external quality control

Differences		
Item	**GEM Premier 4000 with iQM and GEM CVP**	**Predicate Devices**
	measurement for all analytes including co-oximetry. Reference values for analytes in 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.	solutions on a regular basis for error detection. • Traditional controls may not detect the error for 8 or more hours, based on the frequency of running the control solutions.

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

None identified.

L. Test Principle:

The GEM Premier 4000 analyzer uses potentiometric sensors to measure *p*CO_2, pH, Na^+, K^+, Cl^- and Ca^{++}, amperometric electrodes to measure *p*O2, glucose and lactate concentrations and blood conductivity to measure hematocrit. CO-Oximetry measurements involve chemically lysing the whole blood sample and then utilizing a broad spectrum spectrometer to evaluate the sample at a variety of wavelengths.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

To verify the performance of the GEM Premier 4000, whole blood precision testing was performed in-house on 6 to 12 different GEM Premier 4000 instruments, depending on the analyte. Six levels for pH, blood gases, potassium, glucose and lactate, 7 levels for sodium, calcium and chloride, 8 levels for hematocrit and 5 to 9 levels for CO-Oximetry were evaluated using whole blood from healthy adult volunteers.

Samples were altered with various levels of analytes (salts, gases, or plasma) to span the claimed measuring range and tested in 3 replicates per run on each instrument. All parameters were tested once in week two of the cartridge use life. The data was used to show within run standard deviations and %CV pooled. Results are summarized below.

pH			
N per Level	Mean	SD	% CV
35	7.030	0.008	0.12
36	7.086	0.007	0.10
35	7.235	0.009	0.12
35	7.350	0.010	0.13
36	7.483	0.011	0.14
33	7.675	0.024	0.31
pCO_2			
N per Level	Mean (mmHg)	SD	% CV
34	11.3	0.60	5.33
36	24.5	0.07	0.29
35	39.9	0.89	2.24
35	59.6	0.72	1.21
36	105.8	0.92	0.87
35	125.2	1.26	1.01
pO_2			
N per Level	Mean (mmHg)	SD	% CV
36	28.5	0.94	3.31
35	49.0	0.81	1.66
35	105.7	4.35	4.12
35	203.9	4.48	2.20
36	420.5	8.75	2.08
30	714.5	36.80	5.15

Na^+			
N per Level	Mean (mmol/L)	SD	% CV
30	108.9	0.63	0.58
30	121.0	0.55	0.45
29	130.1	1.51	1.16
29	139.2	1.99	1.43
30	156.2	0.89	0.57
30	170.0	0.91	0.54
30	177.2	1.99	1.12
K^+			
N per Level	Mean (mmol/L)	SD	% CV
30	1.98	0.10	4.79
30	4.11	0.11	2.61
27	5.02	0.06	1.24
30	7.50	0.08	1.03
30	10.20	0.07	0.68
30	18.99	0.20	1.05
Ca^{++}			
N per Level	Mean (mmol/L)	SD	% CV
33	0.422	0.005	1.27
33	1.223	0.010	0.78
33	1.509	0.017	1.11
30	1.929	0.015	0.77
33	2.524	0.011	0.43
33	3.747	0.018	0.48
33	4.319	0.039	0.90

Cl^-			
N per Level	Mean (mmol/L)	SD	% CV
33	61.7	0.43	0.69
33	78.5	0.25	0.31
30	100.3	0.41	0.41
33	124.3	0.88	0.71
33	132.0	0.97	0.74
33	143.8	0.66	0.46
33	161.4	0.31	0.19

Glucose			
N per Level	Mean (mg/dL)	SD	% CV
29	46.3	0.69	1.48
30	105.8	2.02	1.91
30	202.2	1.92	0.95
30	340.1	1.51	0.44
29	464.0	4.68	1.01
27	708.3	9.73	1.37

Lactate			
N per Level	Mean (mmol/L)	SD	% CV
33	1.11	0.07	6.49
33	2.38	0.17	7.23
33	4.23	0.11	2.64
33	7.86	0.11	1.37
33	13.75	0.11	0.83
33	17.21	0.36	2.11

Hematocrit			
N per Level	Mean (%)	SD	% CV
36	19.4	0.37	1.92
36	22.1	0.29	1.30
36	25.1	0.17	0.67
36	34.1	0.37	1.09
36	46.4	0.29	0.62
36	65.0	0.65	0.99
36	69.8	0.37	0.53
35	73.0	0.55	0.76

tHb			
N per Level	Mean (g/dL)	SD	% CV
18	6.1	0.1	0.9
18	6.8	0.1	1.1
17	7.7	0.1	1.2
18	10.3	0.2	1.5
107	15.4	0.2	1.2
144	16.8	0.2	1.2
36	17.7	0.3	1.5
18	18.9	0.1	0.7
17	21.6	0.5	2.4

O_2Hb			
N per Level	Mean (%)	SD	% CV
18	0.4	0.3	*
18	2.9	0.2	*
18	26.9	0.1	0.4
18	35.0	0.3	1.0
18	50.2	0.1	0.3
18	66.5	0.4	0.6
35	73.5	0.2	0.2
54	88.8	0.2	0.2
197	95.4	0.7	0.8

* SD calculations were used for the CO-Oximeter fractions with Mean values ≤ 3.0.

COHb			
N per Level	Mean (%)	SD	% CV
124	1.0	0.4	*
160	1.7	0.4	*
18	5.3	0.1	1.0
18	10.4	0.1	0.8
18	24.5	0.1	0.5
18	49.6	0.2	0.3
18	73.2	0.2	0.2
18	99.2	0.6	0.6

MetHb			
N per Level	Mean (%)	SD	% CV
321	0.5	0.4	*
18	3.9	0.2	4.6
18	6.8	0.1	2.0
18	12.3	0.2	2.0
17	27.3	0.2	0.8
HHb			
N per Level	Mean (%)	SD	% CV
225	0.1	0.2	*
77	1.2	0.6	*
36	3.0	0.4	*
18	32.1	0.5	1.4
18	64.0	0.3	0.5
18	96.4	0.2	0.2

***** Only SD calculations were used for the CO-Oximeter fractions with Mean values ≤ 3.0.

To verify the performance of the GEM CVP, precision data were generated using GEM CVP 1 and 2 (Calibration Valuation Product) *with* CO-Ox (two levels for pH, blood gases, electrolytes, metabolites and CO-Oximetry) and GEM CVP 3 and 4 Hematocrit (two levels). The control levels were assayed twice a day in duplicate over 10 days for a total of 20 runs on 3 different GEM Premier 4000 instruments (N=120). The day-to-day and total %CV (or SD) were calculated across all 3 instruments. SD is used for pH and the CO-Oximeter fractions. Results are summarized below.

GEM CVP *with* CO-Ox	Parameter	Mean	Day-to-Day % CV (or SD)	Total % CV (or SD)	Total Spec. % CV (or SD)
	pH	7.156	0.0021 (SD)	0.0060 (SD)	0.020 (SD)
	pCO_2 (mmHg)	68.9	0.87	2.31	4.0

GEM CVP *with* CO-Ox	Parameter	Mean	Day-to-Day % CV (or SD)	Total % CV (or SD)	Total Spec. % CV (or SD)
Level 1	pO_2 (mmHg)	36.0	3.76	10.0	12.5
	Na^+ (mmol/L)	124.9	0.23	0.59	1.60
	K^+ (mmol/L)	2.27	0.72	1.95	11.0
	Ca^{++} (mmol/L)	1.59	0.20	0.71	5.0
	Cl^- (mmol/L)	91.1	0.30	0.53	2.5
	Glucose (mg/dL)	362.3	0.72	2.99	6.0
	Lactate (mmol/L)	7.03	0.81	3.61	7.5
	tHb (g/dL)	16.84	0.95	1.44	2.1
	O_2Hb (%)	86.9	0.00 (SD)	0.00 (SD)	1.0 (SD)
	COHb (%)	3.59	0.01 (SD)	0.03 (SD)	1.0 (SD)
	MetHb (%)	3.90	0.00 (SD)	0.00 (SD)	1.0 (SD)
	HHb (%)	5.69	0.00 (SD)	0.03 (SD)	3.0 (SD)

GEM CVP *with* CO-Ox	Parameter	Mean	Day-to-Day % CV (or SD)	Total % CV (or SD)	Total Spec. % CV (or SD)
Level 2	pH	7.580	0.0006 (SD)	0.0024 (SD)	0.020 (SD)
	pCO_2 (mmHg)	13.8	0.34	4.40	18.12
	pO_2 (mmHg)	123.8	0.83	3.16	5.0
	Na^+ (mmol/L)	154	0.00	0.54	1.3
	K^+ (mmol/L)	7.64	0.35	0.78	3.5
	Ca^{++} (mmol/L)	0.82	0.75	1.10	6.1
	Cl^- (mmol/L)	133.2	0.36	0.58	2.5
	Glucose (mg/dL)	74.9	0.28	2.37	8.0

GEM CVP *with* CO-Ox	Parameter	Mean	Day-to-Day % CV (or SD)	Total % CV (or SD)	Total Spec. % CV (or SD)
	Lactate (mmol/L)	1.60	0.72	4.81	12.5
	tHb (g/dL)	7.63	1.42	2.20	4.59
	O_2Hb (%)	39.20	0.03 (SD)	0.05 (SD)	1.0 (SD)
	COHb (%)	30.70	0.00 (SD)	0.00 (SD)	1.0 (SD)
	MetHb (%)	8.98	0.02 (SD)	0.04 (SD)	1.0 (SD)
	HHb (%)	21.10	0.00 (SD)	0.00 (SD)	3.0 (SD)

GEM CVP Hematocrit	Parameter	Mean	Day-to-Day % CV	Total % CV	Total Spec. % CV
Level 3	Hematocrit (%)	22.4	0.23	0.47	2.0
Level 4	Hematocrit (%)	43.0	0.00	0.16	2.0

b. Linearity/assay reportable range:
The data from the whole blood precision study above were used in the linearity calculations provided below. The following reference analyzers were used:

Description	**510(k)**	**Analyte(s)**
GEM 3000 with iQM and GEM CVP	k052121	pH, electrolytes (except chloride), glucose, lactate and hematocrit [except for Glu levels > 500 mg/dL and Lac levels > 15 mmol/L, which used the ABL 735 analyzer (K991417) and Hct levels > 65%, which used spun crit]
Tonometry	NA	Blood gases
IL Synthesis	K963800	Chloride
IL 682 CO-Oximeter	K945677	CO-Oximeter parameters [except for tHb levels > 20 g/dL, which used the ABL 735 analyzer (K991417)]

Results are summarized below:

Parameter	N per Level	Slope	Intercept	R^2	Range
pH	33 to 36	0.9576	0.3189	0.9971	7.01 to 7.70
pCO_2 (mmHg)	34 to 36	0.9888	0.1274	0.9967	10.5 to 124.9
pO_2 (mmHg)	30 to 36	1.0412	-3.388	0.9938	30.2 to 689.4
Na^+ (mmol/L)	29 to 30	0.9586	6.1116	0.9952	107.3 to 179.7
K^+ (mmol/L)	27 to 30	1.0366	-0.2831	0.9981	2.1 to 19.0
Ca^{++} (mmol/L)	30 to 33	1.0098	-0.0038	0.9953	0.44 to 4.25
Cl^- (mmol/L)	30 to 33	1.0465	-5.3123	0.9984	63 to 158
Glucose (mg/dL)	27 to 30	1.0318	-6.5867	0.9960	44 to 685
Lactate (mmol/L)	33	1.0164	-0.1171	0.9969	1.0 to 17.0
Hct (%)	35 to 36	1.0273	-0.3038	0.9989	19 to 72
tHb (g/dL)	17 to 144	1.0036	-0.1839	0.9956	6.0 to 22.5
O_2Hb (%)	18 to 197	0.9905	0.5235	0.9996	0.0 to 98.0
COHb (%)	18 to 160	0.9943	0.0507	0.9997	0.0 to 99.3
MetHb (%)	17 to 321	0.9944	0.0174	0.9945	0.0 to 27.8
HHb (%)	18 to 225	1.003	0.1054	0.9997	0.0 to 96.2

A separate study was performed to show that the instrument is linear with regards to the lowest detectable limit of glucose indicated in the functional sensitivity study (below). Five levels of glucose (1.3, 6, 18, 54, and 94 mg/dL) were used with 3 replicates per level. Samples were tested on 9 GEM 4000 instruments and were compared to tests run on 3 GEM 3000 instruments resulting in 27 samples per level of glucose. The linearity was summarized as Observed = 1.0552(Expected) +1.2853; $r^2 = 0.9998$.

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

Traceability:

Analytes	Traceability Methods and Materials
pH & Ca^{++}	Per NIST pub. no. 260-53 (Dec.'75) and CLSI no. C46-A for pH and IFCC no. 1994-03-30 and CLSI no. C39-A for Ca^{++}, i.e., direct

Analytes	Traceability Methods and Materials
	potentiometry vs. secondary standards prepared from: • phosphate salts for pH, #186I & 186II • calcium carbonate for Ca^{++}, #915, all from NIST
pCO_2 & pO_2	Per CLSI nos. C21-A & C46-A, i.e., tonometry at 37°C using gas mixtures assured to ± 0.01% vs. NIST.
Na^+ & K^+	Per CLSI No. C29-A and NIST pub. no. 260-60 (Aug.'78) and 260-63 (May'79), i.e., flame photometry vs. secondary standards prepared from NaCl & KCl, #919 & #918, NIST.
Cl^-	Per NIST pub. No. 260-67 (Nov.'79) and CLSI no. RS10-P, i.e., coulometric-amperometric titration with silver ion vs. secondary standards prepared from NaCl, #919, NIST.
Glucose and Lactate	Automated spectrophotometry: • Glucose: hexokinase method per CDC no. 77-8330 and CLSI no. RS1-A using secondary standard prepared from NIST #917. • Lactate: no ref. method established for lactate. Lactate oxidase is used with secondary std. prep'd from Fluka cat. no. 71718 (99%).
Hct	Correlation to blood using centrifugation per CLSI H7-A3. Maintained conductivity from lot to lot by controlling sodium concentration.
tHb	Correlation to blood per CLSI H15-A3 (2000) using hemoglobincyanide colorimetry and cyanMetHb standards.

Stability:
Testing supports the stability claims in the product insert. Stability claims are listed below.

GEM CVP 1 and 2 with CO-Ox: Unopened ampules are stable until the expiration date shown on the label when stored at 2-8○C, or up to 9 months at room temperature (15-25°C), providing storage does not exceed the expiration date.
GEM CVP 3 and 4 Hematocrit: Unopened ampules are stable until the expiration date shown on the label when stored at room temperature 15-25°C. DO NOT FREEZE.
GEM Premier 4000 cartridge: Data support a shelf-life claim of 3 months.

Expected values:
Expected values for the GEM CVP 1, 2, 3, and 4 as well as the cartridge are listed below.

	GEM CVP *with* CO-Ox	
Parameters	Level 1	Level 2
pH	7.15	7.57

Parameters	GEM CVP *with* CO-Ox	
	Level 1	Level 2
pCO_2 (mmHg)	76	14
pO_2 (mmHg)	38	127
Na^+ (mmol/L)	126	155
K^+ (mmol/L)	3.5	7.8
Ca^{++} (mmol/L)	1.61	0.81
Cl^- (mmol/L)	105	132
Glucose (mg/dL)	380	77
Lactate (mmol/L)	7.3	1.7
tHb (g/dL)	17.0	7.8
O_2Hb (%)	87	39
COHb (%)	3	31
MetHb (%)	4	9
HHb (%)	6	21

Parameters	GEM CVP Hematocrit	
	Level 3	Level 4
Hct (%)	23	43

Parameters	Internal GEM Premier 4000 Process Control Solutions			
	A	B	C	D
pH	6.90	7.40	8.00	7.30
pCO_2 (mmHg)	64	34	34	22
pO_2 (mmHg)	115	175	3	80
Na^+ (mmol/L)	105	153		165
K^+ (mmol/L)	7.1	2.0	4.2	14.0

Parameters	Internal GEM Premier 4000 Process Control Solutions			
	A	B	C	D
Ca^{++} (mmol/L)	1.80	0.76		1.25
Cl^- (mmol/L)	48	91		135
Glucose (mg/dL)	144	0		350
Lactate (mmol/L)	3.3	0		8.0
tHb (g/dL)	14.5	0		7.5
O_2Hb (%)	89.5			69.5
COHb (%)	2.5			4.5
MetHb (%)	1.5			4.0
HHb (%)	6.5			22.0
Hct (%)	28	16		

d. Detection limit:

Functional sensitivity was determined for all measured analytes on the GEM Premier 4000. Functional sensitivity was defined by the sponsor as the lowest concentration of an analyte at which quantitative information is available and where a coefficient of variation (CV) of ≤ 20% (within run) is obtained. In this test, a run was performed consisting of 10 replicates of the same whole blood sample on at least 4 different GEM Premier 4000 instruments. Pooled within run SD and % CV were calculated.

Functional sensitivity was used to determine the low limit of the reportable range for all measured analytes on the GEM Premier 4000. The proposed low limit of the reportable range is above the observed functional sensitivity requirement for all analytes.

% CV (Spec. ≤ 20%)	NA	4.0	18.1	3.2	15.6	3.8	0.5	9.2	12.0	3.1	0.9
Low limit (or high for pH) of reportable range	pH 8.00	pCO_2 mmHg 6	pO_2 mmHg 5	Na^+ mmol/L 100	K^+ mmol/L 0.2	Ca^{++} mmol/L 0.10	Cl^- mmol/L 40	Glucose mg/dL 4	Lactate mmol/L 0.3	Hct % 15	tHb g/dL 5.0
N	50	50	40	50	50	50	50	40	60	50	50
Grand Mean	8.000	5.6	4.6	86.6	0.19	0.099	40.0	3.9	0.23	14.7	4.30
Pooled SD	0.020	0.2	0.8	2.8	0.03	0.004	0.2	0.4	0.03	0.5	0.04

Below are the measuring and tested ranges for the GEM Premier 4000 analyzer as indicated in the product labeling. The measuring ranges are the ranges that the system will support in terms of actual numeric values that the system can report. The tested ranges are supported by the linearity study (above), in conjunction with the functional sensitivity data in this section (above).

Parameter	Units	GEM Premier 4000 Measuring Range	GEM Premier 4000 Tested Range
pH	pH Scale	6.8 to 8.0	7.0 to 8.0
pCO_2	mmHg	0 to 150	6 to 125
pO_2	mmHg	0 to 800	5 to 690
Na^+	mmol/L	70 to 200	100 to 180
K^+	mmol/L	0 to 20	0.2 to 19
Ca^{++}	mmol/L	0.10 to 5.00	0.10 to 4.25
Cl^-	mmol/L	40 to 170	40 to 158
Glu	mg/dL	0 to 750	4 to 685
Lac	mmol/L	0 to 20	0.3 to 17
Hct	%	15 to 75	15 to 72
tHb	g/dL	5 to 23	5 to 23
O_2Hb	%	-10 to 110	0 to 98
COHb	%	-10 to 110	0 to 99
MetHb	%	-10 to 110	0 to 28
HHb	%	-10 to 110	0 to 96

e. Analytical specificity:

The following substances did not show noticeable interference with the indicated analytes on the GEM Premier 4000 when tested at the concentrations listed. Interference testing was performed in duplicate on a minimum of three GEM Premier 4000 instruments, with the number of instruments indicated in parentheses in the column entitled “Mean Interference”.

Substance	Possible Affected Analytes	Analyte Conc.	Interferant Concentrations Tested	Mean Interference (N instruments)	SD	± Bias Spec.
Acetaminophen	glucose lactate	80 mg/dL 1.3 mmol/L	20 mg/dL	+2 mg/dL (6) +0.03 mmol/L (6)	1.4 0.04	6 mg/dL 0.2 mmol/L
Acetoacetate	glucose lactate	100 mg/dL 2.5 mmol/L	2 mmol/L	-2.1 mg/dL (4) -0.05 mmol/L (5)	1.3 0.01	6 mg/dL 0.2 mmol/L
Ammonium	Na^+ K^+	140 mmol/L 4.0 mmol/L	80 µmol/L 3000 µmol/L 80 µmol/L 3000 µmol/L	+0.6 mmol/L (5) +1.2 mmol/L (5) +0.03 mmol/L (5) +0.08 mmol/L (5)	1.6 1.4 0.01 0.01	2 mmol/L 0.25 mmol/L
Ascorbic acid	glucose lactate	80 mg/dL 1.3 mmol/L	3 mg/dL	+1.5 mg/dL (5) +0.05 mmol/L (5)	0.8 0.05	6 mg/dL 0.2 mmol/L
Benzalkonium	Na^+	140 mmol/L	5 mg/L 10 mg/L	1.4 mmol/L (8) 1.7 mmol/L (8)	0.7 0.5	2 mmol/L
Bilirubin	tHb O_2Hb COHb MetHb HHb	13.7 g/dL 97.2% 1.5% 0.5% 0.8%	20 mg/dL	0.2 g/dL (5) 0.5% (5) -0.6% (5) -0.8% (5) 0.9% (5)	0.1 0.1 0.1 0.2 0.2	0.35 g/dL 1% 1% 1% 3%
Chlorpromazine	glucose lactate	100 mg/dL 2.5 mmol/L	0.2 mmol/L	-0.9 mg/dL (4) -0.03 mmol/L (5)	2.2 0.02	6 mg/dL 0.2 mmol/L
Citrate	Cl^- glucose lactate	109 mmol/L 85 mg/dL 1.8 mmol/L	12 mmol/L	2.7 mmol/L (7) 1.4 mg/dL (6) 0.2 mmol/L (6)	0.4 3.6 0.1	2.7 mmol/L 6 mg/dL 0.2 mmol/L

[1]Correction for fetal hemoglobin is applied by the instrument and therefore, the reported result would not exhibit any interference.

Substance	Possible Affected Analytes	Analyte Conc.	Interferant Concentrations Tested	Mean Interference (N instruments)	SD	± Bias Spec.
Ethanol	glucose lactate	90 mg/dL 2.2 mmol/L	100 mg/dL 350 mg/dL 100 mg/dL 350 mg/dL	2.5 mg/dL (3) 5.7 mg/dL (3) 0.15 mmol/L (3) 0.19 mmol/L (3)	1.5 1.1 0.10 0.07	6 mg/dL 0.2 mmol/L

Substance	Possible Affected Analytes	Analyte Conc.	Interferant Concentrations Tested	Mean Interference (N instruments)	SD	± Bias Spec.
Evans Blue	tHb	15.7 g/dL	10 mg/L	-0.1 g/dL (5)	0.3	0.35 g/dL
	O_2Hb	97.0%		0.8% (5)	0.3	1%
	COHb	1.3%		0.1% (5)	0.3	1%
	MetHb	0.7%		-0.2% (5)	0.1	1%
	HHb	1.1%		-0.7% (5)	0.1	3%
Fetal hemoglobin[1]	tHb	5.9 g/dL	50%	-0.1g/dL(5)	0.0	0.35 g/dL
	O_2Hb	95.7%		1.1 % (5)	0.3	1%
	COHb	0.4%		1.8 % (5)	0.2	1%
	MetHb	3.3%		-0.3 % (5)	0.2	1%
	HHb	0.7%		-2.6 % (5)	0.2	3%
	tHb	6.8 g/dL	76%	-0.1 g/dL (5)	0.0	0.35 g/dL
	O_2Hb	95.2%		0.8 % (5)	0.2	1%
	COHb	1.0%		2.0 % (5)	0.1	1%
	MetHb	4.2%		0.0 % (5)	0.1	1%
	HHb	-0.3%		-2.9 % (5)	0.1	3%
Flaxedil	glucose	90 mg/dL	2 mg/dL	1.2 mg/dL (4)	0.4	6 mg/dL
			5 mg/dL	0.6 mg/dL (4)	0.8	
	lactate	1.5 mmol/L	2 mg/dL	0.01 mmol/L (4)	0.04	0.2 mmol/L
			5 mg/dL	0.06 mmol/L (4)	0.03	
Halothane	pO_2	92 mmHg	74 µg/mL	3.1 mmHg (4)	3.0	10 mmHg
			374 µg/mL	3.1 mmHg (4)	2.7	

Substance	Possible Affected Analytes	Analyte Conc.	Interferant Concentrations Tested	Mean Interference (N instruments)	SD	± Bias Spec.
Hemoglobin Based Oxygen Carriers (Hemopure®)	tHb	13.5 g/dL	1.0 g/dL	N/A	N/A	0.35 g/dL
	O_2Hb	97.9%		N/A	N/A	1%
	COHb	1.3%		0.3% (5)	0.1	1%
	MetHb	0.0%		0.0% (5)	0.0	1%
	HHb	0.8%		N/A	N/A	3%

Substance	Possible Affected Analytes	Analyte Conc.	Interferant Concentrations Tested	Mean Interference (N instruments)	SD	± Bias Spec.
	tHb	13.5 g/dL	1.5 g/dL	N/A	N/A	0.35 g/dL
	O_2Hb	97.9%		N/A	N/A	1%
	COHb	1.3%		0.5% (5)	0.1	1%
	MetHb	0.0%		0.0% (5)	0.0	1%
	HHb	0.8%		N/A	N/A	3%
	tHb	13.5 g/dL	3.2 g/dL	N/A	N/A	0.35 g/dL
	O_2Hb	97.9%		N/A	N/A	1%
	COHb	1.3%		0.6% (5)	0.1	1%
	MetHb	0.0%		-0.3% (5)	0.0	1%
	HHb	0.8%		N/A	N/A	3%
	tHb	13.5 g/dL	6.4 g/dL	N/A	N/A	0.35 g/dL
	O_2Hb	97.9%		N/A	N/A	1%
	COHb	1.3%		0.8% (5)	0.1	1%
	MetHb	0.0%		-0.8% (5)	0.2	1%
	HHb	0.8%		N/A	N/A	3%
Heparin	Cl^-	109 mmol/L	100 IU/mL	0.7 mmol/L (7)	0.6	2.7 mmol/L
ß-hydroxybutyrate	glucose	100 mg/dL	2 mmol/L	1.0 mg/dL (4)	4.8	6 mg/dL
	lactate	2.5 mmol/L		-0.02 mmol/L (5)	0.01	0.2 mmol/L
Ibuprofen	glucose	100 mg/dL	2 mmol/L	-0.3 mg/dL (4)	2.1	6 mg/dL
	lactate	2.5 mmol/L		-0.01 mmol/L (5)	0.01	0.2 mmol/L
Indocyanine green	tHb	13.7 g/dL	10 mg/L	0.1 g/dL (5)	0.1	0.35 g/dL
	O_2Hb	97.2%		0.0% (5)	0.2	1%
	COHb	1.5%		0.0% (5)	0.2	1%
	MetHb	0.5%		0.0% (5)	0.3	1%
	HHb	0.8%		-0.1% (5)	0.3	3%
Maltose	glucose	100 mg/dL	0.2 mg/mL	-1.8 mg/dL (4)	0.6	6 mg/dL
	lactate	2.5 mmol/L		-0.03 mmol/L (5)	0.01	0.2 mmol/L
Methylene blue	tHb	13.6 g/dL	40 mg/L	-0.4 g/dL (5)	0.0	0.35 g/dL
	O_2Hb	97.4%		-0.5% (5)	0.1	1%

Substance	Possible Affected Analytes	Analyte Conc.	Interferant Concentrations Tested	Mean Interference (N instruments)	SD	± Bias Spec.
	COHb	2.3%		0.8% (5)	0.0	1%
	MetHb	0.1%		0.1% (5)	0.0	1%
	HHb	0.2%		-0.4% (5)	0.1	3%
Pyruvate	glucose	100 mg/dL	2 mmol/L	-2.9 mg/dL (4)	0.7	6 mg/dL
	lactate	2.5 mmol/L		-0.04 mmol/L (5)	0.01	0.2 mmol/L
Thiocyanate	glucose	80 mg/dL	5 mg/dL	0.3 mg/dL (4)	0.9	6 mg/dL
			10 mg/dL	1.6 mg/dL (4)	1.5	
			20 mg/dL	2.0 mg/dL (4)	3.3	
	lactate	1.3 mmol/L	5 mg/dL	0.03 mmol/L (4)	0.01	0.2 mmol/L
			10 mg/dL	0.07 mmol/L (4)	0.06	
			20 mg/dL	0.06 mmol/L (4)	0.06	
Thiopental	Na^+	140 mmol/L	30 mg/L	-1.2 mmol/L (3)	1.3	2 mmol/L
			50 mg/L	0.5 mmol/L (3)	1.6	
Uric acid	lactate	1.3 mmol/L	20 mg/dL	0.16 mmol/L (4)	0.05	0.2 mmol/L

The following substances showed noticeable interference with certain analytes on the GEM Premier 4000, causing falsely elevated results as indicated below:

Substance	Affected Analyte	Analyte Conc.	Interferant Concentration Producing Interference	Mean Interference (N instruments)	SD	± Bias Spec.
Benzalkonium[2]	Ca^{++}	1.20 mmol/L	5 mg/L	0.11 mmol/L (8)	0.01	0.06 mmol/L
Bromide	Cl^-	109 mmol/L	10 mmol/L	151.3 mmol/L (6)	6.4	2.7 mmol/L
Cyanomethemoglobin[3]	tHb	17.5 g/dL	> 4%	1.0 g/dL (5)	0.1	0.35 g/dL
	O_2Hb	97.1%		-0.4 % (5)	0.3	1%
	COHb	2.0%		-0.2 % (5)	0.0	1%
	MetHb	0.5%		0.4 % (5)	0.2	1%
	HHb	0.4%		0.2 % (5)	0.1	3%
Dopamine	glucose	60 mg/dL	5 mg/dL	6.4 mg/dL (7)	8.4	6 mg/dL
	lactate	2.7 mmol/L		-0.06 mmol/L (7)	0.29	0.2 mmol/L

Substance	Affected Analyte	Analyte Conc.	Interferant Concentration Producing Interference	Mean Interference (N instruments)	SD	± Bias Spec.
Dobutamine	glucose lactate	80 mg/dL 2.0 mmol/L	2 mg/dL	6.0 mg/dL (5) 0.17 mmol/L (6)	7.4 0.20	6 mg/dL 0.2 mmol/L
Fluoride	Cl- lactate	109 mmol/L 2.0 mmol/L	500 mg/dL	13.0 mmol/L (4) 0.18 mmol/L (4)	0.9 0.13	2.7 mmol/L 0.2 mmol/L
Glycolic acid	lactate	2.5 mmol/L	1 mmol/L	12.6 mmol/L (4)	0.72	0.2 mmol/L
Hemoglobin Based Oxygen Carriers (Hemopure®)	hematocrit	20%	3.2 g/dL	4 % (4)	0.2	2%
Hydroxyurea	glucose lactate	90 mg/dL 1.4 mmol/L	0.8 mg/dL	25.3 mg/dL (4) 0.97 mmol/L (4)	2.3 0.13	6 mg/dL 0.2 mmol/L
Iodide	Cl-	109 mmol/L	3 mmol/L	8.6 mmol/L (7)	0.7	2.7 mmol/L
Isoniazide	glucose lactate	80 mg/dL 1.3 mmol/L	5 mg/dL	3.6 mg/dL (3) 0.21 mmol/L (3)	4.7 0.04	6 mg/dL 0.2 mmol/L
Oxalate	Cl^- lactate	110 mmol/L 2.0 mmol/L	500 mg/dL	4.8 mmol/L (7) 0.33 mmol/L (7)	0.4 0.06	2.7 mmol/L 0.2 mmol/L
Salicylate	Cl^-	110 mmol/L	4 mmol/L	4.6 mmol/L (4)	0.6	2.7 mmol/L
Sulfhemoglobin[3]	tHb O_2Hb COHb MetHb HHb	13.6 g/dL 97.7% 2.0% 0.5% -0.2%	> 3%	1.2 g/dL(5) -1.0 % (5) -0.1 % (5) 0.9 % (5) 0.2 % (5)	0.1 0.3 0.0 0.1 0.2	0.35 g/dL 1% 1% 1% 3%
Thiopental[2]	pCO_2 Ca^{++}	30 mmHg 1.05 mmol/L	30 mg/L 50 mg/L	96.5 mmHg (3) 0.08 mmol/L (3)	74.8 0.04	4.5 mmHg 0.05 mmol/L
Turbidity[3]	tHb O_2Hb COHb MetHb HHb	13.6 g/dL 97.4% 2.3% 0.1% 0.2%	5% based on turbidity created by Intralipid® fat emulsion	0.0 g/dL (5) 0.5 % (5) -0.5 % (5) -0.6 % (5) 0.6 % (5)	0.0 0.1 0.1 0.2 0.1	0.35 g/dL 1% 1% 1% 3%
Uric acid	glucose	80 mg/dL	20 mg/dL	10.7 mg/dL (3)	2.1	6 mg/dL

[2]The GEM Premier 4000 with iQM (Intelligent Quality Management) employs failure pattern recognition checks. These checks include the presence of positively charged lipophilic compounds (e.g., benzalkonium) and negatively charged lipophilic compounds (e.g., thiopental).

[3]CO-Oximetry interference is detected and flagged by failure pattern recognition checks.

The following substances showed noticeable interference with the glucose channel on the GEM Premier 4000, causing falsely lowered results.

Substance	Affected Analyte	Analyte Conc.	Interferant Concentration Producing Interference	Mean Interference (N instruments)	SD	± Bias Spec.
Oxalate	glucose	85 mg/dL	1000 mg/dL	-16.6 mg/dL (7)	16.6	6 mg/dL
Fluoride	glucose	80 mg/dL	500 mg/dL	-2.2 mg/dL (4)	5.0	6 mg/dL

f. Assay cut-off:
Not Applicable.

2. Comparison studies:

a. Method comparison with predicate device:
The sponsor had method comparison studies performed at 3 point of care sites and 3 laboratory sites. Results of these studies are summarized below.

Point-of-Care Testing Site No. 1:

At the point-of-care setting, a GEM Premier 3000 was used as the reference for pH, blood gases, electrolytes (except chloride), glucose, lactate, hematocrit, and an IL CO-Oximeter 682 was used for CO-Oximetry. Samples were tested for chloride at the central laboratory using a Beckman Synchron CX7 (K910185).

Testing included 70 whole blood samples obtained from patients in a critical care unit submitted for stat analysis over a one-week period. Each sample was assayed in duplicate on the GEM Premier 4000 and the reference devices for a total of N=140 individual results per instrument, with the exceptions noted below.

Summary Statistics

Analyte	N	Slope	Intercept	r	Sample Range
pH	134	1.076	-0.572	0.991	7.19-7.76
pCO_2 (mmHg)	134	0.919	2.16	0.997	25-98
pO_2 (mmHg)	133	1.024	-1.078	0.998	19-491
Na^+ (mmol/L)	134	0.942	8.65	0.958	128-153
K^+ (mmol/L)	134	0.975	0.043	0.992	3.0-5.5
Ca^{++} (mmol/L)	134	0.904	0.118	0.979	0.72-1.38
Cl^- (mmol/L)	42	0.982	3.280	0.901	88-116
Glucose (mg/dL)	43	1.044	0.199	0.992	55-321
Lactate (mmol/L)	134	1.004	0.223	0.996	0.4-5.4
Hct (%)	134	1.003	0.782	0.986	17-51
tHb (g/dL)	133	1.009	-0.356	0.989	6.7-16.0
O_2Hb (%)	133	0.974	2.678	0.998	30.1-98.4
HHb (%)	133	0.979	0.147	0.999	0-67.9

NOTE: For carboxyhemoglobin and methemoglobin results, due to the narrow range of blood samples used in the study, partitioned difference analysis method was used to assess the 95% confidence interval of the bias.

Parameter	N	Range	95% CI of Bias	Bias Spec.
COHb (%)	133	0.8 – 6.9	-0.7 to -0.6	± 1.0
MetHb (%)	133	0 – 2.2	0.0 - 0.1	± 1.0

Point-of-Care Testing Site No. 2:

At the point-of-care setting, a GEM Premier 3000 was used as the reference for pH, blood gases, electrolytes (except chloride), glucose, lactate, hematocrit, and an IL CO-Oximeter 682 was used for CO-Oximetry. Samples were tested for chloride at the central laboratory using a Beckman Synchron CX7 (K910185).

Testing included 72 whole blood samples obtained from patients in a critical care unit submitted for stat analysis over a one-week period. Each sample was assayed in duplicate on the GEM Premier 4000 and the reference devices, except for three samples that were only tested in singlet, for a total of N=141 individual results per instrument, with the exceptions noted below.

Summary Statistics

Analyte	N	Slope	Intercept	r	Sample Range
pH	120	1.132	-0.984	0.985	7.19-7.56
pCO_2 (mmHg)	120	0.970	1.276	0.991	27-71
pO_2 (mmHg)	120	1.064	-5.139	0.997	31-440
Na^+ (mmol/L)	37	1.090	-11.38	0.979	127-152
K^+ (mmol/L)	110	0.995	-0.034	0.985	3.5-8.3
Ca^{++} (mmol/L)	120	0.867	0.178	0.859	0.92-1.41
Cl^- (mmol/L)	17	0.892	14.729	0.805	91-117
Glucose (mg/dL)	120	0.983	8.632	0.993	69-354
Lactate (mmol/L)	120	0.984	0.178	0.989	0.4-3.4
Hct (%)	118	0.959	2.551	0.967	19-51
tHb (g/dL)	112	1.037	-0.485	0.990	7.6-16.0
O_2Hb (%)	112	1.004	-0.512	0.997	60-99
HHb (%)	112	0.997	-0.018	0.999	0-39

NOTE: For carboxyhemoglobin and methemoglobin results, due to the narrow range of blood samples used in the study, partitioned difference analysis method was used to assess the 95% confidence interval of the bias.

Parameter	N	Range	95% CI of Bias	Bias Spec.
COHb (%)	112	0.3 – 6.2	0.0 to 0.3	± 1.0
MetHb (%)	112	-0.3 – 1.8	-0.2 to -0.03	± 1.0

Point-of-Care Testing Site No. 3:

At the point-of-care setting, a GEM Premier 3000 was used as the reference for pH, blood gases, electrolytes (except chloride), glucose, lactate, hematocrit, and an IL CO-Oximeter 682 was used for CO-Oximetry. Samples were tested for chloride at the central laboratory using a J&J Vitros 950 (K946090).

Testing included 65 whole blood samples obtained from patients in an intensive care unit submitted for stat analysis over a one-week period. Each sample was assayed in duplicate on the GEM Premier 4000 and the reference devices for a total of N=130 individual results per instrument, with the exceptions noted below.

Summary Statistics

Analyte	N	Slope	Intercept	r	Sample Range
pH	98	1.089	-0.657	0.988	7.27-7.57
pCO_2 (mmHg)	98	0.989	-0.929	0.994	26-74
pO_2 (mmHg)	98	0.939	6.313	0.997	57-280
Na^+ (mmol/L)	98	0.958	7.274	0.964	124-150
K^+ (mmol/L)	98	0.984	0.031	0.995	2.1-5.8
Ca^{++} (mmol/L)	98	0.902	0.141	0.980	0.78-1.28
Cl^- (mmol/L)	98	0.999	-1.700	0.918	91 - 129
Glucose (mg/dL)	98	1.009	0.480	0.996	87-361
Lactate (mmol/L)	89	0.972	0.171	0.991	0.5-3.2
Hct (%)	98	0.957	1.403	0.989	19-54
tHb (g/dL)	97	0.996	-0.074	0.996	6.2 – 16.6

Analyte	N	Slope	Intercept	r	Sample Range
O_2Hb (%)	97	0.953	4.254	0.971	86.7 – 98.7
HHb (%)	97	0.988	-0.074	0.999	0.1 – 12.6

NOTE: For carboxyhemoglobin and methemoglobin results, due to the narrow range of blood samples used in the study, partitioned difference analysis method was used to assess the 95% confidence interval of the bias.

Parameter	N	Range	95% CI of Bias	Bias Spec.
COHb (%)	97	0 – 1.9	0.6 - 0.7	± 1.0
MetHb (%)	97	0 – 1.8	-0.5 to -0.3	± 1.0

Laboratory Testing Site No. 1:

A GEM Premier 3000 was used as the reference for pH, blood gases, electrolytes (except chloride), glucose, lactate, hematocrit, a J&J Vitros 950 (K946090) was used for chloride, and an IL CO-Oximeter 682 was used for CO-Oximetry.

Testing included 165 whole blood samples obtained from patients in the hospital submitted for stat analysis over a three-week period. Each sample was assayed in duplicate on the GEM Premier 4000 and the reference devices. However, 22 samples were missing values on the reference device and 7 samples were not measured on the GEM Premier 4000, bringing the final total to N=301.

Summary Statistics

Analyte	N	Slope	Intercept	r	Sample Range
pH	297	0.989	0.080	0.992	7.06-7.57
pCO_2 (mmHg)	297	0.922	2.178	0.996	26-105
pO_2 (mmHg)	286	0.992	-1.271	0.993	48-470
Na^+ (mmol/L)	297	0.849	22.248	0.887	123-154
K^+ (mmol/L)	297	1.022	-0.147	0.990	2.7-6.1

Analyte	N	Slope	Intercept	r	Sample Range
Ca^{++} (mmol/L)	297	0.920	0.088	0.958	0.88-1.79
Cl^{-} (mmol/L)	140	1.275	-30.081	0.949	93-120
Glucose (mg/dL)	157	0.954	7.039	0.989	67-269
Lactate (mmol/L)	297	1.162	-0.105	0.989	0.4-13.0
Hct (%)	277	1.002	0.430	0.987	17-53
tHb (g/dL)	273	0.994	-0.200	0.995	6.4 – 16.7
O_2Hb (%)	273	0.977	3.322	0.968	82.7 – 99.2
HHb (%)	273	0.983	-0.456	0.981	0 – 14.7

NOTE: For carboxyhemoglobin and methemoglobin results, due to the narrow range of blood samples used in the study, partitioned difference analysis method was used to assess the 95% confidence interval of the bias.

Parameter	N	Range	95% CI of Bias	Bias Spec.
COHb (%)	273	0.3 – 6.5	-0.3 to -0.2	± 1.0
MetHb (%)	273	0 – 2.5	-0.5 to -0.4	± 1.0

Laboratory Testing Site No. 2:

A GEM Premier 3000 was used as the reference for pH, blood gases, electrolytes (except chloride), glucose, lactate, hematocrit, a Beckman Synchron LX20 (K965240) was used for chloride, and an IL CO-Oximeter 682 was used for CO-Oximetry.

Testing included 159 whole blood samples obtained from hospital patients submitted for routine and stat analysis over a three-week period. Each sample was assayed in duplicate on the GEM Premier 4000 and the reference devices for a total of N=318 individual results per instrument, with the exceptions noted below.

Summary Statistics

Analyte	N	Slope	Intercept	r	Sample Range
pH	290	1.094	-0.702	0.990	7.12 – 7.55
pCO_2 (mmHg)	291	0.978	0.161	0.989	22 - 98
pO_2 (mmHg)	291	0.951	7.919	0.995	27 - 538
Na^+ (mmol/L)	291	0.876	16.185	0.953	124 - 152
K^+ (mmol/L)	291	1.039	-0.200	0.991	2.6 – 6.9
Ca^{++} (mmol/L)	291	0.950	0.062	0.979	0.82 – 1.89
Cl^- (mmol/L)	116	0.984	2.333	0.912	82-125
Lactate (mmol/L)	289	0.983	0.189	0.995	0.4 – 13.0
tHb (g/dL)	280	1.061	-0.274	0.994	7.1 – 16.7
O_2Hb (%)	280	0.980	2.031	0.995	47 – 98.9
HHb (%)	280	0.999	-0.398	0.997	0 – 50.7

NOTE: For carboxyhemoglobin and methemoglobin results, due to the narrow range of blood samples used in the study, partitioned difference analysis method was used to assess the 95% confidence interval of the bias.

Parameter	N	Range	95% CI of Bias	Bias Spec.
COHb (%)	280	-0.1 – 3.3	0.17 - 0.24	±1.0
MetHb (%)	280	0.3 – 2.3	0.0 to 0.1	±1.0

Laboratory Testing Site No. 3:

A GEM Premier 3000 was used as the reference for pH, blood gases, electrolytes (except chloride), glucose, lactate, hematocrit, and an IL CO-Oximeter 682 was used for CO-Oximetry. Chloride was not run at this site.

Testing included 97 whole blood samples obtained from patients in the hospital submitted for stat analysis over a one-week period. Each sample was assayed in

duplicate on the GEM Premier 4000 and the reference devices. However, two sample results were unavailable (one on the reference device and one on the GEM Premier 4000), bringing the total to N=192 individual results per instrument, with the exceptions noted below.

Summary Statistics

Analyte	N	Slope	Intercept	r	Sample Range
pH	184	1.076	-0.574	0.995	7.01-7.57
pCO_2 (mmHg)	184	0.962	0.325	0.994	27-79
pO_2 (mmHg)	184	0.954	1.028	0.993	28-321
Na^+ (mmol/L)	184	0.924	11.372	0.975	130-150
K^+ (mmol/L)	184	1.018	-0.103	0.995	2.6-6.0
Ca^{++} (mmol/L)	184	0.985	0.048	0.988	0.91-1.49
Glucose (mg/dL)	98	0.977	2.190	0.995	57-237
Lactate (mmol/L)	184	0.946	0.057	0.999	0.7-12.3
Hct (%)	184	1.002	1.243	0.981	21-51
tHb (g/dL)	175	0.989	-0.153	0.987	7.5 – 17.2
O_2Hb (%)	175	1.002	0.316	0.996	52.1 – 98.2
HHb (%)	175	1.010	-0.433	0.999	0 – 46.3

NOTE: For carboxyhemoglobin and methemoglobin results, due to the narrow range of blood samples used in the study, partitioned difference analysis method was used to assess the 95% confidence interval of the bias.

Parameter	N	Range	95% CI of Bias	Bias Spec.
COHb (%)	175	0 – 6.7	0.1 - 0.3	± 1.0
MetHb (%)	175	0.2 – 1.4	-0.3 to -0.2	± 1.0

b. Matrix comparison:

A study was performed to demonstrate equivalence between the normal, capillary and micro sampling modes on the GEM Premier 4000. Each day, two whole blood sample preparations (Level 1 and Level 2) were tested in duplicate twice per day for 10 days on each of three different GEM Premier 4000 for a total of 40 samples per instrument and a pooled total of N=120 per level.

To compensate for day-to-day sample preparation variation, the evaluation utilized normalization techniques. The following reference instruments were run to monitor any sample degradation thus allowing for these normalization techniques:

Description	510(k)	Analyte(s)
GEM 3000 with iQM and GEM CVP	K022158	pH, blood gases, electrolytes (except chloride), glucose, lactate and hematocrit
IL Synthesis	K963800	Chloride
IL 682 CO-Oximeter	K945677	CO-Oximeter parameters

- The micro mode is not applicable to the CO-Oximetry parameters.

The table below and on the following pages contain the pooled SD for each analyte on the three different GEM Premier 4000 instruments, for each sampling mode, for two concentration levels. The specifications for within run and total SD are provided in each table for each level.

Level 1	pH				
Sampling Mode	N	Mean	Within Run SD	Day-to-Day SD	Total SD
Normal	120	7.05	0.009	0.005	0.011
Capillary	120	7.05	0.008	0.005	0.010
Micro	120	7.07	0.011	0.007	0.015
Spec. (SD)			0.015		0.020

Level 2	pH				
Sampling Mode	N	Mean	Within Run SD	Day-to-Day SD	Total SD
Normal	120	7.36	0.007	0.007	0.010
Capillary	120	7.36	0.007	0.007	0.013
Micro	120	7.35	0.009	0.007	0.012
Spec. (SD)			0.015		0.020

Level 1	pCO_2				
Sampling Mode	N	Mean mmHg	Within Run SD	Day-to-Day SD	Total SD
Normal	120	58.6	1.2	0.4	1.7
Capillary	120	57.7	1.0	1.0	1.6
Micro	120	61.3	1.7	1.0	2.5
Spec. (SD)			1.88 (2.3 Micro)		2.5 (3.0 Micro)

Level 2	pCO_2				
Sampling Mode	N	Mean mmHg	Within Run SD	Day-to-Day SD	Total SD
Normal	120	40.9	0.7	0.4	1.0
Capillary	120	40.2	0.9	0.0	1.3
Micro	120	40.6	1.3	0.2	1.7
Spec. (SD)			1.88 (2.3 Micro)		2.5 (3.0 Micro)

Level 1	pO_2				
Sampling Mode	N	Mean mmHg	Within Run SD	Day-to-Day SD	Total SD
Normal	108	30	1.9	1.1	2.6
Capillary	108	29	0.8	0.5	1.7
Micro	108	29	1.1	0.9	2.4
Spec. (SD)			3.4		4.5

Level 2	pO_2				
Sampling Mode	N	Mean mmHg	Within Run SD	Day-to-Day SD	Total SD
Normal	108	53	2.2	1.0	2.5
Capillary	108	51	1.6	0.7	2.0
Micro	108	55	1.2	0.1	2.1
Spec. (SD)			3.4		4.5

Level 1	Sodium				
Sampling Mode	N	Mean mmol/L	Within Run SD	Day-to-Day SD	Total SD
Normal	120	123	0.8	0.1	1.0
Capillary	120	124	0.7	0.8	1.2
Micro	120	120	0.7	1.0	1.4
Spec. (SD)			1.5		2.0

Level 2	Sodium				
Sampling Mode	N	Mean mmol/L	Within Run SD	Day-to-Day SD	Total SD
Normal	120	148	0.9	0.0	2.0
Capillary	120	150	1.1	0.5	1.8
Micro	120	147	1.0	1.2	2.0
Spec. (SD)			1.5		2.0

Level 1	Potassium				
Sampling Mode	N	Mean mmol/L	Within Run SD	Day-to-Day SD	Total SD
Normal	120	2.0	0.15	0.00	0.18
Capillary	120	1.9	0.04	0.06	0.08
Micro	120	2.2	0.03	0.03	0.12
Spec. (SD)			0.17		0.25

Level 2	Potassium				
Sampling Mode	N	Mean mmol/L	Within Run SD	Day-to-Day SD	Total SD
Normal	120	6.8	0.14	0.04	0.17
Capillary	120	6.6	0.13	0.00	0.18
Micro	120	6.9	0.08	0.07	0.16
Spec. (SD)			0.26		0.34

Level 1	Ionized Calcium				
Sampling Mode	N	Mean mmol/L	Within Run SD	Day-to-Day SD	Total SD
Normal	120	0.52	0.01	0.01	0.01
Capillary	120	0.52	0.01	0.01	0.01
Micro	120	0.46	0.01	0.01	0.01
Spec. (SD)			0.04		0.05

Level 2	Ionized Calcium				
Sampling Mode	N	Mean mmol/L	Within Run SD	Day-to-Day SD	Total SD
Normal	120	1.15	0.01	0.01	0.02
Capillary	120	1.15	0.02	0.01	0.02
Micro	120	1.16	0.02	0.01	0.02
Spec. (SD)			0.04		0.05

Level 1	Chloride				
Sampling Mode	N	Mean mmol/L	Within Run SD	Day-to-Day SD	Total SD
Normal	120	62	0.5	0.2	0.7
Capillary	120	62	0.5	0.3	0.7
Micro	120	62	0.4	0.5	0.8
Spec. (SD)			1.1		1.5

Level 2	Chloride				
Sampling Mode	N	Mean mmol/L	Within Run SD	Day-to-Day SD	Total SD
Normal	120	106	0.5	0.6	0.9
Capillary	120	106	0.7	0.4	0.9
Micro	120	106	0.7	0.7	1.0
Spec. (SD)			2.0		2.7

Level 1	Glucose				
Sampling Mode	N	Mean mg/dL	Within Run SD	Day-to-Day SD	Total SD
Normal	80	34	1.3	1.1	1.8
Capillary	80	34	1.2	0.8	2.3
Micro	80	32	0.8	0.5	1.8
Spec. (SD)			2.25		3.00

Level 2	Glucose				
Sampling Mode	N	Mean mg/dL	Within Run SD	Day-to-Day SD	Total SD
Normal	80	180	2.0	4.2	7.9
Capillary	80	178	2.0	3.7	7.9
Micro	80	181	2.4	4.0	7.4
Spec. (SD)			6.56		8.75

Level 1	Lactate				
Sampling Mode	N	Mean mmol/L	Within Run SD	Day-to-Day SD	Total SD
Normal	120	1.7	0.07	0.02	0.08
Capillary	120	1.7	0.08	0.03	0.10
Micro	120	1.6	0.06	0.05	0.10
Spec. (SD)			0.15		0.20

Level 2	Lactate				
Sampling Mode	N	Mean mmol/L	Within Run SD	Day-to-Day SD	Total SD
Normal	120	5.4	0.12	0.11	0.16
Capillary	120	5.4	0.14	0.09	0.17
Micro	120	5.3	0.11	0.05	0.18
Spec. (SD)			0.32		0.42

Level 1	Hematocrit				
Sampling Mode	N	Mean %	Within Run SD	Day-to-Day SD	Total SD
Normal	120	26.33	0.51	0.42	0.80
Capillary	120	26.30	0.44	0.55	0.87
Micro	120	26.67	0.75	0.62	1.10
Spec. (SD)			1.50		2.00

Level 2	Hematocrit				
Sampling Mode	N	Mean %	Within Run SD	Day-to-Day SD	Total SD
Normal	120	45.50	0.64	0.17	0.88
Capillary	120	45.37	0.65	0.29	0.88
Micro	120	46.23	0.80	0.54	1.21
Spec. (SD)			1.50		2.00

Level 1	Total Hemoglobin				
Sampling Mode	N	Mean g/dL	Within Run SD	Day-to-Day SD	Total SD
Normal	120	10.43	0.065	0.098	0.141
Capillary	120	10.58	0.078	0.108	0.157
Spec. (SD)			0.260		0.350

Level 2	Total Hemoglobin				
Sampling Mode	N	Mean g/dL	Within Run SD	Day-to-Day SD	Total SD
Normal	120	14.82	0.145	0.070	0.251
Capillary	120	14.89	0.188	0.083	0.225
Spec. (SD)			0.260		0.350

Level 1	O_2Hb				
Sampling Mode	N	Mean %	Within Run SD	Day-to-Day SD	Total SD
Normal	120	88.9	0.19	0.47	0.56
Capillary	120	88.8	0.17	0.47	0.54
Spec. (SD)			0.75		1.00

Level 2	O_2Hb				
Sampling Mode	N	Mean %	Within Run SD	Day-to-Day SD	Total SD
Normal	120	36.0	0.50	0.21	0.63
Capillary	120	36.1	0.37	0.02	0.41
Spec. (SD)			0.75		1.00

Level 1	COHb				
Sampling Mode	N	Mean %	Within Run SD	Day-to-Day SD	Total SD
Normal	120	10.66	0.11	0.20	0.32
Capillary	120	10.71	0.20	0.28	0.42
Spec. (SD)			0.75		1.00

Level 2	COHb				
Sampling Mode	N	Mean %	Within Run SD	Day-to-Day SD	Total SD
Normal	120	0.84	0.14	0.13	0.20
Capillary	120	0.84	0.15	0.11	0.20
Spec. (SD)			0.75		1.00

Level 1	MetHb				
Sampling Mode	N	Mean %	Within Run SD	Day-to-Day SD	Total SD
Normal	120	3.30	0.14	0.15	0.26

Level 2	MetHb				
Sampling Mode	N	Mean %	Within Run SD	Day-to-Day SD	Total SD
Normal	120	6.20	0.16	0.22	0.30

Capillary	120	3.29	0.15	0.20	0.28
Spec. (SD)			0.75		1.00

Level 1	HHb				
Sampling Mode	N	Mean %	Within Run SD	Day-to-Day SD	Total SD
Normal	120	0.00	0.15	0.32	0.37
Capillary	120	0.00	0.27	0.34	0.43
Spec. (SD)			2.25		3.00

Capillary	120	6.12	0.17	0.28	0.37
Spec. (SD)			0.75		1.00

Level 2	HHb				
Sampling Mode	N	Mean %	Within Run SD	Day-to-Day SD	Total SD
Normal	120	63.0	0.47	0.40	0.72
Capillary	120	62.9	0.37	0.13	0.43
Spec. (SD)			2.25		3.00

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):
   See the Method Comparison section above.

4. Clinical cut-off:
   Not Applicable.

5. Expected values/Reference range:
   The following table provides general reference ranges from published literature. The sponsor recommends that each laboratory should establish its own reference ranges.

Measured Analyte	**Units**	**Arterial Reference Range (Adult)**
pH	n/a	7.35 to 7.45
pCO_2	mmHg	35 to 48
pO_2	mmHg	83 to 108
Na^+	mmol/L	136 to 145 [1,2]
K^+	mmol/L	3.4 to 4.5 [1]
Ca^{++}	mmol/L	1.15 to 1.35
Cl^-	mmol/L	98 to 107 [1,2]
Glu	mg/dL	60 to 95

Measured Analyte	Units	Arterial Reference Range (Adult)
Lac	mmol/L	0.5 to 2.2
Hct	%	35 to 51
tHb	g/dL	11.7 to 17.4
O_2Hb	%	94 to 97
COHb	%	0.5 to 1.5 (non-smoking)
MetHb	%	< 1.0
HHb	%	0 to 5

[1] Plasma (Hep)[2]Serum

References:

- Henry, JB, Clinical Diagnosis & Management by Laboratory Methods, WB Saunders Co., Philadelphia, 18th Edition, 1991.
- Tietz, NW, Fundamentals of Clinical Chemistry, WB Saunders Co., Philadelphia, 4th Edition, 1996.
- Bishop, ML, Duben-Engelkirk, JL, Fody, EP, Clinical Chemistry – Principles Procedures Correlations, JB Lippincott Co., 2nd Edition, 1992.

N. Instrument Name:

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

O. System Descriptions:

1. Modes of Operation:
   The instrument has three modes of operation: normal, capillary, and micro mode. The system's core operation module (the PAK cartridge) can also be purchased in different configurations of analyte measuring capabilities (e.g. with or without electrolyte testing).
2. Software:
   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:
   Yes ___X____ or No _____
3. Specimen Identification:
   Sample identification is performed through an interface which instructs the device which sample types are to be detected.
4. Specimen Sampling and Handling:
   The sponsor indicates in the operator's manual that it is recommended that the samples be well mixed prior to introduction into the analyzer. In the operator's manual, topics

covered by training videos on the system are identified with icons. The videos cover topics such as sample handling, patient sampling, and inserting and removing the cartridge. The sponsor also cautions the user that only sodium or lithium anticoagulant be used with samples.

5. Calibration:
   As part of this program, GEM CVP (Calibration Valuation Product) with CO-Ox and GEM CVP Hematocrit are external solutions intended to complete the calibration process and final accuracy assessment of the iQM cartridge calibration after initial warm-up. The reported values for the four levels of GEM CVP (two levels for pH, blood gases, electrolytes, metabolites and CO-Oximetry; two levels for hematocrit) must meet specifications before the iQM cartridge can be used for patient sample measurements. Once the cartridge calibration is verified, the internal iQM program monitors the status of the system during the cartridge use life. The GEM CVP solutions are pre-tonometered and contain known quantities of the analytes and dyes tested using CLSI and NIST traceable reference standards.
6. Quality Control:
   The sensors of the instrument are calibrated and monitored with four Process Control Solutions A, B, C and D. These solutions are pre-tonometered and contain known quantities of the analytes and dyes tested using NIST traceable reference standards. The solutions are sealed in gas impermeable bags with no headspace.

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

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.