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

A. 510(k) Number:

k160412

B. Purpose for Submission:

New device

C. Measurand:

pH, pCO_2, and pO_2 in whole blood

D. Type of Test:

Potentiometry for pH and pCO_2

Amperometry for pO_2

E. Applicant:

Instrumentation Laboratory Co.

F. Proprietary and Established Names:

GEM® Premier 5000 (Measured Parameters: pH, pCO_2, and pO_2)

G. Regulatory Information:

1. Regulation section:

   21 CFR § 862.1120 Blood gases (pCO_2 and pO_2) and blood pH test system.

2. Classification:

   Class II

3. Product code:

   CHL

4. Panel:

   Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See indications for use below.

2. Indication(s) for use:

   The GEM Premier 5000 system 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 pH and pO_2 from venous, arterial and capillary heparinized whole blood, as well as quantitative measurements of pCO_2 from venous and arterial heparinized whole blood. These parameters, along with derived parameters, aid in the diagnosis of a patient's acid/base status.

   pH, pCO_2 and pO_2 measurements in whole blood are used in the diagnosis and treatment of life-threatening acid-base disturbances.

3. Special conditions for use statement(s):

   For prescription use only.

   For clinical laboratory and point-of-care use.

4. Special instrument requirements:

   GEM Premier 5000 analyzer

I. Device Description:

The GEM Premier 5000 system contains two key components: the GEM Premier 5000 analyzer and the GEM Premier 5000 PAK (cartridge):

GEM Premier 5000 PAK
The GEM® Premier 5000 PAK is a disposable, multi- assay cartridge which includes measurements of pH, pCO_2 and pO_2. The cartridge is used exclusively with the GEM Premier 5000 analyzer. The cartridge houses all required components to test heparin whole blood samples for pH, pCO_2 and pO_2. The components include the sensors, reagents, CO-Ox optical cell, Process Control Solutions, sampler, pump tubing, distribution valve, and waste bag. The cartridge contains sufficient materials to operate the analyzer for 75 to 600 tests.

The five Process Control Solutions (A, B, C, D, and E) contained on the GEM Premier 5000 PAK are control materials and calibration verifiers. These materials are tonometered to specific levels of pO_2 and pCO_2, and contain known pH values tested using CLSI and NIST traceable reference standards. The solutions are sealed in gas impermeable bags with no headspace.

GEM Premier 5000 analyzer
The GEM Premier 5000 analyzer 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.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   GEM® Premier 4000 for pH, pCO_2, and pO_2

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

   k133407

3. Comparison with predicate:

Similarities		
Item	Candidate Device k160412 GEM Premier 5000 for pH, pCO_2, and pO_2	Predicate k133407 GEM Premier 4000 for pH, pCO_2, and pO_2
Intended use	The GEM Premier 5000 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, and pO_2.	Same
Intended user	Central Laboratory and Point-of-Care sites	Same
Type of Measurement	Potentiometry: pH and pCO2	Same

Similarities		
	Amperometry: pO2	
Sample type	Lithium heparin whole blood	Same
Sampling devices	Heparinized syringe and heparinized capillary tube	Same
Measuring modes and sample volumes	Normal Mode for syringe: 150 µL Normal Mode for capillary tube: 150 µL tBili/CO-Ox for capillary tube: 100 µL Micro Mode for capillary tube: 65 µL	Same
Time to analysis	Analyze samples within 15 minutes from draw.	Same
Calibration	2-point calibration	Same

Differences		
Item	Candidate Device k160412 GEM Premier 5000 for pH, pCO_2, and pO_2	Predicate k133407 GEM Premier 4000 for pH, pCO_2, and pO_2
Measurement ranges	pH 7.00 to 7.92 pCO_2 6 to 125 mmHg pO_2 6 to 690 mmHg	pH 7.00 to 8.00 pCO_2 6 to 125 mmHg pO_2 5 to 690 mmHg
Specimens	pH: Arterial, capillary, and venous pCO_2: Arterial and venous pO_2: Arterial, capillary, and venous	pH: Arterial, capillary, and venous pCO_2: Arterial, capillary, and venous pO_2: Arterial, capillary, and venous

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

CLSI EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline, 3rd Edition.

CLSI EP06-A: Evaluation of Linearity of Quantitative Measurement Procedures; A Statistical Approach; Approved Guideline. First Edition.

CLSI EP07-A2. Interference Testing in Clinical Chemistry; Approved Guideline. Second Edition.

CLSI EP09-A3 Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline.

CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline. Second Edition.

CLSI EP25-A: Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline.

L. Test Principle:

Assay principles:

pH — pH is measured using an ion selective electrode on the GEM Premier 5000 PAK. The result may be corrected for actual patient temperature if different than 37°C.

pCO_2 — pCO_2 is measured by potentiometry using a sensor on the GEM Premier 5000 PAK. The result may be corrected for actual patient temperature if different than 37°C.

pO_2 — pO_2 is measured amperometrically using a three electrode cell configuration with platinum working electrode. The result may be corrected for actual patient temperature if different than 37°C.

Derived parameters:
The following are derived parameters which utilize measured pH, pCO_2, and pO_2 values:

Total Carbon Dioxide, Base Excess of Extracellular Fluid, Base Excess of Blood, Arterial partial pressure / inspired oxygen ratio, Alveolar oxygen partial pressure, Arterial oxygen content, Oxygen content, Partial pressure of O_2 in a hemoglobin solution, Alveolar-arterial oxygen gradient, Arterial-alveolar oxygen ratio, Respiratory index, End pulmonary capillary oxygen content, Arterial-mixed venous oxygen gradient mixed venous oxygen content, Estimated shunt, Physiological shunt, Actual bicarbonate, and Calculated oxygen saturation.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Four separate precision studies were conducted to evaluate the precision of the GEM Premier 5000 system for pH, pCO_2, and pO_2 and were conducted according to CLSI EP05-A3 guidance document.

#1 Internal precision study using control material – GEM System Evaluators
An internal precision study was performed on the GEM Premier 5000 for pH, pCO_2, and pO_2 using GEM System Evaluators 1, 2 and 3 control materials.

The GEM System Evaluators 1, 2, 3 (previously cleared in k093623) are ampules of three levels of assayed quality control material intended for evaluating performance characteristics of pH, pCO_2, pO_2, and other analytes on the GEM Premier 5000 analyzer.

Each of the control levels was run on three GEM Premier 5000 analyzers for 20 days, with two runs per day and one replicate measured per run per level for a total of n=120 replicates. The samples were introduced into the analyzer using the QC sample drawn mode. The results are given as follows:

Analyte	Level	Mean	N	Within Analyzer SD	Within Analyzer %CV	Total SD	Total %CV
pH	1	7.14	120	0.008	0.1%	0.008	0.1%
	2	7.38	120	0.004	0.1%	0.006	0.1%
	3	7.57	120	0.003	0.0%	0.003	0.0%
pCO_2 (mmHg)	1	87	120	2.3	2.7%	2.3	2.7%
	2	35	120	0.7	1.9%	0.8	2.3%
	3	14	120	0.3	2.2%	0.3	2.3%
pO_2 (mmHg)	1	31	120	1.9	6.1%	2.4	7.9%
	2	88	120	1.2	1.4%	2.2	2.4%
	3	370	120	4.8	1.3%	5.9	1.6%

#2 Internal precision study using whole blood samples
Note: Capillary not claimed for pCO_2 on the GEM Premier 5000.

An internal precision study was performed on the GEM Premier 5000 for pH, pCO_2, and pO_2 using lithium heparin whole blood samples.

Donor venous blood was collected in balanced lithium heparinized blood collection tubes. For the pO_2 and pCO_2, five levels were prepared by tonometrization. For pH, whole blood was adjusted to the five levels using carbonate.

For pH and the pO_2 each sample was tested in two sampling modes: normal using 150 µL with syringe and micro using 65 µL with capillary tube. For pCO_2 each sample was tested in normal using 150 µL with syringe. The samples were run on three GEM Premier 5000 analyzers per sample mode for five days, with one run per day and 8 replicates measured per run per level for a total of 120 replicates per level.

Day-to-day variability was not assessed due to the in vitro instability of whole blood. Fresh blood samples at each level were prepared daily. The results are given as follows:

Analyte	Mode	Level	Mean	N	Within Run SD	Within Run %CV	Total SD*	Total %CV*
pH	Normal	1	7.11	120	0.004	0.1%	0.005	0.1%
		2	7.33	120	0.007	0.1%	0.007	0.1%
		3	7.35	120	0.004	0.1%	0.005	0.1%
		4	7.42	120	0.005	0.1%	0.006	0.1%
		5	7.68	120	0.012	0.1%	0.014	0.2%
	Micro	1	7.10	120	0.006	0.1%	0.007	0.1%
		2	7.32	120	0.004	0.1%	0.006	0.1%
		3	7.35	120	0.004	0.1%	0.005	0.1%
		4	7.41	120	0.005	0.1%	0.006	0.1%
		5	7.67	120	0.013	0.2%	0.015	0.2%
pCO2** (mmHg)	Normal	1	112	120	2.7	2.4%	2.9	2.3%
		2	70	120	1.1	1.5%	1.5	2.0%
		3	50	120	0.6	1.2%	0.8	1.5%
		4	36	120	0.5	1.3%	0.8	1.9%
		5	10	120	0.5	4.6%	0.8	7.7%
pO2 (mmHg)	Normal	1	32	120	0.4	1.2%	0.9	2.7%
		2	62	120	0.7	1.1%	0.9	1.2%
		3	204	120	2.3	1.1%	3.1	1.4%
		4	415	120	8.6	2.1%	13.0	2.8%
		5	722	120	18.6	2.6%	32.7	4.3%
	Micro	1	31	120	0.9	3.0%	1.6	5.3%
		2	62	120	0.7	1.1%	0.9	1.4%
		3	204	120	4.3	2.1%	5.5	2.5%
		4	402	120	15.3	3.8%	16.4	3.8%
		5	693	120	26.5	3.8%	34.0	4.8%

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

** The candidate device is not intended for the measurement of pCO_2 in capillary samples; therefore, only pCO_2 data from syringe samples tested under normal mode is shown in the table.

#3 Point of Care setting using control material - GEM System Evaluators
A reproducibility study at three point of care sites in hospital settings was performed on the GEM Premier 5000 for pH, pCO_2, and pO_2 using the GEM System Evaluators 1, 2 and 3 control material.

The studies were conducted by 9 different operators (perfusionists and respiratory therapists) on three different GEM Premier 5000 instruments using a single lot of GEM Premier 5000 PAKs. Each site used the same lot of GEM System Evaluators and running each control level in triplicate, twice a day for 5 days, for a total of 30 replicates per level per site. The samples were introduced into the analyzer using the QC sample drawn mode. The results are given as follows:

Point of care site 1:

Analyte	Level	N	Mean	Repeatability		Within Site	
				SD	%CV	SD	%CV
pH	1	30	7.14	0.003	0.0%	0.003	0.0%
	2	30	7.39	0.005	0.1%	0.007	0.1%
	3	30	7.57	0.000	0.0%	0.000	0.0%
pCO_2 (mmHg)	1	30	87	0.6	0.7%	1.1	1.3%
	2	30	34	0.7	1.9%	0.7	2.0%
	3	30	13	0.4	3.1%	0.4	3.3%
pO_2 (mmHg)	1	30	30	0.8	2.6%	1.0	3.3%
	2	30	87	1.5	1.7%	1.6	1.8%
	3	30	351	8.2	2.3%	8.6	2.5%

Point of care site 2:

Analyte	Level	N	Mean	Repeatability		Within Site	
				SD	%CV	SD	%CV
pH	1	30	7.14	0.002	0.0%	0.003	0.0%
	2	30	7.39	0.010	0.1%	0.011	0.1%
	3	30	7.57	0.002	0.0%	0.005	0.1%
pCO2 (mmHg)	1	30	87	0.2	0.2%	1.2	1.4%
	2	30	34	1.2	3.5%	1.3	3.8%
	3	30	13	0.4	3.0%	0.4	3.0%
pO2 (mmHg)	1	30	28	0.6	2.1%	1.0	3.6%
	2	30	87	1.7	2.0%	1.7	2.0%
	3	30	360	9.1	2.5%	9.0	2.5%

Point of care site 3:

Analyte	Level	N	Mean	Repeatability		Within Site	
				SD	%CV	SD	%CV
pH	1	30	7.14	0.000	0.0%	0.000	0.0%
	2	30	7.38	0.003	0.0%	0.005	0.1%
	3	30	7.57	0.003	0.0%	0.003	0.0%
pCO2 (mmHg)	1	30	87	0.4	0.5%	0.8	1.0%
	2	30	34	0.5	1.5%	0.6	1.6%
	3	30	13	0.5	3.6%	0.5	3.9%
pO2 (mmHg)	1	30	27	0.6	2.1%	1.0	3.6%
	2	30	85	1.2	1.4%	1.3	1.6%
	3	30	359	6.3	1.7%	6.5	1.8%

All 3 point of care sites combined:

Analyte	Level	N	Mean	Repeatability		Reproducibility	
				SD	%CV	SD	%CV
pH	1	90	7.14	0.002	0.0%	0.002	0.0%
	2	90	7.39	0.007	0.1%	0.008	0.1%
	3	90	7.57	0.002	0.0%	0.003	0.0%
pCO_2 (mmHg)	1	90	87	0.4	0.5%	1.1	1.2%
	2	90	34	0.9	2.5%	0.9	2.7%
	3	90	13	0.4	3.3%	0.5	3.5%
pO_2 (mmHg)	1	90	28	0.7	2.3%	1.9	6.7%
	2	90	87	1.4	1.7%	1.9	2.2%
	3	90	357	7.9	2.2%	9.3	2.6%

#4 Point of Care setting using whole blood samples

Note: Capillary not claimed for pCO_2 on the GEM Premier 5000.

A precision study at two central laboratories, one company internal customer simulation laboratory, and three point of care sites in hospital settings was performed on the GEM Premier 5000 for pH, pCO_2, and pO_2 using lithium heparinized whole blood patient samples.

All samples were arterial or venous native whole blood patient samples from individual donors. At least two whole blood specimens were analyzed in triplicate daily for 5 days in two sampling modes: normal using 150 µL with syringe and micro using 65 µL with capillary tube. A new specimen was used for each sample mode.

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.

Reproducibility was not assessed due to the in vitro instability of whole blood. Fresh blood samples were collected daily. The repeatability results are given as follows:

Analyte	Sample Mode	Site	N	Mean	Min	Max	Within sample SD
pH	Normal Mode	POC1	54	7.36	7.21	7.47	0.008
		POC2	42	7.33	7.14	7.43	0.009
		POC3	30	7.35	7.06	7.51	0.008
		POC-All	126	7.35	7.06	7.51	0.008
		CSL	30	7.32	7.28	7.39	0.009
		Lab1	30	7.36	7.20	7.44	0.009
		Lab2	30	7.32	7.24	7.44	0.007
		Lab-All	90	7.33	7.20	7.44	0.008
	Micro Mode	POC1	30	7.29	7.17	7.42	0.009
		POC2	36	7.32	7.18	7.45	0.012
		POC3	36	7.28	6.97	7.45	0.012
		POC-All	102	7.30	6.97	7.45	0.011
		CSL	30	7.30	7.26	7.37	0.008
		Lab1	30	7.33	7.21	7.48	0.007
		Lab2	30	7.26	6.94	7.46	0.009
		Lab-All	90	7.30	6.94	7.48	0.008

Analyte	Sample Mode	Site	N	Mean	Min	Max	Within sample SD
pCO_2* mmHg	Normal Mode	POC1	48	43	33	54	1.1
		POC2	39	42	28	56	0.8
		POC3	30	49	40	61	1.7
		POC-All	117	44	28	61	1.2
		CSL	24	53	48	61	1.3
		Lab1	30	46	40	58	1.3
		Lab2	24	46	28	56	0.8
		Lab-All	78	48	28	61	1.2

Analyte	Sample Mode	Site	N	Mean	Min	Max	Within sample SD or CV%
pO_2 (mmHg)	Normal Mode	POC1	27	52	35	85	1.5
		POC2	12	63	55	70	0.4
		POC3	12	71	51	86	2.0
		POC-All	51	59	35	86	1.5
		CSL	30	52	32	79	0.6
		Lab1	21	55	42	85	0.8
		Lab2	15	50	26	95	3.9
		Lab-All	66	53	26	95	0.8
		POC1	27	147	82	191	6.0%
		POC2	30	175	97	402	2.6%
		POC3	18	154	103	218	3.4%
		POC-All	75	160	82	402	4.0%
		Lab1	9	110	92	130	1.1%
		Lab2	15	145	112	195	2.1%
		Lab-All	24	132	92	195	1.7%
pO_2 (mmHg)	Micro Mode	POC1	21	53	46	65	1.5
		POC2	6	45	33	59	1.2
		POC3	18	58	43	82	1.1
		POC-All	45	54	33	82	1.3
		CSL	30	54	31	83	0.8
		Lab1	24	60	40	89	1.0
		Lab2	18	52	39	67	1.1
		Lab-All	72	56	31	89	1.0
		POC1	9	130	94	186	2.3%
		POC2	30	216	90	413	4.4%
		POC3	18	135	83	199	4.2%
		POC-All	57	177	83	413	4.0%
		Lab1	6	124	119.0	128.0	3.3%
		Lab2	12	149	100.0	214.0	2.6%
		Lab-All	18	141	100	214	2.8%

* The candidate device is not intended for the measurement of pCO_2 in capillary samples; therefore, only pCO_2 data from syringe samples tested under normal mode is shown in the table.

b. Linearity/assay reportable range:

The linearity studies were performed on GEM Premier 5000 pH, pO_2 and pCO_2 following CLSI EP06-A guidance.

To challenge the measuring range, pH was tested for linearity at 8 levels, and pO_2 and pCO_2 were tested at 9 levels. The samples were venous whole blood from healthy volunteers that were adjusted to different levels by addition of carbonate for pH samples, and tonometrization for pO_2 and pCO_2 samples. The concentrations for pH were assigned using the Radiometer ABL 837 as a reference device. For pO_2 and pCO_2 the concentrations were assigned by tonometry using commercially available gases.

The whole blood concentration pools were adjusted so that one pool exceeded the upper end of the range by 20-30% and one pool exceeded the lower end of the range by 20-30%, wherever possible. For pH, the upper end of the reference analyzer measuring range was the same as the anticipated GEM Premier 5000 claimed measuring range, thus the sample level exceeding the upper limit was omitted. For pO_2, test samples could not be adjusted beyond 756 mmHg under ambient atmospheric conditions, thus the upper end of the claimed measuring range was not exceeded. Each blood sample was analyzed in triplicate on three GEM Premier 5000 analyzers and results compared to the reference measurements.

For pH, regression analysis found a statistically significant coefficient for a second order polynomial fit which indicated possible non-linearity. Linearity was further assessed by comparing the deviation of the regression line from linearity. At each level, the deviation from linearity was less than ±0.04 pH units.

For pCO_2, regression analysis found a statistically significant coefficient for a third order polynomial fit which indicated possible non-linearity. Linearity was further assessed by comparing the deviation of the regression line from linearity. At each level, the deviation from linearity was less than ±5 mmHg.

For pO_2, regression analysis found that the coefficients for a second or third order polynomial fit were not statistically significant. Therefore, the pO_2 results demonstrate a satisfactory linear response over the measuring range.

The linear regression results are given in the table below:

Analyte	Slope	Intercept	R^2	Tested Range	GEM Premier 5000 Claimed Measuring Range
pH	0.972	0.191	0.998	6.67 to 7.97	7.00 to 7.92
pCO_2 (mmHg)	1.045	-2.027	0.998	1 to 149	6 to 125
pO_2 (mmHg)	1.028	-4.069	0.995	5 to 727	6 to 690

Based on these results, the sponsor concluded that the linearity data support the claimed measuring range for pH, pCO_2, and pO_2.

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

Traceability:
The GEM Premier 5000 PAK measurement for pCO_2 is traceable to tonometry at 37°C using NIST traceable gas mixtures.

The GEM Premier 5000 PAK measurement for pO_2 is traceable to tonometry at 37°C using NIST traceable gas mixtures.

The GEM Premier 5000 PAK measurement for pH is traceable to NIST Standard Reference Material 186g.

Stability:
Stability studies were performed with GEM Premier 5000 PAK for pH, pCO_2, and pO_2. The protocols for stability and acceptance criteria were reviewed and found to be adequate.

Shelf life stability studies demonstrated that GEM Premier 5000 PAK is stable for 180 days when stored in the claimed range of 15-25°C. The on-board stability of the GEM Premier 5000 PAK is 31 days or for 600 sample usage. The cartridges are stable when exposed to transport conditions for days at 10-38°C and up to 10,000 feet altitude.

d. *Detection limit:*

Linearity studies were used to support the lower end of the measuring range for pH, pCO_2, and pO_2.

e. *Analytical specificity:*

In accordance with EP07-A2, an interference study was conducted on the GEM Premier 5000 for pH, pCO_2, and pO_2.

Heparinized whole blood from healthy volunteers was collected daily for the samples. With these samples, an interference screening test was conducted at 2 levels of pH, pCO_2, and pO_2. At each level, a potential interfering substance was spiked at a worse case high concentration. The substances tested represent anesthetics and medications often prescribed for critically ill patients and endogenous substances. Interference was calculated as the bias between the average test result with interfering substance and average control measurement across the three GEM Premier 5000 analyzers. The control sample was prepared by spiking diluent only.

The sponsor stated that interference was considered to be non-significant if the bias between the test and control sample was within the following criteria:

Analyte	Unit	Significant interference criteria, within:
pH		± 0.02
pCO2	mmHg	± 8%
pO2	mmHg	± 10%

No significant interference was observed with the substances tested on pH, pCO_2, and pO_2. The table below lists substances that were tested:

Endogenous substances:

Substance	Highest conc. tested without significant interference in pH, pO_2, and pCO_2
Albumin (Human)	60 g/L
Bilirubin	20 mg/dL
Hemoglobin (Hemolysis)	2000 mg/dL (20%)
Triglycerides (as INTRALIPID® 20%)	4012 mg/dL

Exogenous substances:

Substance	Highest conc. tested without significant interference in pH, pO_2, and pCO_2
Acetaminophen	1324 µmol/L
Amoxicillin	206 µmol/L
Aprotinin	50 mg/L
Atracurium	50 mg/L
Benzalkonium (Chloride)	5 mg/L
Ceftriaxone	1460 µmol/L
Ciprofloxin	30.2 µmol/L
Diazepam	18 µmol/L
Epinephrine	0.5 µmol/L
Ethanol	86.8 mmol/L
Etomidate	50 mg/L
Fentanyl	0.02 µg/ml
Gentamycin	21 µmol/L
Halothane	759 µmol/L
Lithium (Chloride)	3.2 mmol/L
Methadone	6.46 µmol/L
Midazolam	0.5 µg/mL
Morphine	1.75 µmol/L
Omeprazole	17.4 µmol/L
Phenobarbital	431 µmol/L
Propofol	0.05 mg/mL
Suxamethonium	68 µmol/L
Thiopental	248 µmol/L
Thyroxine	1.29 µmol/L

Hematocrit:
The sponsor conducted a screening interference study to demonstrate that changes in hematocrit do not affect the pH, pCO_2, and pO_2 measurements. Whole blood samples at two levels of hematocrit (25% and 75%) representing the lowest and highest hematocrit levels were tested at two levels for each of the blood gases and compared to the same samples with normal hematocrit. The results demonstrated bias less than the significant interference criteria (see table above). Based on the hematocrit study results, the sponsor concluded that hematocrit levels between 25% to 75% do not significantly interfere with the pH, pCO_2, and pO_2 measurements.

Altitude study:
A study was conducted to demonstrate that altitudes between sea level and 10,000 feet (3050 meters) have no significant effect on the GEM Premier 5000 for pH, pCO_2 and pO_2 measurements. Two sites were selected with altitudes of 10,152 feet (high altitude site) and 135 feet (low altitude site). At each site, samples were prepared from heparinized whole blood using gas mixtures to create different pH and blood gas levels. Since identical analyte levels could not be achieved at each of the two sites, the altitude study analysis consisted of: (1) fitting a linear regression line to the values obtain with the six levels for each site, (2) deriving the measurement bias between the two sites by calculating the difference between the regression lines at target levels for pH, pO_2, and pCO_2, and (3) comparing the measurement bias to the significant interference criteria (see table above).

Target Levels		
pH	pO_2	pCO_2
7.00	10	10
7.20	30	35
7.30	45	50
7.35	60	70
7.45	200	100
7.70	450	125

The concentration of each sample was assigned based on the following:

Analyte	Reference Method
pH	GEM Premier 3000
pCO_2	Tonometry
pO_2	Tonometry

Three replicates of heparinized whole blood were run per analyte level on the GEM Premier 5000 and the reference methods at each site. The results are as follows:

pH			
Target	Low Altitude result	High Altitude result	High Altitude Bias at the target level
7.00	7.01	7.00	-0.01
7.20	7.20	7.20	0.00
7.30	7.30	7.30	0.00
7.35	7.34	7.35	0.00
7.45	7.44	7.44	0.00
7.70	7.68	7.69	0.01

pCO_2			
Target (mmHg)	Low Altitude result	High Altitude result	High Altitude Bias at the target level
10	12.3	10.9	-1.4
35	36.2	36.5	0.3
50	50.5	51.8	1.3
70	69.6	72.3	3.9%
100	98.2	103.0	4.8%
125	122.0	128.5	5.2%

pO_2			
Target(mmHg)	Low Altitude result	High Altitude result	High Altitude Bias at the target level
10	10.8	14.7	3.9
30	30.5	34.9	4.4
45	45.3	50.1	4.8
60	60.2	65.3	5.1
200	198.5	207.1	4.3%
450	445.4	460.3	3.3%

Based on the altitude study results, the sponsor concluded that the candidate device operates up to 10,000 feet altitude for pH, pCO_2, and pO_2.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

Method comparison studies were performed following CLSI EP9-A3.

#1. Point-of-Care Method Comparison for pH, pO_2, and pCO_2 using normal syringe mode

A POC method comparison study was performed to establish the accuracy performance of the GEM Premier 5000 for pH, pO_2, and pCO_2 at three external point-of-care (POC) settings.

A minimum of one operator at each POC site participated in sample analysis. Each site used one GEM Premier 5000 analyzer and one GEM Premier 4000 analyzer. The samples were leftover native whole blood samples from the routine hospital population. These samples comprised both venous and arterial collections.

A subset of about 12% of the total samples was adjusted to cover medical decision levels that could not be sourced by native specimens. These results were combined with each POC sites results.

Samples were tested in the normal syringe mode (150 µL). Patient samples were run in singlicate on one GEM Premier 5000 and the results were compared to those obtained on the predicate device (GEM Premier 4000) by the same operator.
The linear regression analysis from the combined POC sites is presented below:

Analyte	N	Slope	95% CI for Slope	Intercept	95% CI for Intercept	r^2	Sample range tested
pH	479	0.941	0.927, 0.955	0.427	0.325, 0.530	0.991	7.01 to 7.92
pO_2	506	0.992	0.984, 1.000	5.093	4.000, 5.717	0.996	6 to 685
pCO_2	492	0.955	0.941, 0.971	3.545	2.743, 4.176	0.991	11 to 117

#2. Point-of-Care Method Comparison for pH and pO2 using normal capillary mode with capillary specimens

Note: Capillary not claimed for pCO_2 on the GEM Premier 5000.

A POC method comparison study was performed to establish the accuracy performance of the GEM Premier 5000 for pH and pO_2 at an external POC site in a hospital and an internal laboratory which simulated a POC site.

The samples were prospectively collected whole blood capillary specimens. On each patient, two skin puncture specimens were collected consecutively into two capillary tubes containing lithium heparin. A minimum of 300 µL whole blood per patient was collected. The internal site tested healthy donors and the external site used samples

from a Cardiac Care Unit and a Progressive Cardiac Care Unit. There were 99 males and 55 females in the study. The age range was 18 to 84 years.

Each site used one GEM Premier 5000 analyzer and one GEM Premier 4000 analyzer. There were two POC operators at the external site and three POC operators at the internal site. The operators were hospital staff with no formal laboratory training.

After collection, the samples were immediately tested in normal capillary mode on the GEM Premier 5000 and GEM Premier 4000 (predicate) by the same POC operator. The results based on native capillary samples at Medical Decision Level are summarized below.

Analyte	Range Min	Range Max	Medical decision level (MDL)	Bias at MDL	95% CI of Bias at MDL
pH (N=171)	7.36	7.59	7.30	0.002	-0.015 to 0.020
			7.35	0.005	-0.006 to 0.016
			7.45	0.010	0.005 to 0.014
pO_2 (N=167)	52	105	30	6.1	1.3 to 11.6
			45	5.1	2.0 to 8.6
			60	4.1	2.0 to 5.7

The data from this POC method comparison study with native capillary samples was combined with contrived samples and tested internally in order to cover the claimed measuring range.

Linear regression analysis from the combined data is presented below:

Analyte	N	Slope	95% CI for Slope	Intercept	95% CI for Intercept	r^2	Range
pH	189	0.935	0.899, 0.970	0.494	0.228, 0.760	0.975	7.07 to 7.89
pO2	218	1.008	0.994, 1.040	2.545	0.858, 4.000	0.996	6 to 676

b. Matrix comparison:

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

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable.

b. Clinical specificity:

Not applicable.

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable.

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

The following are the reference ranges for pH, pCO_2, and pO_2 taken from published literature.

pH	7.35 to 7.45, arterial adult blood 7.32 to 7.42, venous blood
pCO_2	35 to 48 mmHg, adult male arterial blood 32 to 35 mmHg, adult female arterial blood 6 to 7 mmHg, venous blood (right atrium), reported as an increase over arterial blood
pO_2	83 to 108 mmHg, arterial adult blood

The sponsor recommends that each laboratory establish their own reference ranges.

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

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.