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

A. 510(k) Number:

k183549

B. Purpose for Submission:

New device

C. Measurand:

Sodium, potassium, ionized calcium and chloride

D. Type of Test:

Quantitative, potentiometric method.

E. Applicant:

Instrumentation Laboratory Co.

F. Proprietary and Established Names:

GEM Premier ChemSTAT

G. Regulatory Information:

Regulation section	Classification	Product code	Panel
21CFR§862.1665 Sodium test system	Class II	JGS	Chemistry (75)
21CFR§862.1600 Potassium test system		CEM	
21CFR§862.1145 Calcium test system		JFP	
21CFR§862.1170 Chloride test system		CGZ	
21 CFR 862.2160 Discrete Photometric Analyzer Chemistry For Clinical Use	Class I, exempt	JJE	

H. Intended Use:

1. Intended use(s):

   See Indication(s) for Use below.

2. Indication(s) for use:

   The GEM Premier ChemSTAT is a portable critical care system for use by health care professionals to rapidly analyze lithium heparinized whole blood samples at the point of health care delivery in a clinical setting and in a central laboratory. The instrument provides quantitative measurements of sodium (Na^+), potassium (K^+), ionized calcium (Ca^{++}) and chloride (Cl^-) from arterial and venous heparinized whole blood. These parameters, along with derived parameters, aid in the diagnosis of a patient's electrolyte balance.

   Electrolytes in the human body have multiple roles. Nearly all metabolic processes depend on or vary with electrolytes:
   - Sodium (Na^+) measurements are used in the diagnosis and treatment of aldosteronism, diabetes insipidus, adrenal hypertension, Addison's disease, dehydration, inappropriate antidiuretic secretion, or other diseases involving electrolyte imbalance.
   - Potassium (K^+) measurements are used to monitor electrolyte balance in the diagnosis and treatment of disease conditions characterized by low or high blood potassium levels.
   - Ionized calcium (Ca^{++}) measurements are used in the diagnosis and treatment of parathyroid disease, a variety of bone diseases, chronic renal disease and tetany.
   - Chloride (Cl^-) measurements are used in the diagnosis and treatment of electrolyte and metabolic disorders, such as, cystic fibrosis and diabetic acidosis.

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 ChemSTAT analyzer

I. Device Description:

The GEM Premier ChemSTAT is a portable system that analyzes arterial and venous lithium heparinized whole blood at the point of health care delivery in a clinical setting and in a central laboratory for Na^+, K^+, Ca^{++} and Cl^-. All tests are included in a single self-contained, disposable GEM Premier ChemSTAT PAK (cartridge).

The GEM Premier ChemSTAT analyzer has the internal logic and processing power necessary to perform analysis. It employs a unique touch-sensitive color 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.

The disposable, multi-use GEM Premier ChemSTAT PAK is a completely closed cartridge that houses all components necessary to operate the instrument once the GEM PAK is validated. These components include the sensors, Process Control (PC) solutions, sampler, and waste bag. The values of all PC solutions are read from the GEM PAK Electronically Erasable Programmable Read Only Memory (EEPROM) chip. The components and processes used to manufacture the PC Solutions in the GEM PAK are traceable to National Institute of Standards and Technology (NIST) standards, Clinical & Laboratory Standards Institute (CLSI) procedures or other internal standards, where available and appropriate. The GEM Premier ChemSTAT PAK has flexible menus to assist facilities in maximizing efficiency. As part of this program, GEM ChemSTAT CVP (Calibration Valuation Products) are external solutions intended to complete the calibration process and final accuracy assessment of the iQM cartridge calibration following warm-up.

Intelligent Quality Management (iQM) is used as the quality control and assessment system for the GEM Premier ChemSTAT system. iQM is an active quality process control program designed to provide continuous monitoring of the analytical process before and after sample measurement with real-time, automatic error detection, automatic correction and automatic documentation of all corrective actions. iQM performs 4 types of continuous, quality checks to monitor the performance of the GEM PAK, sensors, and reagents throughout the cartridge use-life. These checks include System, Sensor, Pattern Recognition (PR) and Stability Checks.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   GEM Premier 4000

2. Predicate 510(k) number(s):
   k133407

3. Comparison with predicate:

Item	GEM Premier ChemSTAT (k183549) (Candidate Device)	GEM Premier 4000 (k133407) (Predicate Device)
Indications for Use	For the quantitative measurements of sodium (Na^+), potassium (K^+), ionized calcium (Ca^{++}) and chloride (Cl^-) from arterial and venous heparinized whole blood.	Same

Item	GEM Premier ChemSTAT (k183549) (Candidate Device)		GEM Premier 4000 (k133407) (Predicate Device)
Intended User	Healthcare provider in Central Laboratory and Point-of-Care settings (e.g., health practitioners, nurse caregivers, phlebotomists).		Same
Measurement Methodology	Potentiometry		Same
Sample Volume	150 µL		65 to 150 µL (dependent on sample mode)
Sample Type	Lithium heparinized whole blood (arterial and venous)		Lithium heparinized whole blood (arterial, venous and capillary)
Reportable Range	Na^+	100 to 180 mmol/L	Same
	K^+	0.3 to 19.0 mmol/L	0.2 to 19.0 mmol/L
	Ca^{++}	0.10 to 4.25 mmol/L	Same
	Cl^-	40 to 158 mmol/L	Same
PAK Storage Temperature	15-25°C		Same
Calibration	2-point calibration		Same
Instrument Sample Introduction	Aspiration		Same
Instrument Operating Temperature	12-32°C		Same
Software Operating System	Linux-based		Same
Instrument User Interface	Menu Driven Touch Screen		Same

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

- CLSI EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline, 3rd Edition, 2014.
- CLSI EP06-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline, 2003.
- CLSI EP07: Interference Testing in Clinical Chemistry; Approved Guideline-Third Edition, 2018.
- CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline - Second Edition, 2012.
- CLSI EP25-A: Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline, 2009.
- CLSI EP37: Supplemental Tables for Interference Testing in Clinical Chemistry; First Edition, 2018.

L. Test Principle:

The electrolyte sensors (Na^+, K^+, Ca^{++} and Cl^-) are based on the principle of ion- selective electrodes in which electrical potential can be established across a membrane resulting from chemical selectivity of the membrane to a specific ion. The potential can be described by this simplified form of the Nernst equation E=E' +(S * Log C), where E is the electrode potential, E' is the standard potential for that membrane, S is the sensitivity (slope), and C is the ion activity. E' and S can be determined by the sensor response to the Process Control Solutions, and the equation can be solved for the activity of the ion of interest. The electrolyte sensors are polyvinyl chloride (PVC) based ion selective electrodes, consisting of an internal Ag/AgCl reference electrode and an internal electrolyte layer. Their potentials are measured against the card reference electrode (Ag/ Ag+).

The card reference consists of an Ag/Ag+ electrode with an open liquid junction between the silver electrode and the sensor chamber. Every time a sample is pumped into the sensor chamber, fresh reference solution containing silver nitrate flows into the reference chamber and comes in contact with the sample. This process provides a stable and reliable liquid junction potential independent of the sample composition.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   Internal Precision Study – Whole Blood
   A precision study was performed at an internal site by two operators using five different concentrations of whole blood per analyte, each run on three GEM Premier ChemSTAT analyzers/cartridges for five days, with one run per day and eight replicates measured per run per level (N=120). The study was performed following the CLSI EP05-A3 guideline. The summary results are included in the table below.

Analyte	Whole Blood Level	Mean	Within Run		Between Analyzer/Lot		Total Imprecision	
			SD	%CV	SD	%CV	SD	%CV
Na^+ (mmol/L)	Level 1	106	0.5	0.5%	0.4	0.3%	0.6	0.6%
	Level 2	118	0.4	0.4%	0.4	0.4%	0.6	0.5%
	Level 3	132	0.5	0.4%	0.0	0.0%	0.5	0.4%
	Level 4	152	0.7	0.4%	0.3	0.2%	0.8	0.5%
	Level 5	175	0.6	0.3%	0.6	0.3%	0.8	0.5%
K^+ (mmol/L)	Level 1	1.5	0.03	2.2%	0.01	0.8%	0.04	2.3%
	Level 2	3.4	0.03	0.9%	0.01	0.4%	0.03	0.9%
	Level 3	5.8	0.04	0.7%	0.02	0.4%	0.04	0.7%
	Level 4	7.9	0.04	0.5%	0.02	0.3%	0.05	0.6%

Analyte	Whole Blood Level	Mean	Within Run		Between Analyzer/Lot		Total Imprecision	
			SD	%CV	SD	%CV	SD	%CV
	Level 5	18.1	0.04	0.2%	0.11	0.6%	0.12	0.6%
Ca^{++} (mmol/L)	Level 1	0.19	0.003	1.7%	0.004	2.3%	0.005	2.8%
	Level 2	0.38	0.004	1.1%	0.003	0.7%	0.005	1.3%
	Level 3	0.82	0.007	0.8%	0.3%	0.3%	0.007	0.8%
	Level 4	1.60	0.012	0.7%	0.010	0.7%	0.016	1.0%
	Level 5	3.79	0.029	0.8%	0.039	1.0%	0.048	1.3%
Cl^- (mmol/L)	Level 1	54	0.4	0.7%	0.5	0.9%	0.6	1.1%
	Level 2	75	0.3	0.4%	0.6	0.8%	0.7	0.9%
	Level 3	90	0.5	0.5%	0.8	0.9%	0.9	1.0%
	Level 4	118	0.6	0.5%	1.4	1.2%	1.5	1.3%
	Level 5	142	0.5	0.3%	2.0	1.4%	2.1	1.5%

Reproducibility Study with Aqueous Controls – Point-of-Care Setting

A reproducibility study was performed with aqueous control solutions at three clinical point-of-care (POC) sites following the CLSI EP05-A3 guideline. The studies were run by a total of nine different operators on six different GEM Premier ChemSTAT instruments, using a single lot of GEM Premier ChemSTAT PAKs (cartridges). Each site used seven levels of quality control material for each analyte (two levels of GEM ChemSTAT CVP and five levels of GEM ChemSTAT PVP), running each control level in triplicate, twice a day for 5 days, for a total of 30 replicates per level (N=90 pooled across three sites). Summary results at all sites combined are shown in the below table.

Na^+(mmol/L) - Pooled Multi-Site POC Data											
Control Level	Mean	Repeatability		Between-Run		Between-Day		Between-Site		Reproducibility	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
CVP 1	124	0.8	0.7%	0.4	0.3%	0.0	0.0%	0.5	0.4%	1.0	0.8%
CVP 2	156	0.7	0.4%	0.4	0.2%	0.2	0.1%	0.0	0.0%	0.8	0.5%
PVP 1	106	0.5	0.4%	0.0	0.0%	0.2	0.2%	0.3	0.3%	0.6	0.6%
PVP 2	125	0.4	0.3%	0.3	0.2%	0.0	0.0%	0.4	0.3%	0.6	0.5%
PVP 3	140	0.6	0.4%	0.6	0.4%	0.0	0.0%	0.1	0.1%	0.8	0.6%
PVP 4	155	0.6	0.4%	0.3	0.2%	0.2	0.1%	0.2	0.1%	0.7	0.5%
PVP 5	177	0.9	0.5%	0.1	0.0%	0.5	0.3%	0.7	0.4%	1.2	0.7%

K^+(mmol/L) - Pooled Multi-Site POC Data											
Control Level	Mean	Repeatability		Between-Run		Between-Day		Between-Site		Reproducibility	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
CVP 1	2.5	0.00	0.0%	0.02	0.7%	0.00	0.0%	0.00	0.0%	0.02	0.7%
CVP 2	7.4	0.03	0.4%	0.05	0.7%	0.00	0.0%	0.01	0.1%	0.06	0.8%
PVP 1	1.2	0.00	0.0%	0.00	0.0%	0.00	0.0%	0.00	0.0%	0.00	0.0%
PVP 2	2.5	0.00	0.0%	0.00	0.0%	0.00	0.0%	0.00	0.0%	0.00	0.0%
PVP 3	4.6	0.03	0.6%	0.04	0.9%	0.00	0.0%	0.02	0.5%	0.05	1.2%
PVP 4	7.3	0.03	0.4%	0.02	0.3%	0.00	0.0%	0.02	0.2%	0.04	0.5%
PVP 5	9.6	0.04	0.5%	0.01	0.1%	0.02	0.2%	0.06	0.6%	0.08	0.8%

Ca^{++}(mmol/L) - Pooled Multi-Site POC Data											
Control Level	Mean	Repeatability		Between-Run		Between-Day		Between-Site		Reproducibility	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
CVP 1	0.89	0.009	1.0%	0.001	0.1%	0.000	0.0%	0.002	0.3%	0.010	1.1%
CVP 2	1.54	0.009	0.6%	0.007	0.4%	0.000	0.0%	0.002	0.1%	0.011	0.7%
PVP 1	0.37	0.004	1.1%	0.003	0.9%	0.000	0.0%	0.003	0.9%	0.006	1.7%
PVP 2	0.90	0.006	0.6%	0.005	0.5%	0.000	0.0%	0.003	0.4%	0.008	0.9%
PVP 3	1.10	0.007	0.7%	0.008	0.7%	0.000	0.0%	0.000	0.0%	0.011	1.0%
PVP 4	1.56	0.009	0.6%	0.006	0.4%	0.000	0.0%	0.002	0.2%	0.011	0.7%
PVP 5	2.23	0.015	0.7%	0.011	0.5%	0.003	0.1%	0.000	0.0%	0.019	0.9%

Cl^-(mmol/L) - Pooled Multi-Site POC Data											
Control Level	Mean	Repeatability		Between-Run		Between-Day		Between-Site		Reproducibility	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
CVP 1	91	0.6	0.6%	0.3	0.3%	0.2	0.2%	0.3	0.3%	0.7	0.8%
CVP 2	135	0.4	0.3%	0.1	0.1%	0.1	0.1%	2.1	1.5%	2.1	1.6%
PVP 1	72	0.3	0.5%	0.0	0.0%	0.3	0.4%	2.3	3.2%	2.3	3.3%
PVP 2	92	0.5	0.6%	0.2	0.2%	0.2	0.2%	0.3	0.3%	0.7	0.8%
PVP 3	106	0.5	0.4%	0.3	0.3%	0.0	0.0%	0.7	0.7%	0.9	0.9%
PVP 4	135	0.6	0.4%	0.4	0.3%	0.1	0.1%	2.1	1.5%	2.2	1.6%
PVP 5	152	0.8	0.5%	0.0	0.0%	0.4	0.3%	2.7	1.8%	2.9	1.9%

External Precision – Whole Blood

A precision study was performed with whole blood patient samples at three external clinical point-of-care sites. The studies were run over five days by six different operators on three different GEM Premier ChemSTAT instruments (one analyzer per site), using a single lot of GEM Premier ChemSTAT PAKs (cartridges). Each whole blood patient sample was run in triplicate on a single GEM Premier ChemSTAT

instrument. At each site a minimum of twenty two whole blood samples were analyzed to cover the medical decision levels. Reproducibility was not assessed for whole blood samples. Due to the use of unique whole blood samples at each clinical site, only repeatability was evaluated. The assessment of precision is based on a pooled analysis of the imprecision of a minimum of twenty individual samples per site, as shown below.

Analyte	Site	N	Mean	Within Sample SD or %CV
Na^+ (mmol/L)	POC 1	69	139	1.0
	POC 2	63	140	1.0
	POC 3	63	140	1.3
	Pooled	195	140	1.1
	POC 1	3	106	0.6
	POC 2	3	106	0.0
	POC 3	3	103	0.6
	Pooled	9	105	0.5
K^+ (mmol/L)	POC 1	69	4.1	0.12
	POC 2	63	4.0	0.03
	POC 3	63	3.6	0.04
	Pooled	195	3.9	0.08
	POC 1	3	8.2	0.7%
	POC 2	3	7.3	0.0%
	POC 3	3	7.9	0.7%
	Pooled	9	7.8	0.5%

Analyte	Site	N	Mean	Within Sample SD or %CV
Ca^{++} (mmol/L)	POC 1	3	0.34	0.006
	POC 2	3	0.38	0.006
	POC 3	3	0.41	0.006
	Pooled	9	0.38	0.006
	POC 1	69	1.20	1.1%
	POC 2	63	1.22	1.4%
	POC 3	63	1.22	1.8%
	Pooled	195	1.21	1.4%
Cl^- (mmol/L)	POC 1	3	73	0.0
	POC 2	3	40	0.0
	POC 3	3	44	0.0
	Pooled	9	52	0.0
	POC 1	69	102	0.5%
	POC 2	63	105	0.7%
	POC 3	63	105	0.5%
	Pooled	195	104	0.6%

b. *Linearity/assay reportable range:*

A linearity study was conducted for each analyte following the CLSI EP06-A guideline. Nine levels per analyte were prepared by spiking or diluting whole blood to challenge the claimed reportable range for Na^+, K^+, Ca^{++} and Cl^-. Each blood level was analyzed in triplicate on six GEM Premier ChemSTAT test analyzers (N=18) and results compared to the reference analyzer. The summary results are shown below. The lower limits of the claimed reportable ranges were determined based on the combined data from limit of quantitation and linearity studies.

Analyte	Slope	Intercept	R^2	Tested Range	Claimed Measuring Range
Na^+ (mmol/L)	1.023	-1.189	0.9997	92 to 200	100 to 180
K^+ (mmol/L)	0.995	0.057	0.9998	0.2 to 19.6	0.3 to 19.0
Ca^{++} (mmol/L)	0.986	0.019	0.9984	0.04 to 4.27	0.10 to 4.25
Cl^- (mmol/L)	1.011	-1.909	0.9998	34 to 177	40 to 158

The linear regression results support the claimed measuring ranges, as summarized in the table above.

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

Na^+ assay is traceable to a flame photometry reference method, which uses secondary standards prepared from NIST SRM 919 sodium chloride salt.
K^+ assay is traceable to a flame photometry methods, which uses secondary standards prepared from NIST SRM 918 potassium chloride salt.
Ca^{++} assay is traceable to a direct potentiometry method that uses secondary standards prepared from NIST SRM 915 calcium carbonate salt.
Cl^- assay is traceable to a coulometric-amperometric titration with silver ion method that uses secondary standards prepared from NIST SRM 919 sodium chloride salt.

The real time shelf life stability study and the in-use (cartridge use-life) stability study was performed on three lots of GEM Premier ChemSTAT PAKs (cartridges). Based on the results, the sponsor claims that the GEM Premier ChemSTAT PAKs has a shelf life stability of five months when stored at 15°C to 25°C, and an in-use stability of 450 samples or 21 days when stored on board the analyzer. The stability study protocol and acceptance criteria were found to be adequate.

A transport simulation study was conducted to support the stability claim of the GEM Premier ChemSTAT PAKs (cartridges) when exposed to transport conditions of 10°C to 38°C and an altitude of 10,000 feet for three days.

d. Detection limit:

Detection limit studies were performed following the CLSI EP17-A2 guideline. Limit of blank (LoB), limit of detection (LoD) and limit of quantitation (LoQ) were established for Na^+, K^+, Ca^{++} and Cl^-, using three lots of GEM Premier ChemSTAT PAKs (cartridges) on three different GEM Premier ChemSTAT instruments. Samples tested in these studies were lithium heparinized whole blood samples over three day. The heparinized whole blood samples were prepared fresh each day.

LoB was determined by running three blank samples in sixty replicates per day over three days using three cartridge lots on three analyzers. LoB was independently calculated for each lot using the non-parametric method.

LoD was determine by running three low level samples in sixty replicates per day over three days using three cartridge lots on three analyzers. The LoB used for LoD calculation is the maximum value across the three cartridge lots. The is calculated using the formula $LoD = LoB + 1.645/[1-\{1/(4(L-J))\}]^{-} * SD_L$, where L is the total number of all low level sample results across all cartridge lots and J is the number of low level samples (number of days). The maximal value of the LoDs obtained for the three lots was determined to be the LoD of the device.

LoQ was determined by running low level samples in 60 replicates per day over three days using three lots of cartridges on three analyzers. The LoQ is defined as the lowest concentration at which measured total error is less than the pre-defined total error of 5 mmol/L for sodium, 0.5 mmol/L for potassium, 0.10 mmol/L for ionized calcium and 4 mmol/L for chloride. The total error TE is calculated as:
$TE = [(mean_{GEM\ Premier\ ChemSTAT} - mean_{Predicate\ Device})] + 1.96 * SD_{Low\ Level}$

The combined summary results for LoB, LoD and LoQ are shown below.

Analyte	LoB	LoD	LoQ	Claimed Measuring Range
Na^+ (mmol/L)	69	70	88	100 to 180
K^+ (mmol/L)	0.0	0.1	0.3	0.3 to 19.0
Ca^{++} (mmol/L)	0.00	0.01	0.05	0.10 to 4.25
Cl^- (mmol/L)	4	4	36	40 to 158

e. Analytical specificity:

In accordance with CLSI EP07 3rd Edition, an interference study was conducted for the Na^+, K^+, Ca^{++} and Cl^- assays on three GEM Premier ChemSTAT analyzers using heparinized whole blood at two levels of the analyte of interest. Interference effect was calculated as the difference between the average test and average control measurements across the three analyzers. Clinically non-significant interference limit for each of the four assays is defined by the sponsor as:

Analyte assay	Clinically non-significant interference limit
Na^+ (mmol/L)	≤ ± 4
K^+ (mmol/L)	≤ ± 7%
Ca^{++} (mmol/L)	≤ ± 10%
Cl^- (mmol/L)	≤ ± 5%

The table below shows the substances and the concentrations tested that did not interfere with the analyte assays listed in the third column.

Test Substance	Test Concentration	Tested analytes where interference was not observed
Atracurium	50 mg/L	Sodium, Potassium, Ionized Calcium, Chloride
Benzalkonium (Chloride)	5 mg/L	Sodium, Potassium, Ionized Calcium, Chloride
Bilirubin	40 mg/dL	Sodium, Potassium, Ionized Calcium, Chloride
Ceftriaxone	1510 µmol/L	Sodium, Potassium, Ionized Calcium, Chloride
Epinephrine	0.5 µmol/L	Sodium, Potassium, Ionized Calcium, Chloride
Etomidate	50 mg/L	Sodium, Potassium, Ionized Calcium, Chloride
Fentanyl	0.03 µg/mL	Sodium, Potassium, Ionized Calcium, Chloride
Furosemide	48.1 µmol/L	Sodium, Potassium, Ionized Calcium, Chloride
Gadodiamide	1.4 mmol/L	Sodium, Potassium, Ionized Calcium, Chloride
Hemoglobin (Hemolysis)	1000 mg/dL	Sodium, Ionized Calcium, Chloride
Heparin	100,000 U/L	Sodium, Potassium, Ionized Calcium, Chloride
Ibuprofen	1060 µmol/L	Sodium, Potassium, Ionized Calcium, Chloride
Leflunomide	100 µg/mL	Sodium, Potassium, Ionized Calcium, Chloride
Lithium	3.2 mmol/L	Sodium, Potassium
Methadone	10.3 µmol/L	Sodium, Potassium, Ionized Calcium, Chloride
Midazolam	0.376 mg/dL	Sodium, Potassium, Ionized Calcium, Chloride
Morphine	27.3 µmol/L	Sodium, Potassium, Ionized Calcium, Chloride
N-Acetyl-L-cysteine	920µmol/L	Sodium, Potassium, Ionized Calcium, Chloride
Perchlorate	20 mg/dL	Sodium, Potassium, Ionized Calcium
Phenobarbital	2970 µmol/L	Sodium, Potassium, Ionized Calcium, Chloride
Piperacillin	110 mg/dL	Sodium, Potassium, Ionized Calcium, Chloride
Propofol	4.8 mg/dL	Sodium, Potassium, Ionized Calcium, Chloride
Salicylic acid	0.207 mmol/L	Sodium, Potassium, Ionized Calcium, Chloride
Suxamethonium	68 µmol/L	Sodium, Potassium, Ionized Calcium, Chloride
Tazobactam	3.05 mg/dL	Sodium, Potassium, Ionized Calcium, Chloride
Teriflunomide	100 µg/mL	Sodium, Potassium, Ionized Calcium, Chloride
Thiocyanate	898 µmol/L	Sodium, Potassium, Ionized Calcium, Chloride
Thiopental	1660 µmol/L	Sodium, Potassium, Ionized Calcium, Chloride
Triglycerides	2000 mg/dL	Sodium, Chloride, Ionized Calcium

Test Substance	Test Concentration	Tested analytes where interference was not observed
(Intralipid)	(1% Intralipid)	
Vancomycin	82.8 µmol/L	Sodium, Potassium, Ionized Calcium, Chloride

The list of interfering substances that interferes with the specific analyte assay and the lowest concentration of the interfering substance with analyte impact with the observed positive or negative bias is shown in the below table.

Interfering Substance	Affected Analytes	Analyte Concentration	Interfering Concentration Tested	Bias Observed (Mean)	Lowest Interfering Concentration with Analyte Impact	Bias Observed at the Lowest Concentration
Hemoglobin (Hemolysis)	Potassium	3.5 mmol/L	1000 mg/dL	+16 %	155 mg/dL	+7%
		5.0 mmol/L		+15 %	228 mg/dL	+7%
Perchlorate	Chloride	100 mmol/L	20 mg/dL	+6 %	18 mg/dL	+5%
		110 mmol/L		+5 %	17 mg/dL	+5%
Triglyceride (Intralipid)	Potassium	3.5 mmol/L	2000 mg/dL (1 % Intralipid)	+11 %	689 mg/dL (0.34 %)	+7%
		5.0 mmol/L		No Interference Observed		

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison study was conducted at three external POC sites by at least two POC operators at each site. Both arterial and venous whole blood samples were tested in singlicate on one GEM Premier ChemSTAT analyzer and one GEM Premier 4000 analyzer for sodium, potassium, ionized calcium and chloride. Contrived samples tested in the study were ≤8% of all the samples tested. For analytes with constant SD (sodium), slope, intercept and correlation coefficient (R) were obtained from the Deming regression method. For analytes with mixed variability, including both constant SD and %CV ranges, (potassium, ionized calcium and chloride), slope, intercept and correlation coefficient (R) were obtained from the Passing-Bablok regression method. The summary results from the three sites are shown below:

Analyte	Sample Range	N	Slope	Intercept	R	Regression Method
Na^+ (mmol/L)	100 to 170	436	1.021	-2.157	0.987	Deming
K^+ (mmol/L)	0.5 to 18.2	442	1.000	0.100	0.999	Passing-Bablok
Ca^{++} (mmol/L)	0.26 to 4.08	444	1.000	0.015	0.999	
Cl^- (mmol/L)	45 to 154	435	1.000	1.000	0.994	

b. Matrix comparison:

Not applicable. The four analyte assays are for use with lithium heparinized whole blood (venous and arterial) sample type only.

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 reference ranges for arterial adult blood (unless noted) are cited from the published literature* as shown below.

Analyte	**Reference Range**	**Unit**
Na^+	136 to 145	mmol/L
K^+	3.5 to 5.1	mmol/L
Ca^{++}	1.15 to 1.33	mmol/L
	1.16 to 1.32 (venous)	mmol/L
Cl^-	98 to 107	mmol/L

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

N. Instrument Name:

GEM Premier ChemSTAT Analyzer System.

O. System Descriptions:

1. Modes of Operation:

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

   Yes ___X___ or No _____

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

   Yes ___X___ or No _____

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:

   Specimens may be identified by scanning a barcode or by manually entering the information via the touchscreen.

4. Specimen Sampling and Handling:

   Lithium heparinized arterial and venous whole blood from syringes and open blood collection tubes.

5. Calibration:

   The disposable, multi-use GEM Premier ChemSTAT PAK is a completely closed cartridge that houses all components necessary to operate the instrument once the GEM PAK is validated. These components include the sensors, Process Control (PC) solutions, sampler, and waste bag. The values of all PC Solutions are read from the GEM PAK Electronically Erasable Programmable Read Only Memory (EEPROM) chip. The setup of the instrument consists of inserting the GEM PAK into the instrument. 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 50 minutes. As part of this program, 4-level GEM ChemSTAT CVP (Calibration Valuation Products) are external solutions needed to complete the calibration process to validate the integrity of the PC solutions and final accuracy assessment of the iQM cartridge calibration following warm-up.

Following validation of the PAK, the sensors/analyte parameters are calibrated and monitored with four Process Control (PC) solutions A, B, C, and D. Each PC solution serves a specific function in the iQM process. The four PC solutions (A, B, C, and D) are used continuously each day at defined frequency to confirm sensor PAK performance.

6. Quality Control:

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

In the device labeling the sponsor states "*Facilities should follow local, state and federal regulatory guidelines to ensure that a total quality management system is followed.*"

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

Not applicable.

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Parts 801 and 809, as applicable.

R. Conclusion:

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