510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K252475

B Applicant

Radiometer Medicals ApS

C Proprietary and Established Names

ABL90 FLEX PLUS System

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
JGS	862.1665	Sodium Test System	CH
JFP	862.1145	Calcium Test System	CH
CGZ	862.1170	Chloride Test System	CH

II Submission/Device Overview:

A Purpose for Submission:

Modification to a previously cleared device.

B Measurand:

Sodium (cNa^+), Calcium (cCa^{2+}), and Chloride (cCl^-)

C Type of Test:

Potentiometry

III Intended Use/Indications for Use:

A Intended Use(s):
See Indications for Use below.

B Indication(s) for Use:
The ABL90 FLEX PLUS System is an in vitro diagnostic, portable, automated analyzer that quantitatively measures electrolytes:

- cCl^- in heparinized arterial, venous and capillary whole blood, and
- cCa^{2+} and cNa^+ in heparinized capillary whole blood

The ABL90 FLEX PLUS System is intended for use by trained technologists, nurses, physicians and therapists. It is intended for use in a laboratory environment, near patient, or point-of-care setting.

These tests are only performed under a physician's order.

Calcium (cCa^{2+}): Calcium measurements are used in the diagnosis and treatment of parathyroid disease, a variety of bone diseases, chronic renal disease and tetany.

Sodium (cNa^+): Sodium 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.

Chloride (cCl^-): Chloride measurements are used in the diagnosis and treatment of electrolyte and metabolic disorders such as cystic fibrosis and diabetic acidosis.

C Special Conditions for Use Statement(s):
Rx - For Prescription Use Only

D Special Instrument Requirements:
ABL90 FLEX PLUS System

IV Device/System Characteristics:

A Device Description:
The ABL90 FLEX PLUS System consists of the ABL90 FLEX PLUS analyzer, sensor cassette (SC) and solution pack (SP) consumables, and related accessories for the analyzer as described in K240998. The ABL90 FLEX PLUS System has an automated sample inlet mechanism, which can collect arterial and venous whole blood through two different measuring modes: the S65 syringe mode and the SP65 short probe mode, and capillary whole blood through the C65 capillary mode. For the C65 modes, samples are loaded using safeCLINITUBES which are 70 and 100µL plastic capillary tubes with balanced heparin, mixing wires and end caps.

This submission is for the addition of capillary heparinized whole blood samples for Sodium (cNa^+) and Calcium (cCa^{2+}) and for capillary, arterial and venous heparinized whole blood samples for Chloride (cCl^-).

The ABL90 FLEX PLUS System is cleared for the quantitative measurement of pH, pO2, pCO2, oximetry (sO2, ctHb, FO2Hb, FCOHb, FMetHb, FHHb) cK+, cNa+, cCa2+, cGlu, and cLac using arterial and venous heparinized whole blood samples. The system is cleared for the quantitative measurement of pH, pCO2, ctHb and cGlu using capillary heparinized whole blood sample (K240998, K241037, K252207 and K252488).

B Principle of Operation:
Potentiometry: The potential of an electrode chain is measured by a voltmeter and related to the concentration of the sample (the Nernst equation). The potentiometric measuring principle is applied in cNa^+, cCa^{2+}, and cCl^- sensors.

V Substantial Equivalence Information:

A Predicate Device Name(s):
Stat Profile® Prime Plus Analyzer System

B Predicate 510(k) Number(s):
K200403

C Comparison with Predicate(s):

Device & Predicate Device(s):	K252475	K200403
Device Trade Name	ABL90 FLEX PLUS System	Stat Profile® Prime Plus Analyzer System
General Device Characteristic Similarities		
Intended Use/Indications For Use	Intended for the quantitative measurements of sodium, ionized calcium and chloride	Same
Intended Use Environment	Laboratory environment, near patient or point-of-care setting	Same
General Device Characteristic Differences		
Sample Type	Heparinized capillary whole blood for cCl^- and heparinized arterial and	Heparinized arterial and venous whole blood

Device & Predicate Device(s):	K252475	K200403
	venous whole blood for cCl^-, cNa^+, and cCa^{2+}	
Analytes	cNa^+, cCa^{2+}, and cCl^-	K^+, Na^+, iCa^{2+}, Cl^-, iMg^{2+}

VI Standards/Guidance Documents Referenced:

Clinical and Laboratory Standards Institute (CLSI) EP05-A3 – Evaluation of Precision of Quantitative Measurement Procedures
CLSI EP09c 3rd Edition – Measurement Procedure Comparison and Bias Estimation Using Patient Samples
CLSI EP17-A2 2nd Edition – Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline
CLSI EP06-2nd Edition – Evaluation of Linearity of Quantitative Measurement Procedures
CLSI EP07-3rd Edition – Interference Testing in Clinical Chemistry
CLSI EP37 1st Edition – Supplemental Tables for Interference Testing in Clinical Chemistry
CLSI EP39 1st Edition – A Hierarchical Approach to Selecting Surrogate Samples for the Evaluation of In Vitro Medical Laboratory Tests

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:
Point of care precision (aqueous control material):
A multi-day precision study was performed at one internal site using three concentrations of aqueous control solutions and three reagent lots. Each level was tested on three analyzers as two replicates per run, two runs per day, for twenty days. Repeatability, within-laboratory precision, and reproducibility results are reported below:

Parameters (units)	QC Level	N	Mean (mmol/L)	Repeatability		Within Lab Precision		Reproducibility	
				SD	CV%	SD	CV%	SD	CV%
cCl^- (mmol/L)	L1	234	93	0.1	0.1	0.2	0.3	0.2	0.3
	L2	234	99	0.1	0.1	0.2	0.2	0.2	0.2
	L3	240	140	0.2	0.1	0.4	0.3	0.4	0.3

A multi-day precision study was performed at three POC sites using three concentrations of aqueous control solutions and three reagent lots. At each site, each level was tested as three replicates per run, two runs per day, for at least five days. At least two POC operators were included at each site. Repeatability, within-laboratory precision, and reproducibility results are reported below:

Parameters (units)	QC Level	N	Mean (mmol/L)	Repeatability		Within Lab Precision		Reproducibility	
				SD	CV%	SD	CV%	SD	CV%
cCl^- (mmol/L)	L1	101	93	0.1	0.1	0.3	0.4	0.4	0.4
	L2	102	99	0.1	0.1	0.2	0.2	0.2	0.2
	L3	101	140	0.1	0.1	0.3	0.2	0.3	0.2

Whole Blood for Chloride

Point of Care precision (Arterial and Venous Whole Blood) cCl^- in S65 and SP65 Mode:

A multi-day precision study was performed at three POC sites by at least three POC operators at each site, using balanced heparinized whole blood targeted to levels within the reportable range of cCl^-. The whole blood precision was assessed using duplicate test results collected across multiple point of care sites using both the S65 and SP65 sampling modes. Samples were grouped into subintervals based on their mean values. The results are summarized below.

Parameter (mmol/L)	N	Test interval	Mean	Repeatability	
				SD	CV%
S65 Mode					
cCl^-	30	80 - <98	95.857	0.154	0.16
	108	98 - 107	103.62	0.124	0.12
	90	>107 - <130	110.46	0.102	0.09
	18	130 - <150	141.59	0.108	0.08
SP65 Mode					
cCl^-	34	80 - <98	95.612	0.064	0.07
	108	98 - 107	103.62	0.073	0.07
	84	>107 - <130	110.50	0.071	0.06
	18	130 - <150	141.34	0.058	0.04

Capillary (C65) Mode for Calcium, Chloride, and Sodium

A precision study was performed at two POC sites with at least two POC operators in capillary (C65) mode using native heparinized capillary whole blood and two reagent lots. The study spanned 15 days, testing two subjects per day with two samples collected from each subject. A total of 39 subjects were included in the study.

Parameter (units)	N	Test Interval	Mean	Repeatability	
				Std	CV (%)
cCa^{2+} (mg/dL)	8	3.4 - <4.8	4.677	0.017	0.35
	42	4.8 - <5.0	4.921	0.045	0.91
	28	5.0 - <5.812	5.143	0.074	1.43
cCl^- (mmol/L)	28	80 - <107	104.76	0.793	0.76
	26	107 - <110	108.58	0.803	0.74
	24	110 - <130	112.45	0.686	0.61

Parameter (units)	N	Test Interval	Mean	Repeatability	
				Std	CV (%)
cNa^+ (mmol/L)	4	120 - <136	130.98	1.278	0.98
	66	136 - <146	142.25	0.749	0.53
	8	146 - <155	147.76	0.662	0.45

2. Linearity:

Linearity testing for cCl^- was conducted in general accordance with CLSI EP06-A2. The linearity of the ABL90 FLEX PLUS System for cCl^- measurements was evaluated by preparing heparinized venous whole blood samples at low and high concentrations. Eleven test concentrations were then generated by mixing of these high and low samples. At least 20 replicates were run for each level. The maximum deviation from linearity was -0.42%.

Parameter (units)	Reportable Range	Tested Linearity Range	Slope	Intercept	R2
cCl^- (mmol/L)	86 - 151	70.1 - 165	0.998	1.022	1.00

Linearity for cNa^+ and cCa^{2+} was previously established in K241037.

3. Analytical Specificity/Interference:

Interference testing for cCl^- was conducted in two parts: paired-difference testing and dose-response experiments and in general accordance with CLSI EP07.

a) The paired-difference testing was conducted on all potential interferents. Matched samples were tested, one with no interferent and the other with the interferent. If no interference was found, no further testing was performed.
b) The dose-response experiment was only conducted on interferents found to have an effect via the paired-difference testing. This was carried out to determine the concentration at which clinically significant interference occurred.

Freshly drawn heparinized adult venous whole blood samples were used as starting material for the interference studies. Interference testing was conducted at two cCl^- levels (i.e., 100 mmol/L and 110 mmol/L). The following table lists the concentrations of each substance at which no significant interference was found.

Highest concentration tested at which no significant interference is observed.

Potential Interferent for cCl-	Concentration
Acetylsalicylic acid	65 mg/dL
Acetyltryptophane	3.0 mg/dL
Ammonium chloride	5.3 mg/dL
Ascorbate (sodium-) Na salt	392 mg/dL
Benzalkonium chloride	2.4 mg/dL
Bicarbonate (HCO_3^-) at low level	42 mg/dL
Bicarbonate (HCO_3^-) at high level	378 mg/dL

Potential Interferent for cCl-	Concentration
Bilirubin, conjugated	40 mg/dL
Bilirubin, unconjugated	40 mg/dL
Biotin	0.351 mg/dL
Caprylic acid	1.73 mg/dL
Citrate (trisodium citrate 2H2O)	1176 mg/dL
Fluoride (sodium-) (>99%)	210 mg/dL
Hemolysis	20%
Intralipid	2000 mg/dL
Lactate (sodium-)	280 mg/dL
Leflunomide	30 mg/dL
Nortriptyline (hydrochloride solution)	0.113 mg/dL
Oxalate (sodium-)	134 mg/dL
pH at high level	8.0
Propofol	4.8 mg/dL
Salicylic acid	59.4 mg/dL
Teriflunomide	30 mg/dL

For those substances that on initial screening were found to interfere, dose response testing was conducted to establish the concentration limit below which no significant interference is expected. The results are summarized in the table below:

Interferent	Maximum test concentration	Highest concentration level without interference	Impact on result
cCl- (test level: 100 mmol/L)			
Bromide (sodium-)	391 mg/dL	24.4 mg/dL	80.22 mmol/L
Iodide (sodium-)	45 mg/dL	11.25 mg/dL	11.57 mmol/L
Perchlorate ClO_4 (potassium-)	20.8 mg/dL	15.6 mg/dL	6.351 mmol/L
pH at low level	6.8	Cl^- is corrected for bicarbonate, calculated from pH and pCO_2. pH interference on Cl sensor will also depend on pCO_2 level.	10.91 mmol/L (measured at pCO_2 84 mmHg)
Thiocyanate (sodium-)	195mg/dL	3.66 mg/dL	51.90 mmol/L
cCl- (test level: 110 mmol/L)			
Bromide (sodium-)	391 mg/dL	24.4 mg/dL	80.23 mmol/L
Iodide (sodium-)	45 mg/dL	11.25 mg/dL	12.12 mmol/L
Perchlorate ClO_4 (potassium-)	20.8 mg/dL	No interference	N/A

Interferent	Maximum test concentration	Highest concentration level without interference	Impact on result
pH at low level	6.8	Cl^- is corrected for bicarbonate, calculated from pH and pCO^2. pH interference on Cl sensor will also depend on pCO^2 level.	9.93 mmol/L (measured at pCO^2 108 mmHg)
Thiocyanate (sodium-)	195 mg/dL	4.88 mg/dL	58.746 mmol/L

The sponsor included the following in their labeling:
The chloride measurement is corrected for bicarbonate, calculated from pH and pCO_2. There is no indication of clinically significant interference at pH above 7.1. The combination of very low pH and very high pCO_2 level may interfere with the chloride measurements. Clinically significant interference has been observed at pH 6.8 and pCO_2 levels around 100 mmHg. For pH measurements below 7.1, it is recommended to always interpret results of chloride in conjunction with the other measurements reported by the ABL90 FLEX PLUS analyzer and the overall clinical context.

4. Assay Reportable Range:

The reportable range for $cCl^{-\text{ is } 86}$ – 151 mmol/L. The reportable ranges for cNa^+ and cCa^{2+} were previously established in K241037.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

cCl^- is traceable to SRM999 NIST Standard Reference Material. Refer to K241037 for traceability information for cNa^+ and cCa^{2+}.

6. Detection Limit:
Detection capability for limit of quantitation (LoQ) was conducted in general accordance with CLSI EP17-A2. Testing was performed using 4 independent heparinized venous whole blood samples, three reagent lots, nine instruments, over the course of nine days, with at least 5 replicates/sample, and 60 replicates/reagent lot, using the S65 mode.

Parameter	Unit	LoQ
cCl^-	mmol/L	77

B Comparison Studies:

1. Method Comparison with Predicate Device:

Method comparison studies were conducted in general accordance with CLSI EP09c-ED3.

Method comparison for cCl^- using heparinized arterial and venous whole blood specimens in S65 and SP65 mode and for cNa^+, cCa^{2+}, and cCl^- in heparinized capillary whole blood samples in C65 mode on the ABL90 FLEX PLUS System was done in general accordance with CLSI EP09c-ED3. A minimum of 100 heparinized arterial (A), venous (V), and capillary whole blood specimens (maximum of 10% contrived) were collected across 3 POC sites by at least 2 operators per site. Capillary blood samples were collected in 2 safeCLINITUBE capillary tubes and were compared to venous and arterial whole blood specimens tested on a comparator method. Specifically, each capillary whole blood sample was measured once on the candidate device in C65 mode and once on the comparator device. A comparison between the measurements was performed using Deming regression analysis. The results are summarized below.

Method Comparison- cCl^- in arterial and venous whole blood

Parameter	Sample type	Mode	n	Min-max	Intercept	Slope	R^2	MDLs (mmol/L)	Bias at MDLs
cCl^-	A	S65	222	88-148.1	-0.26	1.00	1.00	98	-0.374
								107	-0.385
		SP65	215	89.2-148.2	0.02	1.00	1.00	98	-0.334
								107	-0.366
	V	S65	231	86.2-148.1	-0.22	1.00	1.00	98	-0.339
								107	-0.350
		SP65	221	86.5-148.2	-0.09	1.00	1.00	98	-0.319
								107	-0.340

Method Comparison- cCa^{2+}, cNa^+, and cCl^- in capillary whole blood

Parameter	Blood type of Comparator	N	Contrived (%)	Min-max	Slope	Intercept	R2	MDLs (mmol/L)	Bias at MDLs
cNa^+ (mmol/L)	Arterial	116	9.5	117-179	1.02	-0.542	0.93	136	2.05
								146	2.24
	Venous	116	9.5	117-179	1.02	-0.964	0.93	136	1.85
								146	2.06
cCa^{2+} (mg/dL)	Arterial	111	8.1	2.53-9.78	0.94	0.442	0.97	3.41	0.24
								4.60	0.17
								5.17	0.14
								5.81	0.1
	Venous	111	8.1	2.53-9.78	0.95	0.338	0.96	3.41	0.17
								4.60	0.11
								5.17	0.08
								5.81	0.05

Parameter	Blood type of Comparator	N	Contrived (%)	Min-max	Slope	Intercept	R2	MDLs (mmol/L)	Bias at MDLs
cCl^- (mmol/L)	Arterial	115	8.7	88.4-148.7	1.02	-1.512	0.96	98	0.54
								107	0.73
	Venous	116	8.7	88.4-148.7	1	2.753	0.96	98	2.39
								107	2.35

2. Matrix Comparison:

Not applicable.

C Clinical Studies:

1. Clinical Sensitivity:

Not applicable.

2. Clinical Specificity:

Not applicable.

3. Clinical Cut-Off:

Not applicable.

4. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Not applicable.

D Expected Values/Reference Range:

The reference range for cCl^-, cited from literature, for a normal, healthy population is 98-107 mmol/L[1]. Refer to K241037 for reference range information for cNa^+ and cCa^{2+}.

[1]Burtis CA, Ashwood ER, Bruns DE. Tietz textbook of clinical chemistry and molecular diagnostics. 5th ed. St. Louis: Saunders Elsevier, 2012.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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