510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K252207

B Applicant

Radiometer Medicals ApS

C Proprietary and Established Names

ABL90 FLEX PLUS System, safeCLINITUBES

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
CHL	Class II	21 CFR 862.1120 - Blood Gases (PCO2, PO2) And Blood Ph Test System	CH - Clinical Chemistry
GKR	Class II	21 CFR 864.5620 - Automated hemoglobin system	HE - Hematology
JKA	Class II	21 CFR 862.1675 - Blood specimen collection device	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

Modification to a previously cleared device.

B Measurand:

1. pH (acidity)
2. pCO2 (partial pressure of carbon dioxide)
3. ctHB (total hemoglobin concentration)

C Type of Test:
Quantitative - Sensors using Potentiometry for pH and pCO2 measurement; Spectrophotometry for the measurement of ctHb.

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:
-blood gas (pCO2) in heparinized arterial, venous and capillary whole blood, and
-pH and oximetry (ctHb) 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.

pH and pCO2: pH and pCO2 measurements are used in the diagnosis and treatment of life-threatening acid-base disturbances.

ctHb (Total Hemoglobin): Total hemoglobin measurements are used to measure the hemoglobin content of whole blood for the detection of anemia in venous and arterial whole blood. Capillary whole blood is used to estimate the presence of ctHb.

safeCLINITUBES are intended for the collection, mixing, and dispensing of capillary whole blood samples on the ABL90 FLEX PLUS System.

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. This submission is for the addition of capillary heparinized whole blood samples for pH and ctHB, and for capillary, arterial and venous heparinized whole blood samples for pCO2. 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.

safeCLINITUBES are 70 and 100µL plastic capillary tubes with balanced heparin, mixing wires and end caps.

The ABL90 FLEX PLUS System was cleared in K241037 for the quantitative measurement of cK+, cNa+, cCa2+, glucose and lactate using arterial and venous heparinized whole blood samples. The system was cleared for the quantitative measurement of pH, blood gas (pO2), Oximetry (sO2, ctHb, FO2Hb, FCOHb, FMetHb, and FHHb) using arterial and venous heparinized whole blood samples in K240998.

B Principle of Operation:

There are two different measuring principles employed by the ABL90 FLEX PLUS System: Potentiometry and spectrophotometry.

- 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 the pH and pCO2 sensors.
- Spectrophotometry: Light passes through a cuvette that contains a hemolyzed blood sample. The absorption spectrum is used to calculate oximetry parameters. This measuring principle is used for ctHb.

V Substantial Equivalence Information:

A Predicate Device Name(s):

ABL90 FLEX PLUS

B Predicate 510(k) Number(s):

K160153

C Comparison with Predicate(s):

Device & Predicate Device(s):	K252207	K160153
Device Trade Name	ABL90 FLEX PLUS System	ABL90 FLEX PLUS
General Device Characteristic Similarities		
Intended Use/Indications For Use	In vitro diagnostic that quantitatively measures	Same

Device & Predicate Device(s):	K252207	K160153
	pH, blood gases, and oximetry.	
Intended Use and Environment	Intended for use by trained technologists, nurses, physicians, and therapists in a laboratory environment, near patient, or point-of-care setting.	Same
Prescription/OTC Use	Prescription Use	Same
General Device Characteristic Differences		
Sample type	Balanced heparinized capillary whole blood for pH, ctHb and PCO2 using the safeCLINITUBES	No capillary whole blood claim for pH, ctHb and PCO2

VI Standards/Guidance Documents Referenced:

Clinical and Laboratory Standards Institute (CLSI) EP05-A3 – Evaluation of Precision of Quantitative Measurement Procedures
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 EP09c 3rd Edition – Measurement Procedure Comparison and Bias Estimation Using Patient Samples
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 three point of care (POC) sites using four concentrations of aqueous control solutions. At each site, each level was tested as two replicates per run, two runs per day, for twenty days. At least three POC operators were

included at each site. Repeatability, within-laboratory precision, and reproducibility results are reported below:

Parameter	QC Level	N	Mean	Repeatability		Within Lab-Precision		Reproducibility	
				SD	CV%	SD	CV%	SD	CV%
pCO2 (mmHg)	L 1	243*	70.5	0.53	0.7	1.13	1.6	1.16	1.6
	L 2	244	42.7	0.23	0.5	0.5	1.2	0.50	1.2
	L 3	244	23.1	0.12	0.5	0.27	1.2	0.29	1.2
	L 4	244	97.3	1.17	1.2	1.81	1.9	2.08	2.1

*One L1 sample replicate was excluded due to insufficient sample being loaded onto the instrument.

Point of Care precision (Whole Blood) pCO2 in S65 and SP65 Mode:
A multi-day precision study was performed at three sites by at least three POC operators at each site, using balanced heparinized whole blood targeted to levels within the reportable range of pCO2. 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 (unit)	N	Test interval	Mean	Repeatability	
				SD	CV%
S65 Mode					
*p*CO2 (mmHg)	4	25 - <32	27.775	0.320	1.15
	166	32 - <48	40.417	0.271	0.67
	50	48 - <60	52.030	0.266	0.51
	26	60 - <80	67.908	0.495	0.73
SP65 Mode					
*p*CO2 (mmHg)	4	25 - <32	29.375	1.005	3.42
	160	32 - <48	40.448	0.168	0.42
	50	48 - <60	51.742	0.231	0.45
	27	60 - <80	68.989	0.334	0.48

Within Sample Precision - Capillary Mode Fingerstick

A multi-day precision study to assess heparinized capillary whole blood sample within run precision in capillary mode was performed at two sites by at least two POC operators at each site. Capillary whole blood from 39 donors via finger stick puncture from two (2) fingers into 2 *safe*CLINITUBE capillary tubes was collected. Blood from each capillary pair was analyzed in singlet in capillary mode on one ABL90 FLEX PLUS analyzer. Samples were grouped into subintervals based on their mean values. The results are summarized below.

Parameter (unit)	N	Test interval	Mean	Repeatability	
				SD	CV%
pH	20	7.2 - <7.35	7.325	0.012	0.17
	40	7.35 - <7.40	7.374	0.011	0.15
	18	7.40 - <7.55	7.430	0.016	0.21
*p*CO2 (mmHg)	6	25 - <35	32.233	1.626	5.04
	58	35 - <48	41.002	1.207	2.94
	14	48 - <60	51.636	2.770	5.36
*c*tHb (g/dL)	30	8 - <13.5	11.487	0.285	2.48
	46	13.5 - <17.5	14.930	0.248	1.66

2. Linearity:

Linearity testing was conducted in general accordance with CLSI EP06-A2. The linearity of the ABL90 FLEX PLUS System test for pCO2 was evaluated by preparing balanced heparinized venous whole blood samples. To achieve target concentrations, samples for pCO2 were prepared via tonometry. At least 10 replicates were run for each level. The results are summarized below. Linearity for pH, and ctHb was previously established in K240998.

Parameter (units)	Reportable Range	Tested Range	Slope	Intercept	R2
pC02 (mmHg)	15.4-98.3	9.4 – 99.89	1.009	0	0.9995

3. Analytical Specificity/Interference:

Interference testing was performed according to CLSI EP07-ED3 and CLSI EP37-ED1 and consisted of two parts: paired-difference testing and dose-response experiments.

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 was used as starting material for the interference studies. Interference testing was conducted at two levels (i.e., low and high) for

pCO2. The following tables list 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 parameter pCO2	Concentration
Bilirubin, conjugated	40 mg/dL
Bilirubin, unconjugated	40 mg/dL
Biotin	3510 ng/mL
Hemolysis	20%
Intralipid	2000 mg/dL
Propofol	4.8 mg/dL

Interference for pH, and ctHb was previously established in K240998.

4. Assay Reportable Range:

The reportable ranges are

Parameter	Unit	Reportable Range
pH	pH Scale	6.818 - 7.797
*p*CO2	mmHg	15.4 - 98.3
*c*tHb	g/dL	0.1 - 24.0

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

pCO2: Traceable to the International System of Units (SI) via commercially available certified specialty medical gas standards.

Refer to K240998 for traceability information for pH and ctHB

6. Detection Limit:

Detection capability testing was conducted in general accordance with CLSI EP17-A2. To achieve target concentrations, heparinized venous whole blood samples for pCO2 were prepared via tonometry. Testing was performed on the ABL90 FLEX PLUS System using 3 reagent lots, 9 instruments, over the course of 9 days, using 4 independent samples, with at least 5 replicates/sample, and 60 replicates/reagent lot.

Parameter (units)	Reportable Range	LoQ results
pCO2 (mmHg)	15.4-98.3 mmHg	8.9

Detection limits for pH and ctHB were previously established in K240998

7. Assay Cut-Off:

   Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:
   Method comparison for pCO2 using heparinized arterial and venous whole blood specimens in S65 and SP65 mode and for pH, pCO2, and ctHb in heparinized capillary whole blood samples in C65 mode on the ABL90 FLEX PLUS System was done in general accordance with CLSI EP09c-ED3. Heparinized arterial and venous whole blood specimens (maximum of 10% contrived) that spanned the measuring range were collected across 3 POC sites to evaluate pCO2 measurements. Capillary blood samples (maximum of 10% contrived) collected across 2 POC sites in 2 *safe*CLINITUBE capillary tubes, with at least two POC users per site was compared to 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 two measurements was performed using linear regression analysis. The regression analysis are summarized below.

Method Comparison - pCO2 in Arterial and Venous Whole Blood

Parameter	n	Range Min	Range Max	Intercept	Slope	R2	Medical decision level (MDL)	Bias at MDL
S65								
*p*CO2 (mmHg)	446	16.1	95	0.55	0.99	1.0	32	0.20
							48	0.03
SP65								
*p*CO2 (mmHg)	429	16.3	97.1	0.60	0.99	1.0	32	0.21
							48	0.02

Method comparison – capillary whole blood

Parameter	N	Intercept	Slope	R^2	MDL	Bias at MDL
pH (pH scale)	115	-0.118	1.01	0.93	7.35	-0.01
					7.45	-0.01
pCO2 (mmHg)	119	3.094	0.95	0.93	32	1.6
					48	0.85
ctHb (g/dL)	110	0.713	0.99	0.95	7	0.66
					10	0.63
					17.5	0.57

Parameter	N	Range Min	Range Max	MDL	Bias at MDL
pH	115	6.87	7.78	7.35	-0.01
				7.45	-0.01
pCO2 (mmHg)	119	17	92.9	32	1.6
				48	0.85
ctHb (g/dL)	110	0.36	22	7	0.66
				10	0.63
				17.5	0.57

2. Matrix Comparison:

   Not applicable.

C Clinical Studies:

1. Clinical Sensitivity:
   Not applicable.

2. Clinical Specificity:

   Not applicable.

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

D Clinical Cut-Off:
Not applicable.

E Expected Values/Reference Range:

Below are general reference ranges, cited from literature, for a normal, healthy population.

Parameter	Unit	Reference range
*p*CO2	mmHg; Torr	35-481 (male) 32-451 (female)
	kPa	4.67-6.401 (male) 4.27-6.001 (female)
ctHb	(g/dL)	13.5 – 17.53 (male) / 12.0 – 16.03 (female) [2]
pH		7.35 – 7.45[1]

[1] Tietz NW, Logan NM. Reference ranges, In: Fundamentals of clinical chemistry. 3rd ed. Philadelphia: WB Saunders Company 1987: 944-75.
[2] 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.