510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
INSTRUMENT AND ASSAY TEMPLATE

A. 510(k) Number:

k111188

B. Purpose for Submission:

New Device

C. Measurand:

pH, pO2, pCO2, sodium, potassium, ionized calcium, Hct, tHb, O2Hb, HHb, COHb, MetHb, SO2, lactic acid, glucose

D. Type of Test:

Quantitative

E. Applicant:

Roche Diagnostics Corporation

F. Proprietary and Established Names:

Cobas® b 123 POC System**, Cobas® b** 123 AutoQC Pack Tri-Level**, Cobas® b** 123 AutoCVC Pack, Roche COMBITROL PLUS B

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
CHL	Class II	21 CFR § 862.1120 Blood gases (pCO2, pO2) and blood pH test system	75
JGS	Class II	21 CFR § 862.1665 Sodium test system	75
CEM	Class II	21 CFR § 862.1600 Potassium test system	75
JFP	Class II	21 CFR § 862.1145	75

		Calcium test system	
GKF	ass II	21 CFR § 864.5600 Hematocrit automated instrument	81
CGA	Class II	21 CFR § 862.1345 Glucose test system	75
KHP	Class I, meets limitations of exemptions per 21 CFR § 862.9 (c)(9)	21 CFR § 862.1450 Lactic acid test system	75
KHG	Class II	21 CFR § 864.7500 Whole blood hemoglobin assays (tHb)	81
GGZ	Class II	21 CFR § 864.7500 Whole blood hemoglobin assays (Oxyhemoglobin)	81
GKA	Class II	21 CFR § 864.7500 Deoxyhemoglobin	81
GHS	Class II	21 CFR § 864.7425 Carboxyhemoglobin	81
KHG	Class II	21 CFR § 864.5620 Methemoglobin	81
GLY	Class II	870.1230 Oximeter Oxygen Saturation	81
JJY	Class I, reserved	21 CFR § 862.1660 Quality control material (assayed and unassayed)	75

H. Intended Use:

1. Intended use(s):

   See indications for use statements below.

2. Indication(s) for use:

Device Name: cobas® b 123 POC System

The **cobas b** 123 POC system is a fully automated POC system for whole blood in vitro measurement of pH, blood gases (BG), electrolytes Na^+, K^+, iCa^{2+} (ISE), hematocrit (Hct), metabolites (Glu, Lac), total hemoglobin (tHb), hemoglobin derivatives (O_2Hb, HHb, COHb, MetHb), and oxygen saturation (SO_2). In addition, the **cobas b** 123 POC system calculates derived parameters.

It is dedicated for use in a Point-of-Care environment and laboratory. The integrated AutoQC module and the oximeter module are available as an option.

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

Sodium (Na^+): 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.

Potassium (K^+): potassium measurements are used to monitor electrolyte balance in the diagnosis and treatment of disease conditions characterized by low or high blood potassium levels.

Calcium (Ca^{2+}): calcium measurements are used in the diagnosis and treatment of parathyroid disease, a variety of bone diseases, chronic renal disease and tetany (intermittent muscular contractions or spasms).

Hematocrit (Hct): hematocrit measurements are used to distinguish normal from abnormal states of whole blood, such as anemia and erythrocytosis (an increase in the number of red cells).

Glucose (Glu): glucose measurements are used in the diagnosis and treatment of carbohydrate metabolism disorders including diabetes mellitus and idiopathic hypoglycemia, and of pancreatic islet cell carcinoma.

Lactate (Lac): Lactate measurements are used to evaluate the acid-base status and are used in the diagnosis and treatment of lactic acidosis (abnormally high acidity of the blood.)

Total Hemoglobin (tHb): total hemoglobin measurements are used to measure the hemoglobin content of whole blood for the detection of anemia.

O_2Hb: oxyhemoglobin as a fraction of total hemoglobin.

COHb: carboxyhemoglobin measurements are used to determine the carboxyhemoglobin content of human blood as an aid in the diagnosis of carbon monoxide poisoning.

MetHb: methemoglobin as a fraction of total hemoglobin.

HHb: reduced hemoglobin as a fraction of total hemoglobin.

SO_2: oxygen saturation, more specifically the ratio between the concentration of oxyhemoglobin and oxyhemoglobin plus reduced hemoglobin.

Device Name: cobas® b 123 AutoQC Pack Tri-Level

The **cobas b** 123 AutoQC pack Tri-Level is a multi-analyte control intended for use as control material to monitor the measurement of pH, PCO_2, PO_2, SO_2, Na^+, K^+, iCa^{2+}, Hct, tHb and Hb derivatives as well as glucose and lactate on **cobas b** 123 systems with an AutoQC module.

Device Name: cobas® b 123 AutoCVC Pack

The **cobas b** 123 AutoCVC Pack is a multi-analyte control, intended for use in calibration verification of the measuring range established by the **cobas b** 123 POC system for pH, PCO_2, PO_2, SO_2, Na^+, K^+, iCa^{2+}, Hct, tHb and Hb derivatives as well as glucose and lactate on **cobas b** 123 systems with an AutoQC module.

Device Name: Roche COMBITROL PLUS B

COMBITROL PLUS B is a multi-analyte control intended for use as control material to monitor the measurement of pH, PCO_2, PO_2, SO_2, Na^+, K^+, iCa^{2+}, Hct, tHb and Hb derivatives as well as glucose, lactate, urea/BUN and bilirubin on Roche OMNI S or **cobas b** 221 analyzers with an oximeter module, and **cobas b** 123 analyzers (except urea/BUN, and bilirubin). COMBITROL PLUS B control material is not intended for use with analyzers from other manufacturers.

3. Special conditions for use statement(s):

   For prescription use.

   For Point of Care

4. Special instrument requirements:

   Cobas b 123 POC System

I. Device Description:

The **cobas b** 123 POC system consists of a modular system analyzer which contains the following components:

An electrochemical sensor system independent of the reagent delivery system for the following analytes:

- pCO2, pH, calcium, potassium, and sodium (potentiometric measurement)
- pO2 (amperometric measurement)
- Hct (conductivity measurement)
- Glucose and Lactate enzyme (amperometric measurement)

An optionally integrated oximeter module consisting of a spectrometer, measurement and calibration light source, respectively, an ultrasonic hemolyzer and thermostatic components measure SO2, tHb, O2Hb, HHb, COHb, and MetHb

A disposable, self-contained sample and reagent delivery system containing liquid reagents, calibrators and waste container, built-in safety shielded sample port, built-in oximeter cuvette, two peristaltic pump fluidics systems, and built in air filter

The system also includes an optional integrated Auto QC module that uses a disposable cassette containing three levels of QC material.

A smart memory chip is incorporated into each biosensor, reagent pack (sample and reagent delivery system) and AutoQC cassette which tracks and monitors the sensor,reagent pack, AutoQC and AutoCVC cassette usage

Cobas b 123 AutoQC Pack Tri-Level:

- 24 single glass ampoules of multi-analyte controls in 3 levels

Cobas b 123 AutoCVC Pack:

- 24 single glass ampoules of multi-analyte controls in 6 levels

Roche COMBITROL PLUS B:

- Multi-analyte controls available in 3 levels

J. Substantial Equivalence Information:

The **cobas b** 123 POC System is equivalent to **cobas b** 221 (OMNI S Analyzer) k032311 for the following parameters:

- pH
- pO2
- pCO2
- Na+
- K+

- Ca2+
- Hct
- tHb
- O2Hb
- HHb
- COHb
- MetHb
- SO2

The **cobas b** 123 POC system is equivalent to Roche Gluco-Quant Glucose/HK assay on the Hitachi 902 (k921661) and the Roche Glucose HK Assay on the **cobas c 501 analyzer** (k060373/A001) for the measurement of glucose.

The **cobas b** 123 POC system is equivalent to the Roche Lactate assay on the Hitachi 902 analyzer (k921661) and the Lactate Generation 2 (Gen.2) assay on the **cobas c** 501 analyzer (k060373) for the measurement of lactate.

The **cobas b** 123 AutoQC Pack Tri-Level, **cobas b** 123 AutoCVC Pack, and COMBITROL PLUS B materials are substantially equivalent to the Roche AUTOTROL PLUS B and Roche COMBITROL PLUS B materials – k032453.

Similarities between candidate and predicate devices:

Characteristic	Candidate Device: cobas b 123 POC System	Predicate Device: cobas b 221 (k032311)
Intended Use	The **cobas b** 123 POC system is a fully automated POC system to measure pH, blood gases (BG), electrolytes (ISE), hematocrit (Hct), metabolites (Glu, Lac), total hemoglobin (tHb), hemoglobin derivatives (O_2Hb, HHb, COHb, MetHb), and oxygen saturation (SO_2). In addition, the **cobas b** 123 POC system calculates derived parameters. It is dedicated for use in a Point-of-Care environment and laboratory. The integrated AutoQC module and the oximeter module are available as an option. Depending on the equipment configuration of the instrument, the Sensor Cartridge and the Fluid Pack used, the following parameters are measured in human whole blood and QC materials.	Same

Test Principle	Enzymatic (Lactate) Enzymatic (Glucose)	Same
Blood Gas Measurement	pH and pCO_2 by potentiometry pO_2 by amperometry	Same
Electrolyte Measurement	K^+, Na^+, and Ca^{2+} by potentiometry	Same
Metabolite Measurement	Glucose and Lactate by amperometry	Same
Hemoglobin Measurement	tHb, SO2, O2Hb, HHb, COHb, MetHb:Spectrophotometric	Same
Hematocrit Measurement	Conductivity	Same
Sensor Technology	Amperometric and potentiometric thick film microelectrode array technology for Glucose and Lactate	Same
Sample Introduction	Syringe and capillary aspiration	Same
On-Board (In-Use) Reagent Stability	Up to 42 days	Same
Reagent Tracking	Memory chip technology for identification, lot specifications, usage tracking and traceability allowing pack to be moved from one system to another	Same
QC Material	COMBITROL PLUS B (manual QC) and AUTOTROL PLUS B (automated QC)	Same
Calibration	Two-point liquid calibration	Same
Graphical User Interface	Menu-driven touch screen	Same
Additional Analyzer Hardware	Hard drive and printer	Same
Operating System Software	Linux-based	Same
System Operating Temperature	15-32°C	Same

Characteristic	Candidate Device cobas b 123 AutoQC Pack Tri-Level	Predicate Device Roche AUTOTROL PLUS B (k032453)
Intended use	Intended for use as a quality control material	same
Number of Levels	3	Same
Matrix	Buffered, aqueous electrolyte solution equilibrated with carbon dioxide and oxygen gas mixture	Same
Technological Characteristics	The material consists of buffered aqueous electrolyte solutions with clinically relevant concentrations of the targeted analytes, tonometered with precision gas mixtures of carbon dioxide and oxygen to achieve pH and blood gas values that span the range of values typical for such products with the same intended use. A mixture of dyes is used to simulate absorbance of hemoglobin derivatives. Hematocrit is simulated by conductivity.	Same

Characteristic	Candidate Device Modified COMBITROL PLUS B	Predicate Device Roche AUTOTROL PLUS B (k032453)
Intended Use	intended for use as a quality control material	same
Number of Levels	3	Same
Fill Volume	1.7 mL	Same
Matrix	Buffered, aqueous electrolyte solution equilibrated with carbon dioxide and oxygen gas mixture	Same
Technological Characteristics	The material consists of buffered aqueous electrolyte solutions with clinically relevant concentrations of	Same

	the targeted analytes, tonometered with precision gas mixtures of carbon dioxide and oxygen to achieve pH and blood gas values that span the range of values typical for such products with the same intended use. A mixture of dyes is used to simulate absorbance of hemoglobin derivatives. Hematocrit is simulated by conductivity.	

Characteristic	**Candidate Device cobas b 123 AutoCVC Pack**	**Predicate Device Roche AUTOTROL PLUS B (k032453)**
Intended use	Intended for use as a quality control material	same
Matrix	Buffered, aqueous electrolyte solution equilibrated with carbon dioxide and oxygen gas mixture	Same
Technological Characteristics	The material consists of buffered aqueous electrolyte solutions with clinically relevant concentrations of the targeted analytes, tonometered with precision gas mixtures of carbon dioxide and oxygen to achieve pH and blood gas values that span the range of values typical for such products with the same intended use. A mixture of dyes is used to simulate absorbance of hemoglobin derivatives. Hematocrit is simulated by conductivity.	Same

Differences between candidate and predicate devices:

Characteristic	Candidate Device cobas b 123 POC System	Predicate Device cobas b 221 (k032311)
Sample Volume	123 µl	210 µl
Electrochemical Sensors	pH, PO_2, PCO_2, K^+, Na^+, Ca^{2+}, Glucose, Reference microelectrode array sensor with up to 28 days in-use life **Note:** Sensors with Lactate are stable up to 21 days.	pH, PO_2, PCO_2, K^+, Na^+, Cl, Ca^{2+} Reference electrodes with 6 to 16 months in-use life, depending on the electrode type.
Electrochemical sensor storage stability	Sensor: 2°C – 8°C for 4 months	Sensor: 25°C for 18 or 24 months, depending on electrode type
Auto QC Module	AutoQC Module holds one AutoQC Pack, which is comprised of 24 AUTOTROL PLUS B tri-level ampoules.	QC module holds 120 AUTOTROL PLUS B tri-level ampoules.

Characteristic	Candidate Device cobas b 123 POC System	Predicate Device Roche Hitachi Glucose HK Assays: Hitachi 902 (k921661) and cobas c 501 (k060373)
Sample Type	Whole Blood	Serum, plasma, urine, CSF, and hemolysate
Measurement Principle	Amperometric measurement of the detectable product (H_2O_2) under a polarization voltage of 350 mV.	UV photometric measurement of the detectable product (NADPH) at 340 nm.

Characteristic	Candidate Device cobas b 123 POC System	Predicate Device Roche Hitachi Lactate Assays: Hitachi 902 (k921661) and cobas c 501 (k060373)
Measurement Principle	Amperometric measurement of the detectable product (H_2O_2) under a polarization voltage of 350 mV.	UV photometric measurement of the detectable product (chromogen) at 340 nm.

Characteristic	Candidate Device cobas b 123 AutoQC Pack Tri-Level	Predicate Device Roche AUTOTROL PLUS B (k032453)
Auto QC Pack	The AutoQC Pack is comprised of 24 AUTOTROL PLUS B tri-level ampoules. The AutoQC Pack also contains a smart memory chip for tracking and traceability, allowing the pack to be moved from one system to another.	The QC Pack holds 120 AUTOTROL PLUS B tri-level ampoules. The QC Pack does not contain a smart memory chip.
Fill Volume	1.0 mL	1.7 mL

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

1. EP5-A2: Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline

2. EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline

3. EP7-A2: Interference Testing in Clinical Testing; Approved Guideline – Second Edition

4. EP9-A2: Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Second Edition

5. EP17-A: Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline

6. IEC 61326-1: Electrical Equipment for Measurement, Control and Lab Use-EMC Requirements (Part 1: General Requirements)

7. IEC 61326-2: Electrical Equipment for Measurement, Control and Lab Use- EMC Requirements (Part 2-6: IVD Equipment)

L. Test Principle:

The cobas b 123 POC system measures the analytes pH, K+, Ca2+, and Na+ use potentiometric sensors which transmit direct signals that relate the content of the sample to be measured. A reference electrode is used to provide a stable, fixed

potential against which other potential differences can be measured.

Amperometry is used to measure glucose, lactate, and pO2. For this method of measurement, the magnitude of an electrical flow of current proportional to the concentration of the substance being oxidized or reduced at an electrode results in a measurement of glucose, lactate, and pO2 in the blood.

Spectrophotometry is used to measure the analytes: tHb, SO2, O2Hb, HHb, COHb, MetHb. For this method, light passes through the blood samples; specific wavelengths are absorbed and their intensity generates an absorption spectrum used to calculate oximetry parameters.

M. Performance Characteristics (if/when applicable):

All performance studies were conducted on the **cobas b** 123 POC system.

1. Analytical performance:

   a. Precision/Reproducibility:

   A precision study was performed following CLSI EP5-A2 guidance. Within – run and total precision were conducted using control materials and/or tonometered whole blood samples in duplicate in two runs per day for 20 days (N=80). Testing was conducted using the cobas b 123 POC syringe mode. Results of the precision studies are as follows:

pH Precision Data						
Sample	**Mean (pH Units)**	**N**	**Within run SD**	**Within run % CV**	**Total imprecision SD**	**Total Imprecision %CV**
Level 1	7.149	80	0.007	0.04	0.020	0.08
Level 2	7.393	80	0.007	0.02	0.020	0.06
Level 3	7.543	80	0.007	0.02	0.020	0.06
Level 4	6.883	80	0.012	0.02	0.028	0.12
Level 5	7.731	80	0.014	0.02	0.033	0.08

pO2 Precision Data						
Sample	**Mean (mmHg)**	**N**	**Within run SD**	**Within run % CV**	**Total imprecision SD**	**Total Imprecision %CV**
Blood 1	145.4	80	1.629	0.51	3.039	2.23
Blood 2	40.5	80	1.974	1.70	3.306	6.09
Blood 3	352.2	80	6.614	0.59	12.553	2.49
Level 1	58.5	80	4.550	1.79	5.076	3.00

Level 2	98.7	80	4.775	1.69	5.358	3.57
Level 3	147.6	80	5.442	0.78	6.188	3.17
Level 4	28.9	80	6.595	6.32	7.643	8.31
Level 5	448.5	80	23.168	1.25	29.963	3.76

pCO2 Precision Data						
Sample	**Mean (mmHg)**	**N**	**Within run SD**	**Within run % CV**	**Total imprecision SD**	**Total Imprecision %CV**
Blood 1	23.5	80	1.150	0.50	1.725	2.21
Blood 2	72.7	80	1.570	0.51	2.180	3.18
Blood 3	128.6	80	5.047	1.39	6.868	2.61
Level 1	64.2	80	1.349	0.69	1.856	1.64
Level 2	41.9	80	1.151	0.64	1.656	1.44
Level 3	25.7	80	1.007	0.36	1.510	1.69
Level 4	123.5	80	4.729	0.60	6.412	2.70
Level 5	19.2	80	1.578	0.75	2.368	2.12

Na Precision Data						
Sample	**Mean (mmHg)**	**N**	**Within run SD**	**Within run % CV**	**Total imprecision SD**	**Total Imprecision %CV**
Level 1	117.4	80	1.337	0.34	1.957	0.44
Level 2	141.0	80	1.536	0.11	2.304	0.35
Level 3	153.7	80	1.740	0.29	2.610	0.52
Level 4	113.2	80	1.557	0.16	2.208	0.65
Level 5	177.5	80	2.336	0.11	3.373	0.69

K Precision Data						
Sample	**Mean (mmHg)**	**N**	**Within run SD**	**Within run % CV**	**Total imprecision SD**	**Total Imprecision %CV**
Level 1	2.98	80	0.051	0.37	0.102	0.57
Level 2	4.72	80	0.066	0.15	0.134	0.37
Level 3	7.01	80	0.088	0.32	0.177	0.74
Level 4	9.25	80	0.153	0.16	0.352	1.26
Level 5	2.02	80	0.088	0.30	0.198	1.44

iCa Precision Data						
Sample	**Mean (mg/dL)**	**N**	**Within run SD**	**Within run % CV**	**Total imprecision SD**	**Total Imprecision %CV**
Level 1	6.80	80	0.040	0.61	0.067	0.77
Level 2	4.80	80	0.030	0.24	0.050	0.37
Level 3	2.64	80	0.030	0.74	0.050	0.92
Level 4	8.63	80	0.062	0.25	0.103	0.78
Level 5	1.60	80	0.030	0.63	0.050	1.89

Hct Precision Data						
Sample	**Mean (%)**	**N**	**Within run SD**	**Within run % CV**	**Total imprecision SD**	**Total Imprecision %CV**
Level 1	58.9	80	0.978	0.24	1.467	0.80
Level 2	40.9	80	0.617	0.21	0.926	1.05
Level 3	32.5	80	0.451	0.22	0.676	1.06
Level 5	19.0	80	1.783	0.38	2.676	1.18
Level 6	63.6	80	1.718	0.09	2.576	0.75

Glucose Precision Data						
Sample	**Mean (mg/dL)**	**N**	**Within run SD**	**Within run % CV**	**Total imprecision SD**	**Total Imprecision %CV**
Level 1	111	80	0.126	0.59	0.304	1.67
Level 2	47.3	80	0.104	0.85	0.177	2.23
Level 3	454.5	80	0.302	0.37	1.253	2.29
Level 5	45.5	80	0.103	0.91	0.176	3.55
Level 6	510	80	0.329	0.77	1.307	2.77

Lactate Precision Data						
Sample	**Mean (mg/dL)**	**N**	**Within run SD**	**Within run % CV**	**Total imprecision SD**	**Total Imprecision %CV**
Level 1	96	80	0.36	0.37	2.24	2.34
Level 2	29	80	0.07	0.24	0.58	2.03
Level 3	15	80	0.05	0.32	0.42	2.65
Level 5	57	80	0.59	1.04	1.34	2.37
Level 6	128	80	0.92	0.72	3.83	3.00

tHb Precision Data						
Sample	**Mean (g/dL)**	**N**	**Within run SD**	**Within run % CV**	**Total imprecision SD**	**Total Imprecision %CV**
Level 1	7.1	80	0.135	0.66	0.174	2.29
Level 2	11.5	80	0.172	0.72	0.222	1.12
Level 3	19.6	80	0.294	0.82	0.344	1.21
Level 5	6.1	80	0.131	0.60	0.166	2.12
Level 6	21.7	80	0.335	0.63	0.402	1.06

O2Hb Precision Data						
Sample	**Mean (%)**	**N**	**Within run SD**	**Within run % CV**	**Total imprecision SD**	**Total Imprecision %CV**
Level 1	48.3	80	1.000	0.25	1.500	0.54
Level 2	75.8	80	1.000	0.55	1.500	0.63
Level 3	92.0	80	1.000	0.40	1.500	0.42
Level 5	42.1	80	1.000	0.28	1.500	0.49
Level 6	94.3	80	1.000	0.40	1.500	0.39

HHb Precision Data						
Sample	**Mean (%)**	**N**	**Within run SD**	**Within run % CV**	**Total imprecision SD**	**Total Imprecision %CV**
Level 1	17.6	80	1.000	0.24	1.500	0.52
Level 2	8.2	80	1.000	1.78	1.500	2.02
Level 3	2.7	80	1.000	4.73	1.500	4.92
Level 5	19.7	80	1.000	0.21	1.500	0.37
Level 6	1.9	80	1.000	6.88	1.500	6.58

COHb Precision Data						
Sample	**Mean (%)**	**N**	**Within run SD**	**Within run % CV**	**Total imprecision SD**	**Total Imprecision %CV**
Level 1	22.4	80	0.350	0.24	0.510	0.52
Level 2	10.4	80	0.250	1.78	0.500	2.03
Level 3	3.5	80	0.250	4.63	0.500	4.82
Level 5	25.1	80	0.350	0.21	0.520	0.37
Level 6	2.5	80	0.250	6.65	0.500	6.36

MetHb Precision Data						
Sample	**Mean (%)**	**N**	**Within run SD**	**Within run % CV**	**Total imprecision SD**	**Total Imprecision %CV**
Level 1	11.7	80	0.286	0.21	0.545	0.46
Level 2	5.7	80	0.250	1.49	0.500	1.70
Level 3	2.0	80	0.250	3.98	0.500	4.13
Level 5	13.1	80	0.314	0.18	0.583	0.33
Level 6	1.4	80	0.250	5.67	0.500	5.41

SO2 Precision Data						
Sample	**Mean (%)**	**N**	**Within run SD**	**Within run % CV**	**Total imprecision SD**	**Total Imprecision %CV**
Level 1	73.4	80	1.500	0.13	2.000	0.28
Level 2	90.3	80	1.500	0.23	2.000	0.26
Level 3	97.1	80	1.500	0.15	2.000	0.15
Level 5	68.2	80	1.500	0.16	2.000	0.27
Level 6	98.0	80	1.500	0.15	2.000	0.14

An additional precision study was performed between the syringe mode and the capillary mode using whole blood samples. The syringe mode results provided by the sponsor demonstrated comparable results to the capillary mode. Within-run precision for all analytes (parameters) for the capillary mode are summarized below:

Analyte	**Unit of Measure**	**Sample**	**Capillary**			
			Mean	**S_R**	**CV (%)**	**n**
pH	pH Units	1	7.18	0.003	0.04	24
		2	7.36	0.002	0.02	32
pO_2	mmHg	1	75.42	0.31	0.40	24
		2	132.75	1.349	1.00	32
pCO_2	mmHg	1	68.13	0.192	0.28	24
		2	31.43	0.199	0.63	32
Na^+	mEq/L	1	98.77	0.485	0.5	12
		2	113.51	0.187	0.2	12
		3	141.34	0.676	0.5	12
		4	160.68	0.498	0.3	12
		5	183.69	0.431	0.2	12
K^+	mEq/L	1	2.08	0.020	1.0	12
		2	4.88	0.048	1.0	12
		3	3.93	0.019	0.5	12
		4	12.48	0.041	0.3	12
		5	19.40	0.042	0.2	12

iCa^{2+}	mg/dL	1	2.20	0.020	0.9	12
		2	4.88	0.036	0.8	12
		3	11.69	0.108	0.9	12
		4	7.13	0.024	0.3	12
Hct	%	1	64.81	0.123	0.20	8
		2	49.97	0.305	0.61	8
		3	42.10	0.080	0.20	8
		4	28.70	0.062	0.20	8
		5	20.39	0.134	0.70	8
Glucose	mg/dL	1	101.44	0.025	0.5	8
		2	71.71	0.031	0.8	8
		3	81.08	0.032	0.7	8
		4	49.55	0.008	0.3	8
		5	274.05	0.071	0.5	8
Lactate	mg/dL	1	24.68	0.033	1.2	12
		2	34.77	0.034	0.9	12
		3	28.92	0.052	1.6	12
		4	59.82	0.028	0.4	12
		5	53.96	0.047	0.8	12
tHb	g/dL	1	15.49	0.182	1.18	24
		2	6.94	0.071	1.02	20
		3	19.32	0.243	1.26	20

Whole blood precision study (capillary mode):

An additional precision study was conducted following guidance from CLSI EP5-A2. Whole blood was collected for use in an "in-house" precision study and utilized twenty (20) cobas b 123 POC analyzers, two sensor lots, samples tested in one run per day, in two replicates, and with samples at three clinically significant concentrations. The following tables present a summary of results:

Repeatability (Within-Run): Summary of Results for pH

Sample	Mean (pH Units)	SD (pH Units)	CV (%)	n
Blood Sample 1	7.237	0.0029	0.04%	40
Blood Sample 2	7.441	0.0029	0.03%	40
Blood Sample 3	7.568	0.0054	0.07%	40

Repeatability (Within-Run): Summary of Results for pO_2

Sample	Mean (mmHg)	SD (mmHg)	CV (%)	n
Blood 1	145.4	0.7404	0.51	80
Blood 2	40.5	0.6888	1.70	80
Blood 3	352.2	2.0866	0.59	80

Repeatability (Within-Run): Summary of Results for pCO_2

Sample	Mean (mmHg)	SD (mmHg)	CV (%)	n
Blood 1	23.5	0.1174	0.50	80
Blood 2	72.7	0.3728	0.51	80
Blood 3	128.6	1.7942	1.39	80

Repeatability (Within-Run): Summary of Results for Na^+

Sample	Mean (mEq/L)	SD(mEq/L)	CV (%)	n
Blood Sample 1	117.7	0.2845	0.24%	40
Blood Sample 2	138.6	0.2709	0.19%	40
Blood Sample 3	156.2	0.5890	0.37%	40

Repeatability (Within-Run): Summary of Results for K^+

Sample	Mean (mEq/L)	SD (mEq/L)	CV (%)	n
Blood Sample 1	3.05	0.0221	0.72%	40
Blood Sample 2	5.00	0.0148	0.29%	40
Blood Sample 3	6.10	0.0198	0.32%	40

Repeatability (Within-Run): Summary of Results for Ca^{2+}

Sample	Mean (mg/dL)	SD (mg/dL)	CV (%)	n
Blood Sample 1	2.90	0.03	1.065%	40
Blood Sample 2	4.74	0.04	0.79%	40
Blood Sample 3	5.60	0.07	1.25%	40

Repeatability (Within-Run): Summary of Results for Hct

Sample	Mean (%)	SD (%)	CV (%)	n
Blood Sample 1	22.1	0.2461	1.11%	40
Blood Sample 2	38.5	0.1597	0.41%	40
Blood Sample 3	62.3	0.2370	0.38%	40

Repeatability (Within-Run): Summary of Results for Glucose

Sample	Mean (mg/dL)	SD (mg/dL)	CV (%)	n
Blood Sample 1	47	1.1	2.28%	40
Blood Sample 2	90	1.1	1.27%	40
Blood Sample 3	488	2.8	0.56%	40

Repeatability (Within-Run): Summary of Results for Lactate

Sample	Mean (mg/dL)	SD (mg/dL)	CV (%)	n
Blood Sample 1	8	0.10	1.18%	40
Blood Sample 2	13	0.09	0.69%	40
Blood Sample 3	32	0.51	1.56%	40

Repeatability (Within-Run): Summary of Results for tHb

Sample	Mean (g/dL)	SD (g/dL)	CV (%)	n
Blood Sample 1	6.5	0.1058	1.62%	40
Blood Sample 2	12.9	0.0874	0.67%	40
Blood Sample 3	20.7	0.0703	0.33%	40

Repeatability (Within-Run): Summary of Results for O_2Hb

Sample	Mean (%)	SD (%)	CV (%)	n
Blood Sample 1	80.6	1.2296	1.52%	40
Blood Sample 2	94.5	0.5108	0.54%	40
Blood Sample 3	97.4	0.1342	0.13%	40

Repeatability (Within-Run): Summary of Results for HHb

Sample	Mean (%)	SD (%)	CV (%)	n
Blood Sample 1	5.2	0.1828	3.51%	40
Blood Sample 2	9.5	0.2190	2.31%	40
Blood Sample 3	17.0	1.2248	7.20%	40

Repeatability (Within-Run): Summary of Results for COHb

Sample	Mean (%)	SD (%)	CV (%)	n
Blood Sample 1	2.0	0.0946	4.73%	40
Blood Sample 2	5.4	0.0688	1.27%	40
Blood Sample 3	13.4	0.0894	0.66%	40

Repeatability (Within-Run): Summary of Results for MetHb

Sample	Mean (%)	SD (%)	CV (%)	n
Blood Sample 1	1.3	0.0672	5.16%	40
Blood Sample 2	5.8	0.1125	1.93%	40
Blood Sample 3	30.7	0.3221	1.04%	40

Repeatability (Within-Run): Summary of Results for SO_2

Sample	Mean (%)	SD (%)	CV (%)	n
Blood Sample 1	82.6	1.2561	1.52%	40
Blood Sample 2	96.8	0.4976	0.51%	40
Blood Sample 3	99.7	0.1190	0.11%	40

A POC precision study was conducted at 6 external POC sites. The following table is a summary of precision studies conducted at the external POC sites using the cobas b 123 AutoQC Pack Tri-Level QC material:

	QC Level	Analyte Concentration (Mean)	Within-Run (SD)	Within-Run (% CV)	Total Precision (SD)	Total Precision (% CV)
Ca	Level 1	6.85 mg/dL	0.01 mg/dL	0.17	0.04 mg/dL	0.37
	Level 2	4.93 mg/dL	0.01 mg/dL	0.24	0.02 mg/dL	0.37
	Level 3	2.69 mg/dL	0.02 mg/dL	0.57	0.04 mg/dL	0.81
K	Level 1	2.99 mEq/L	0.01 mEq/L	0.19	0.01 mEq/L	0.45
	Level 2	4.71 mEq/L	0.01 mEq/L	0.2	0.01 mEq/L	0.26
	Level 3	6.97 mEq/L	0.01 mEq/L	0.16	0.02 mEq/L	0.34
Na	Level 1	117.5 mEq/L	0.14 mEq/L	0.12	0.33 mEq/L	0.28
	Level 2	140.4 mEq/L	0.24 mEq/L	0.17	0.34 mEq/L	0.24
	Level 3	153.1 mEq/L	0.22 mEq/L	0.14	0.33 mEq/L	0.22
Glu	Level 1	110 mg/dL	0.72 mg/dL	0.66	1.4 mg/dL	1.29
	Level 2	45 mg/dL	0.72 mg/dL	1.74	0.90 mg/dL	1.98
	Level 3	443 mg/dL	2.3 mg/dL	0.55	6.3 mg/dL	1.49
Lac	Level 1	94.6 mg/dL	0.54 mg/dL	0.56	1.4 mg/dL	1.51

	Level 2	27.9 mg/dL	0.27 mg/dL	0.87	0.45 mg/dL	1.56
	Level 3	15.3 mg/dL	0.18 mg/dL	1.21	0.36 mg/dL	2.43
Hct	Level 1	59.4%	0.10%	0.17	0.24%	0.4
	Level 2	41.4 %	0.14%	0.33	0.19%	0.47
	Level 3	33.0 %	0.12%	0.37	0.16%	0.49
PCO2	Level 1	64.6 mmHg	0.45 mmHg	0.7	0.76 mmHg	1.17
	Level 2	42.2 mmHg	0.17 mmHg	0.4	0.37 mmHg	0.88
	Level 3	25.9 mmHg	0.15 mmHg	0.57	0.42 mmHg	1.62
PO2	Level 1	60.0 mmHg	0.92 mmHg	1.57	1.89 mmHg	3.22
	Level 2	100.0 mmHg	1.00 mmHg	1.01	2.00 mmHg	2.02
	Level 3	148.0 mmHg	1.47 mmHg	1	2.44 mmHg	1.66
pH	Level 1	7.140	0.002	0.03	0.003	0.05
	Level 2	7.385	0.001	0.02	0.002	0.03
	Level 3	7.542	0.001	0.01	0.002	0.03
COHb	Level 1	22.5 %	0.12%	0.53	0.14%	0.64
	Level 2	10.4 %	0.20%	1.96	0.22%	2.07
	Level 3	3.5 %	0.25%	6.98	0.26%	7.32
HHb	Level 1	17.6%	0.10%	0.55	0.12%	0.67
	Level 2	8.1 %	0.16%	1.98	0.17%	2.08
	Level 3	2.9 %	0.19%	7.14	0.20%	7.45
MetHb	Level 1	11.8 %	0.06%	0.51	0.07%	0.61
	Level 2	5.7 %	0.10%	1.69	0.10%	1.82
	Level 3	1.9 %	0.12%	6.12	0.12%	6.3
O2Hb	Level 1	48.2 %	0.26%	0.55	0.32%	0.66
	Level 2	76.0 %	0.45%	0.6	0.48%	0.63
	Level 3	92.1 %	0.55%	0.6	0.57%	0.62
SO2	Level 1	73.2 %	0.20%	0.28	0.25%	0.34
	Level 2	90.3 %	0.23%	0.25	0.24%	0.27
	Level 3	96.9 %	0.21%	0.22	0.22%	0.23
tHb	Level 1	7.1 g/dL	0.10 g/dL	1.35	0.12 g/dL	1.64
	Level 2	11.6 g/dL	0.11 g/dL	0.98	0.15 g/dL	1.28
	Level 3	19.8 g/dL	0.17 g/dL	0.87	0.25 g/dL	1.25

b. Linearity/assay reportable range:

A linearity study was designed based on CLSI EP6 guidance for each analyte. Samples were prepared by spiking 10 different levels of analyte into whole blood for each of the analyte tested. Each sample concentration was tonometered to the expected concentrations prior to running samples on the candidate device. Samples were tested in a single run in replicates of 5 on a single instrument. The observed values were plotted against expected values. Results of this study are summarized in the following table:

Analyte	Slope	Intercept	Correlation Coefficient (r^2)	Linear Range Tested	Claimed Measuring Range
pO2	1.011	-2.993	0.9966	8.900 – 685.9 mmHg	10 – 685 mmHg
pCO2	0.976	1.812	0.9990	9.296 – 167.660 mmHg	10 – 150 mmHg
tHb	0.9895	0.0926	0.9972	3.132 – 27.013 g/dL	4 – 25 g/dL
O2Hb	0.9979	0.2813	0.9991	3.2 – 100 %	30 – 100 %
HHb	1.017	-0.1198	0.9989	0.19 – 96.6 %	0.5 – 70 %
COHb	0.9821	0.062	0.9999	1.0 – 78.9 %	1.1 – 70 %
MetHb	0.9996	-0.0898	1.00	0.6 – 79.2 %	0.95 – 70 %
SO2	1.0032	-0.3379	0.9990	30 – 100 %	30 – 100 %

An additional linearity study was performed using whole blood samples for the following analytes: pH, Na^+, K^+, Ca^{2+}, glucose, and lactate. The results are as follows:

Analyte	Slope	Intercept	(r^2)	Linear Range Tested	Claimed Measuring Range
pH	1.007	-0.032	0.9996	6.499 – 8.319 pH units	6.5 – 8.0 pH units
Na^+	1.006	-1.456	0.9993	88.16 – 212.3 mEq/L	100 – 200 mEq/L
K^+	1.018	0.010	0.9989	0.752 – 16.61 mEq/L	1.0 – 15 mEq/L
iCa^{2+}	0.985	-0.162	0.9769	0.756 – 12.842 mg/dL	1.09 – 10.02 mg/dL
Glucose	1.009	-6.236	0.9942	11.1 – 543.4 mg/ dL	18 – 540mg/dL

Lactate	1.027	-3.993	0.9969	4.1 – 214.3 mg/dL	9 – 180mg/dL
Hct	1.097	-4.095	0.9934	8.3 – 81.0 %	10 – 75 %

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

Traceability:

All the analytes in the control/calibrator solutions are traceable to a reference method and the analyte targets are assigned based on the reference methods or other commercially available methods. See table below for traceability for calibrators and controls.

Analyte	**Traceability**
pH	NIST SRM 2181 HEPES and NIST SRM 2182 Na Salt
pO_2	Fresh human blood tonometered with PRMs (Primary Reference Materials): • Linde O2 4.5 : purity =99.995% and • N2 4.6 : purity = 99.996% These standards are prepared gravimetrically by National Standards Institutes using guideline ISO6142 (2) as the primary standard gas mixture. The gas mixture is created by using a high precision gas mixing system from LNI.
pCO_2	Fresh human blood tonometered with PRMs (Primary Reference Materials): • Linde CO2 4.5: purity = 99.995% This standard is prepared gravimetrically by National Standards Institutes using guideline ISO6142 (2) as the primary standard gas mixture. The gas mixture is created by using a high precision gas mixing system from LNI.
Na^+	• NIST SRM 2201: Sodium Chloride • Merck Sodium Bicarbonate /Sodium Carbonate 1962 (traceable to NIST SRM 191b: Sodium Bicarbonate and NIST

	SRM 192a: Sodium Carbonate) • Merck Sodium Acetate Trihydrate (Extra Pure) 6268: purity = 99.5-100%
K^+	NIST SRM 2202: Potassium Chloride
Ca^{2+}	Merck CertiPUR 119778 Calcium standard solution (traceable to NIST SRM 3109a: Spectrometric Standard Solution Calcium)
Hct	There is no standard reference material available. Fresh human blood samples were analyzed using the Hemafuge® (microcentrifuge) according to CLSI H7-A3: *Procedure for Determining Packed Cell Volume by the Microhematocrit Method; Approved Standard—Third Edition* (Vol. 20, No. 18).
Glucose	NIST SRM 917b: D-Glucose (Dextrose)
Lactate	There is no reference material available. The material used was Fluka 71718 Sodium Lactate: purity ≥ 99.0%.
tHb	There is no reference material available. Oxygenated whole blood samples were analyzed with a Hellma spectrometer using the HiCN reference method in accordance with CLSI H15-A3: *Reference and Selected Procedures for the Quantitative Determination of Hemoglobin in Blood; Approved Standard—Third Edition* (Vol. 20, No. 28). The Hellma spectrometer was calibrated with NIST SRM 930e: Glass Filters for Spectrophotometry.
O_2Hb	There is no reference material available. A pool of human blood was tonometered at sample values of 0% and 100% with PRM (Primary Reference Material): – Linde O2 4.5 : purity =99.995% This standard is prepared gravimetrically by National Standards Institutes using guideline ISO6142 (2) as the primary standard gas mixture. The gas mixture is created by using a high precision gas mixing system from LNI.
HHb	There is no reference material available. A pool of human blood was tonometered at sample values of 0% and 100% with PRM

	(Primary Reference Material): –Linde CO2 4.5: purity = 99.995% This standard is prepared gravimetrically by National Standards Institutes using guideline ISO6142 (2) as the primary standard gas mixture. The gas mixture is created by using a high precision gas mixing system from LNI.
COHb	There is no reference material available. A pool of human blood was tonometered at sample values of 0% and 100% with PRM (Primary Reference Material): • Linde CO 3.7 : purity =99.97% This standard is prepared gravimetrically by National Standards Institutes using guideline ISO6142 (2) as the primary standard gas mixture. The gas mixture is created by using a high precision gas mixing system from LNI.
MetHb	There is no reference material available. A pool of human blood was tonometered with at sample values of 0% and 100% with PRM (Primary Reference Material): – Linde N2 4.6 : purity = 99.996% – Linde NO 2.5 : purity =99.5% These standards are prepared gravimetrically by National Standards Institutes using guideline ISO6142 (2) as the primary standard gas mixture. The gas mixture is created by using a high precision gas mixing system from LNI.
SO_2	There is no reference material available. Whole blood samples were tonometered at sample values of 30% and 100% with PRMs (Primary Reference Materials): • Linde O2 4.5 : purity =99.995% % This standard is prepared gravimetrically by National Standards Institutes using guideline ISO6142 (2) as the primary standard gas mixture. The gas mixture is created by using a high precision gas mixing system from LNI. The primary standard is used to calibrate the reference instrument, the AVL OMNI 12.

Stability:

Shelf life Stability Study:

For this study, three lots of sensor cartridges (BG/ISE/Glu/Lac) were evaluated using five sensors from each lot. Each sensor lot was stored at 2 – 8 ºC and after 4 months the following materials were tested in singlet: Quality Control (QC) material, Calibration Verification Control material, plasma, and whole blood. The results of the study supports the shelf life stability claim of up to 4 months based on real-time testing on three lots for the sensor cartridges.

Shelf life Stability Study (Fluid pack):

For this study, the fluid pack was stored at 15 – 25ºC and tested at the following time intervals: T= 0, 6, 9, and 13 months. Each result obtained at each time point was compared back to baseline (t=0). The results of the study support a shelf life of 9 months when stored unopened at 15 - 25ºC.

On-board stability study:

Six sensor (BG/ISE/Glu/Lac) cartridge lots were stored on-board the system at 37 ºC. Three quality control levels were tested at regular time intervals over a total of 28 days.

The results of the study support an on-board stability of the following:

Stability of up to 28 days at 37ºC for BG (blood gas sensor cartridges)

Stability of up to 28 days at 30ºC for glucose (sensor cartridges) and ISE (ion selective electrode sensor cartridges)

Stability of up to 21 days at 30ºC for lactate sensor cartridges.

On-board stability study (fluid pack):

A study was conducted evaluating the cobas b 123 fluid pack which contains five components: calibration solution 1, calibration solution 2, standby solution, reference solution, and sol-wet solution. The fluid pack's stability was carried out at 32ºC for 42 days. This study supports the on-board stability claim of 42 days.

Value Assignment for Roche AUTOTROL 123:

For lot- specific value assignment, each autoQC pack (containing 8 ampoules per level, 5 of the new lot and 3 of the reference lot) were tested in two runs

on at least three (3) cobas b 123 POC systems. The following table represents the target values for the Roche AUTOTROL 123 levels:

		Target Value		
		Level 1	Level 2	Level 3
Analyte	Units	Mean	Mean	Mean
pH	pH units	7.100 – 7.180	7.345 – 7.425	7.502 – 7.582
pO2	mmHg	48 - 72	88 – 112	136 – 160
pCO2	mmHg	60.6 – 68.6	38.7 – 45.7	22.4 – 29.4
Na	mEq/L	113.0 – 122.0	135.4 – 145.4	147.6 – 158.6
K	mEq/L	2.79 – 3.19	4.41 – 5.01	6.62 – 7.32
Ca	mg/dL	6.252 – 7.455	4.529 – 5.331	2.285 – 3.086
Hct	%	54.4 – 64.4	36.4 – 46.4	28.0 – 38.0
Glucose	mg/dL	94 - 126	36 – 54	389 – 497
Lactate	mg/dL	77 - 113	23 – 32	12 – 19
tHb	g/dL	6.4 – 7.8	10.6 – 12.6	18.4 – 21.2
O2Hb	%	44.2 – 52.2	72.0 – 80.0	88 .1 – 96.1
HHb	%	14.6 – 20.6	5.1 – 11.1	0.0 – 5.7
COHb	%	20.0 – 25.0	7.9 – 12.9	1.0 – 6.0
MetHb	%	10.3 – 13.3	4.2 – 7.2	0.4 – 3.4
SO2	%	71.7 – 75.2	87.8 – 93.4	94.4 – 100.0

Value Assignment for Combitrol Plus B:

For lot- specific value assignment, each COMBITROL PLUS B (levels 1, 2, 3) were tested in duplicate using 8 ampoules per level (5 of the new lot, 3 of the reference lot) with two (2) runs per system. At least three (3) cobas b 123 POC systems were used for the study. The following table represents the target values for the Roche AUTOTROL 123 levels:

		Target Value		
		Level 1	Level 2	Level 3
Analyte	Units	Target range	Target range	Target range
pH	pH units	7.159 – 7.239	7.393 – 7.473	7.515 – 7.595
pO2	mmHg	40 – 64	82 – 106	131 – 155
pCO2	mmHg	61.1 – 69.1	39.1 – 46.1	19.4 – 26.4
Na	mEq/L	120.1 – 129.1	137.8 – 147.8	156.0 – 167.0
K	mEq/L	2.82 – 3.22	4.44 – 5.04	6.77 – 7.47
Ca	mg/dL	6.373 – 7.575	4.569 – 5.371	1.884 – 2.685
Hct	%	47.8 – 57.8	34.8 – 44.8	24.1 – 34.1
Glucose	mg/dL	86 – 119	38.- 56	339 – 447
Lactate	mg/dL	70 – 106	23 – 32	11 - 18
tHb	g/dL	6.7 – 8.1	11.1 – 13.1	18.6 – 21.4
O2Hb	%	43.2 – 51.2	71.0 – 79.0	87.6 – 95.6
HHb	%	15.0 – 21.0	5.5 – 11.5	0.0 – 5.8

COHb	%	20.4 – 25.4	8.3 – 13.3	1.2 – 6.2
MetHb	%	10.5 – 13.5	4.4 – 7.4	0.5 – 3.5
SO2	%	67.3 – 77.3	86.1 – 93.5	93.8 – 100.0

Value Assignment for Calibration Verification Control (CVC):

The six levels of cobas b 123 CVC material are assigned based on the measuring range established by the cobas b 123 POC system. The following table represents the target values of each analyte (parameter):

		Target Value		
		Level 1	**Level 2**	**Level 3**
		Mean	Mean	Mean
pH	pH Units	7.12 – 7.18	7.38 - 7.42	7.52 – 7.58
PO_2	mmHg	55 – 75	92 – 107	135 – 160
PCO_2	mmHg	60 – 70	38 – 46	21 – 27
Na	mEq/L	110-122	133 – 143	150 – 160
K	mEq/L	2.50 – 3.50	4.30 – 5.30	6.30 – 7.50
iCa	mg/dL	6.012 – 6.81	4.329 – 5.13	2.00 – 3.20
Hct	%	54 – 62	36 – 44	26 – 34
Glu	mg/dL	99 – 117	41 – 49	351 – 451
Lac	mg/dL	81 - 99	25 - 29	13 – 15
tHb	g/dL	6.7 – 8.7	11.5 – 13.5	19.5 – 22.5
O2Hb	%	40 – 54	68 – 82	88 – 98
HHb	%	14 – 22	5 – 12	0 – 6
COHb	%	19 – 27	7 – 15	0 – 6
MetHb	%	8 - 16	2 – 10	0 – 6
SO_2	%	65 – 79	85 – 94	94 – 100

d. Detection limit:

Refer to the linearity study data above in M.2.b. for the detection limits claim for all analytes. In addition, the sponsor conducted a Limit of Blank (LoB), Limit of Detection (LoD), and Limit of Quantitation (LoQ) study following the CLSI EP – 17A guideline for the following analytes: Glucose, ICa, and Lactate. To determine LoB, zero level samples were prepared and measured on ten cobas b 123 POC instruments to obtain blank measurements (N=60). To determine the LoD and LoQ, whole blood samples with low levels of analyte (approximately 4 x LoB) were measured on ten instruments (N=200). The LoQ was determined based on the inter-assay precision (%CV). Results of the study are presented in the following table:

Analyte	LoB	LoD	LoQ	%CV for LoQ	Claimed Measuring Range
Glucose	3.1 mg/dL	5.4 mg/dL	13.1 mg/dL	12.1%	18 – 540
iCa	0.000 mg/dL	0.1907 mg/dL	1.057 mg/dL	11.8%	1.09 – 10.02
Lactate	0.00 mg/dL	0.84 mg/dL	5.6 mg/dL	8.5%	9 – 180

e. Analytical specificity:

The interference study was performed according to the CLSI guideline EP7-A2. The study used spiked and diluted human whole blood samples containing potential interferents for pH, pO2, pCO2, sodium, potassium, calcium, Hct, tHb, O2Hb, HHb, COHb, MetHb, SO2, lactic acid, and glucose. Each sample containing interferent was evaluated against a reference whole blood sample without interferent. The following table represents substances that were tested without significant effects on test results:

Interference substance test	Highest concentration tested	Analyte
3- beta - Hydroxybutyrate	20 mmol/L	pH, ISE, Glu, Lac
Acetoacetate	2 mmol/L	pH, ISE, Glu, Lac
Acetone	12.00 mmol/L	BG, pH, ISE, Glu, Lac
Acetylcysteine	10.2 mmol/L	Na, K, , Hct
Albumin	> 9.0%	BG, pH, ISE, Glu, Lac, Hct
Ammonium Chloride	0.107 mmol/L	BG, pH, ISE Glu, Lac
Ampicillin	0.15 mmol/L	BG, pH, ISE, Glu, Lac
Ascorbic Acid	0.34 mmol/L	ISE, Glu, Lac
Aspirin (Acetylsalicylic acid)	3.62 mmol/L	Na, K, , Glu, Lac
Benzalkonium chloride	0.028 mmol/L	pH, K, Ca, , Glu, Lac
Beta-Carotene	2.0 mg/L	tHB, HHb, O2Hb, COHb, MetHb, SO2
Bilirubin	0.342 mmol/L	BG, pH, ISE, Glu, Lac
Calcium chloride	5.0 mmol/L	ISE, Glu, Lac
Cefoxitin	1.546 mmol/L	ISE, Glu, Lac

Chlorpromazine	0.0063 mmol/L	BG, pH, ISE, Glu, Lac
Cyclosporine	0.0043 mmol/L	BG, pH, ISE, Glu, Lac
Creatinine	0.442 mmol/L	BG, pH, ISE, Glu, Lac
Cyanide	0.1 mmol/L	BG, pH, ISE, Glu, Lac
Dobesilate	0.880 mmol/L	BG, ISE, Glu, Lac
Dopamine	0.00587 mmol/L	BG, pH, ISE, Glu, Lac
Dobutamine	0.66 mmol/L	pH, K, Ca, , Glu, Lac
Doxycyline	0.068 mmol/L	BG, pH, ISE, Glu, Lac
EDTA	0.0003 mmol/L	ISE, Glu, Lac
Ethanol	86.80 mmol/L	BG, pH
Ethylene glycol	2.425 mmol/L	BG, pH, ISE, Glu, Lac
Evans blue	5 mg/L	tHB, HHb, O2Hb, COHb, MetHb, SO2
Gelfusine	Dilution 1:1	tHB, HHb, O2Hb, COHb, MetHb, SO2
Gentamicin	0.021 mmol/L	BG, pH, ISE, Glu, Lac
Gentisic Acid	0.117 mmol/L	BG, pH, ISE, Glu, Lac
Glutathione, reduced	3.0 mmol/L	ISE, Glu, Lac
Glycolic Acid	13.05 mmol/L	PO2, Na, K, , Glu
Guaiaco	0.4 mmol/L	BG, pH, ISE, Glu, Lac
HAES-sterile 10%	Dilution 1:1	tHB, HHb, O2Hb, COHb, MetHb, SO2
HAES (Hydroxyethylstarch)	50.0%	BG, ISE, Glu, Lac
Halothane	0.759 mmol/L	PO2
Hemoglobin	2.00 g/L	BG, pH, ISE, Glu, Lac
Hydroxycarbamide (Hydroxyurea)	2.50 mmol/L	BG, pH,ISE
Hydroxocobalmin	0.25 mg/mL	tHb, HHb, O2Hb, COHb, MetHb, SO2
Ibuprofen	2.425 mmol/L	ISE, Glu, Lac

Indocyanine green	5 mg/mL	tHb, HHb, O2Hb, COHb, MetHb, SO2
Isoflurane	3.00 %	BG, pH, ISE, Glu, Lac
Isoniazid	0.29 mmol/L	BG, pH, ISE, Glu, Lac
Intralipid 20%	10 mg/mL	tHB, HHb, O2Hb, COHb, MetHb, SO2
Lactate	6.6 mmol/L	ISE, Glu
Levodopa (L-Dopa)	0.12 mmol/L	BG, pH, ISE, Glu, Lac
Lipfundin 20% with MCT	10 mg/ mL	tHB, HHb, O2Hb, COHb, MetHb, SO2
Lipidem	10 mg/mL	tHB, HHb, O2Hb, COHb, MetHb, SO2
Lithium acetate	3.20 mmol/L	BG, pH, ISE, Glu, Lac
Maltose	13.62 mmol/L	BG, pH, ISE, Glu, Lac
Methyldopa	0.071 mmol/L	BG, pH, ISE, Glu, Lac
Methylene blue	2.5 mg/L	tHB, HHb, O2Hb, COHb, MetHb, SO2
Metronidazole	0.701 mmol/L	pH, ISE, Glu, Lac
Monosodium phosphate	9.0 mmol/L	ISE, Glu, Lac
Norepinephrine	0.12 mmol/L	BG, pH, ISE, Lac
Nitrous Oxide	85%	PO2
Omegaven	5 mg/mL	tHB, HHb, O2Hb, COHb, MetHb, SO2, tHB, HHb, O2Hb, COHb, MetHb, SO2,
Paracetamol(Acetaminophen)	1.320 mmol/L	BG, pH, ISE, Glu, Lac
Patent blue	2.5 mg/L	tHB, HHb, O2Hb, COHb, MetHb, SO2
Perphenazine	0.0.223 μmol/L	BG, pH, ISE, Glu, Lac
pH low	7.1	tHB, HHb, O2Hb, COHb, MetHb,

		SO2
pH high	7.9	tHB, HHb, O2Hb, COHb, MetHb, SO2
Phenobarbital	0.431 mmol/L	BG, pH, ISE, Glu, Lac
Phenylbutazone	1.3 mmol/L	ISE, Glu, Lac
Phenytoin	0.198 mmol/L	BG, pH, ISE, Glu, Lac
Potassium Thiocyanate	6.88 mmol/L	BG, pH, Na, Ca, Lac
Propofol	1.00 %	BG
Propofol 2%	0.11 mg/mL	tHB, HHb, O2Hb, COHb, MetHb, SO2
pCO2	0.00 mm Hg	pO2, ISE, Glu, Lac
pCO2	85.0 mmHg	ISE, Glu, Lac
pO2	600.0 mmHg	BG, pH, ISE, Glu, Lac
pO2	<25 mmHg	BG, pH, ISE, Glu, Lac
Rifampicin	0.078 mmol/L	BG, pH, ISE, Glu, Lac
SMOF Lipid 20%	10 mg/mL	tHB, HHb, O2Hb, COHb, MetHb, SO2
Sodium Bicarbonate	35 mmol/L	ISE, Glu, Lac
Sodium Bromide	37.5 mmol/L	pH, K, Ca, Lac
Sodium Chloride	45 mmol/L	BG, pH, ISE, Glu, Lac
Sodium Fluoride	0.105 mmol/L	BG, pH, ISE, Glu, Lac
Sodium glutamate	0.86 mmol/L	ISE, Glu, Lac
Sodium heparin	3000 IU/L	BG, ISE, Glu, Lac
Sodium Pyruvate	0.309 mmol/L	BG, pH, ISE, Glu, Lac
Albumin	12 g/dL	tHB, HHb, O2Hb, COHb, MetHb, SO2
Triglyceride	37.00 mmol/L	BG, pH, ISE, Glu, Lac
Urea	49.20 mmol/L	BG, pH, ISE, Glu, Lac
Uric Acid	1.40 mmol/L	ISE, Glu
Vancomycin	0.069 mmol/L	BG, pH, ISE, Glu,

		Lac
Voluven 6%	Dilution 1:1	tHB, HHb, O2Hb, COHb, MetHb, SO2
Xylose	4.00 mmol/L	BG, pH, ISE, Glu, Lac

Additional interference study testing the following analytes at two levels (low and high) against additional potential interferents was performed. The following is a summary of what was tested:

Na+, K+, and Ca2+: potential interference with benzalkonium, thiocyanate, salicylate, bromide, iodide

Glucose and Lactate: potential interference with uric acid, ascorbic acid, acetaminophen, dopamine, sodium fluoride, and oxalate

pO2: potential interference with nitrous oxide, halothane, and isoflurane

The results of this adjunctive study showed that there was interference with benzalkonium chloride at low and high sodium concentrations.

The following table represents substances which interfered:

Interference substance tested	Highest concentration of interfering substance (mmol/L)	Analyte (Na)/ concentration (mEq/L)	Effect of the interferent (mEq/L)	± Trueness (mean bias) mEq/L
Benzalkonium chloride	0.0280	116.47	2.81 ± 0.42	2.9
	152.20	152.20	4.07 ± 0.83	3.6
Dobutamine	0.66	137.4	21.2 ± 2.3	3.1
Interference substance tested	Highest concentration of interfering substance (mmol/L)	Analyte (Hct)/ concentration (%)	Effect of the interferent (%)	± Trueness (mean bias) (%)
Sodium Chloride	45.0	43.3	-9.4 ± 0.2	3.000
Interference substance tested	Highest concentration interfering substance (mmol/L)	Analyte (Glucose)/ concentration (mg/dL))	Effect of the interferent (mg/dL)	± Trueness (mean bias) (mg/dL)
Acetylcysteine	4 10.2	73.88	- 25.2 ± 9.01	9.163

Hydroxycarbamide (Hydroxyurea)	2.50	72.08	21.6 ± 12.6	9.010
Norepinephrine	0.118	73.88	-9.01 ± 3.6	9.848
Potassium Thiocyanate	6.88	72.08	21.6 ± 7.2	9.010
Sodium Bromide	37.50	72.08	9.01 ± 5.4	9.010
Interference substance tested	Highest concentration of interfering substance (mmol/L)	Analyte (Lactate)/ concentration (mg/dL))	Effect of the interferent (mg/dL)	± Trueness (mean bias) (mg/dL)
Acetylcysteine	10.20	49.54	-12.6 ± 2.7	6.513
Glycolic acid	13.05	46.84	6.3±4.5	6.313
Hydroxycarbamide (hydroxyurea)	2.50	43.24	-10.8±5.4	6.046
Uric Acid	1.4	54.05	-8.1±0.9	6.760
Interference substance tested	Highest concentration of interfering substance	Analyte (tHb)/ concentration (g/dL)	Effect of the interferent (g/dL)	± Trueness (mean bias) (g/dL)
Methylene blue	40 mg/L	13.7	-1.1	0.5
Hydroxycobalamin	0.90 mg/mL	13.6	-0.5	0.5
Sulfhemoglobin	10%	17.41	"spectral interference detected"	0.5
Cyanomethemoglobin	10%	14.21	"spectral interference detected"	0.5
Fluorescein	0.4 mg/mL	14.53	"spectral interference detected"	0.5
Interference substance tested	Highest concentration of interfering substance	Analyte (O2Hb)/ concentration (%)	Effect of the interferent (%)	± Trueness (mean bias) (%)
Sulfhemoglobin	10%	94.22	"spectral interference detected"	3.00
Cyanomethemoglobin	10%	95.81	"spectral interference detected"	3.00

Fluorescein	0.4 mg/mL	96.91	"spectral interference detected"	3.00
Interference substance tested	Highest concentration of interfering substance	Analyte (HHb)/ concentration (%)	Effect of the interferent (%)	± Trueness (mean bias) (%)
Sulfhemoglobin	10%	3.53	"spectral interference detected"	2.00
Cyanomethemoglobin	10%	2.06	"spectral interference detected"	2.00
Fluorescein	0.4 mg/mL	1.34	"spectral interference detected"	2.00
Interference substance tested	Highest concentration of interfering substance	Analyte (COHb)/ concentration (%)	Effect of the interferent (%)	± Trueness (mean bias) (%)
Sulfhemoglobin	10%	1.68	"spectral interference detected"	1.17
Cyanomethemoglobin	10%	1.45	"spectral interference detected"	1.15
Fluorescein	0.4 mg/mL	1.31	"spectral interference detected"	1.13
Interference substance tested	Highest concentration of interfering substance	Analyte (MetHb)/ concentration (%)	Effect of the interferent (%)	± Trueness (mean bias) (%)
Sulfhemoglobin	10%	0.58	"spectral interference detected"	1.12
Cyanomethemoglobin	10%	0.68	"spectral interference detected"	1.14
Fluorescein	0.4 mg/mL	0.44	"spectral interference detected"	1.09
Interference substance tested	Highest concentration of interfering	Analyte (SO2)/ concentration (%)	Effect of the interferent (%)	± Trueness (mean bias) (%)

	substance			
Sulfhemoglobin	10%	96.39	"spectral interference detected"	2.00
Cyanomethemoglobin	10%	97.89	"spectral interference detected"	2.00
Fluorescein	0.4 mg/mL	98.64	"spectral interference detected"	2.00

f. Assay cut-off: Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

A multi-center clinic evaluation consisting of a total of six clinics (2 laboratory and 4 point-of-care sites) was conducted for the following analytes: pO2, pCO2, pH, Na, K, Ca, Hct, Glucose, Lactate, tHb, O2Hb, HHb, COHb, MetHb, and SO2. Method comparison studies were performed using Roche cobas b 123 and other commercially available devices. In order to cover the hard-to-find sample range, an internal method comparison study was performed using some altered samples that span the entire claimed measuring ranges for all the analytes. Singlet set of data was used for the linear regression analysis. Results are summarized in the table below:

Analyte	**Unit of Measure**	**n**	**Range**	**Slope**	**Intercept**	**r**
pH	pH Units	764	6.59 – 7.89	0.9930	0.0607	0.9940
pO_2	mmHg	737	13.3 – 638.0	0.9685	-0.2771	0.9977
pCO_2	mmHg	731	16.6 – 149.5	0.9698	1.100	0.9921
Na^+	mEq/L	822	102.0 – 199.2	1.0367	-4.855	0.9793
K^+	mEq/L	814	1.43 – 13.54	0.9638	0.1242	0.9982
iCa^{2+}	mg/dL	817	1.180 – 9.535	0.9878	0.0199	0.9808
Hct	%	747	12.5 – 68.7	0.9521	1.506	0.9881
Glucose	mg/dL	719	18.9 – 539.0	1.000	-3.11	0.9880
Lactate	mg/dL	622	9.0 – 171.8	1.0227	0.2406	0.9945
tHb	g/dL	750	4.24 – 22.6	0.9643	-0.0035	0.9888
O_2Hb	%	734	31.5 – 98.3	0.9908	1.3011	0.9976
HHb	%	608	0.5 – 69.5	1.0200	-0.7370	0.9948
COHb	%	695	1.1 – 63.1	1.0000	0.0000	0.9997
MetHb	%	87	1.0 – 59.3	0.9896	0.1093	0.9999
SO_2	%	734	32.0 – 100.0	1.0106	-0.4291	0.9931

b. Matrix comparison:

Not applicable. Only heparinized whole blood samples are used with this 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:

Analyte	**Population**	**Reference range**	**Cited from**
Sodium	Adult	136- 145 mmol/L 136- 145 mEq/L	Tietz 2006[1]
	Adult> 90 years	132- 146 mmol/L 132- 146 mEq/L	Tietz 2006[2]
Potassium (serum)	Adult	3.5 - 5.1 mmol/L 3.5- 5.1 mEq/L	Tietz 2006[3]
Ionized Calcium	Adult, female & male	1.15 – 1.33 mmol/L 4.6 – 5.3 mg/dL	Tietz 2006[4]
Methemoglobin	----------	0.06- 0.24 g/dL 9.3 - 37.2 µmol/L 0.04 - 1.52 % of total Hb 0.0004- 0.0152 mass fraction of total Hb	Tietz 2006[5]
Glucose (whole	Adult	65- 95 mg/dL	Tietz 2006[6]

blood, heparin)		3.5 - 5.3 mmol/L	
Lactate (whole blood)	----------	venous (at bed rest) 5- 15 mg/dL 3-7 mg/dL arterial (at bed rest) 0.56 - 1.39 mmol/L 0.36 - 0.75 mmol/L	Tietz 2006[7]
Analyte	Population	Reference range	Cited from
pH	Arterial whole blood: Adult, children	7.35 - 7.45	Tietz 2006[8]
PO2	Arterial whole blood: Adult, children (2 days-60 years)	83 - 108 mmHg	Tietz 2006[8]
PCO2	Adult (male) arterial whole blood	35 - 48 mmHg	Tietz 2006[9]
	Adult (female) arterial whole blood	32 - 45 mmHg	Tietz 2006[9]
Hct	Adult Male Adult Female	39 – 50 % 35 – 47 %	Tietz 1987[10]
tHb (arterial whole blood)	Adult Male Adult Female	13.1 – 17.2 g/dL 11.7 – 16.0 g/dL	Tietz 1987[10]
SO2	Newborn	40 – 90%	Tietz 2006[8]
	Thereafter (Arterial whole blood)	94 – 98%	Tietz 2006[8]
O2Hb	Whole Blood (Nonsmoker)	94 – 98%	American Environmental Laboratory[11]
HHb	Whole Blood	1 – 5%	American Environmental Laboratory[11]
COHb	Whole Blood (Nonsmoker)	0.5 - 1.5%	Tietz 2006[9]

Citations

1. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics: 4th Edition 2006, p. 2294
2. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics: 4th Edition 2006, p.2295
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5. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics: 4th Edition 2006, p.2317
6. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics: 4th Edition 2006, p.2271
7. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics: 4th Edition 2006, p.2282
8. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics: 4th Edition 2006, p.2289
9. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics: 4th Edition 2006, p.2259
10. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics: 3rd Edition 1987, p.1817
11. American Environmental Laboratory: The Laboratory Assessment of Oxygenation: Robert F. Morgan 1993, 5(4), p. 147 - 153

N. Instrument Name:

Cobas® b 123 POC System

O. System Descriptions:

1. Modes of Operation:

   Single sample

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

   Yes _____ or No ____X__

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:

   Single sample barcode reader

4. Specimen Sampling and Handling:

   This device is intended to be used with whole blood samples.

5. Calibration:

   Two point calibration of all parameters.

6. Quality Control:

   QC consists of the following materials: AutoQC module with AutoQC pack for automated QC measurements

   Combitrol Plus B – control material for manual QC measurements

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

None

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.