

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

A. 510(k) Number:

k101947

B. Purpose for Submission:

New device

C. Measurand:

Blood gases (pCO₂, and pO₂), pH, potassium (K), and glucose

D. Type of Test:

Quantitative, Electrochemical

E. Applicant:

Sphere Medical Ltd.

F. Proprietary and Established Names:

IVD-GE02 (Blood gases analyzer)

G. Regulatory Information:

	Regulation section	Classification	Product Code	Panel
Electrode, Measurement of Blood Gases (pO ₂ , pCO ₂) and Blood pH	21 CFR § 862.1120	II	CHL	Chemistry (75)
Electrode, Ion Specific Potassium	21 CFR § 862.1600	II	CEM	Chemistry (75)
Glucose Oxidase, Glucose	21 CFR § 862.1345	II	CGA	Chemistry (75)
Calibrators	21 CFR § 862.1150	II	JIX	Chemistry (75)

H. Intended Use:

1. Intended use(s):

See indications for use statements below.

2. Indication(s) for use:

The IVD-GE02 system is a blood gases analyzer intended as an in vitro diagnostic device for the quantitative measurement of whole blood samples in a clinical laboratory. The IVD-GE02 system includes sensors for the measurements of pH, pCO₂, pO₂, potassium, and glucose.

Measurements of blood gases (pCO₂, pO₂) and blood pH are used in the diagnosis and treatment of life-threatening acid-base disturbances.

Measurement of potassium is used to monitor electrolyte balance in the diagnosis and treatment of diseases conditions characterized by high or low potassium levels.

Measurement of glucose is used in the diagnosis and treatment of carbohydrate metabolism disorders including diabetes mellitus, neonatal hypoglycemia, idiopathic hypoglycemia, and of pancreatic islet cell carcinoma.

IVD-GE02 calibration solutions are in vitro diagnostic products for the calibration of the IVD-GE02 test system for the measurements of pH, pCO₂, pO₂, potassium and glucose.

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

IVD-GE02 System

I. Device Description:

The IVD-GE02 system is a modular system consisting of the following components:

- An instrument containing
 - o Fluid management components (tubing, pumps and valves)
 - o The cartridge (see below)
 - o An injection port for samples, calibration solutions and QC solutions
 - o Wiring to connect the cartridge to the fluid management component

- A dedicated combined PC and monitor with a touch screen
- A disposable cartridge containing
 - Sensor (A single array chip containing analyte specific sensors)
 - Electronic circuitry, including an Application Specific Integrated Circuit (ASIC) to process sensor signals and drive the fluid management system.
- Syringes with calibration solutions containing electrolytes (Na, K, Cl), glucose, phosphate and dissolved gases in aqueous buffer are packed in sealed foil bags
- Containers with flush solutions containing electrolytes (Na, K, Cl, glucose, phosphate and dissolved gases in aqueous buffer.
- A waste container
- A dedicated printer and associated cables
- An ambient temperature and pressure sensor
- Cables to connect the monitor to the instrument and a power supply unit
- Packaging
- Label copy

J. Substantial Equivalence Information:

1. Predicate device name(s):

Siemens Rapidlab 865 analyzer

2. Predicate K number(s):

k934907

3. Comparison with predicate:

Item	Sphere IVD-GE02 system- Candidate device	Siemens Rapidlab 865 analyzer- Predicate device
Similarities and Difference		
Intended Use	For quantitative measurements of blood gases(pCO ₂ , pO ₂), pH, potassium and glucose in a clinical laboratory	Same
Measured parameters	pH, pCO ₂ , pO ₂ , potassium, glucose	Same, plus Na, Ca, lactate, Cl, tHb, FHHb, FO ₂ Hb, FMetHb, FCOHb
Sample type	Whole blood	Same
Sensor array	Multi-analyte chip	Individual sensors
Test principle	Electrochemical	Same

	(potentiometric, amperometric)	
Individual test sensor type:		
pH	Potentiometric ISFET	Potentiometric ISE
pCO ₂	Potentiometric ISFET	Potentiometric ISE
pO ₂	Amperometric	Same
Potassium	Potentiometric ISFET	Potentiometric ISE
Glucose	Amperometric	Same
Calibrations materials	Aqueous, 2 levels, store at 15-25°C	Aqueous, 2 levels, store at 4-25°C

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

1. ISO 14971:2007 *Medical devices - Application of risk management to medical devices*
2. EN 60601-2-101: 2002 *Safety requirements for electrical equipment for measurement, control and laboratory use – Part 2-101 Particular requirement for in vitro diagnostic (IVD) medical equipment.*
3. FCC Pt 15 Class A – *Conducted Emissions (Compiled with a minimum compliance of – 18.63 dBuV) and Radiated Emissions (Compiled with a minimum compliance of – 10.62 dBuV).*
4. CLSI Guideline, EP5-A2 *Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline Second edition (2004)*
5. CLSI Guideline, EP6-A *Evaluation of the Linearity of Quantitative Analytical Methods; Approved Guideline (2003)*
6. CLSI Guideline, EP7-A2 *Interference Testing in Clinical Chemistry; Approved Guideline- Second edition (2005)*
7. CLSI Guideline, EP9-A2 *Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline Second edition (2002)*

L. Test Principle:

The IVD-GE02 System measures the analytes pH, pCO₂, pO₂, potassium and glucose using electrochemical sensors, based on potentiometric and amperometric phenomenon. The sensors produce electrical signals in response to the analytes in the blood. The signal from each sensor is proportional to the concentration of the analyte. There are two different measuring principles employed, potentiometry and amperometry.

Potentiometry: A potential is recorded using a voltmeter, which relates to the concentration of the sample. A reference electrode is used to provide a stable, fixed potential against which other potential differences can be measured. This measurement technique is used for pH, pCO₂ and potassium.

Amperometry: The magnitude of an electrical flow of current is proportional to the concentration of the substance being oxidized or reduced at an electrode. This measurement technique is used for pO₂ and Glucose.

M. Performance Characteristics (if/when applicable):1. Analytical performance:a. *Precision/Reproducibility:*

Precision study was designed based on the CLSI EP5-A2 guideline. The sponsor conducted within run precision and total precision with three levels of control materials. All samples were tested in duplicate per run, two runs daily for 10 days (N= 40). Results of the precision studies are summarized below.

pH precision data						
QC823	Mean pH reading	N	Within run SD	Within run % CV	Total imprecision SD	Total imprecision %CV
Level 1	7.1727	40	0.0027	0.0376	0.0106	0.1478
Level 2	7.4364	40	0.0018	0.0242	0.0067	0.0901
Level 3	7.6059	40	0.0036	0.0473	0.0113	0.1486

K⁺ precision data (units are mM)						
QC823	Mean K⁺ reading	N	Within run SD	Within run % CV	Total imprecision SD	Total imprecision %CV
Level 1	2.2350	40	0.0316	1.4139	0.1272	5.6913
Level 2	4.8950	40	0.0592	1.2094	0.1671	3.4137
Level 3	7.1350	40	0.0894	1.2530	0.1814	2.5424

O₂ precision data (units are mmHg)						
QC823	Mean O₂ reading	N	Within run SD	Within run % CV	Total imprecision SD	Total imprecision %CV
Level 1	65.1825	40	2.1864	3.3543	5.5164	8.4630
Level 2	112.1450	40	1.4992	1.3368	4.0312	3.5946
Level 3	158.3425	40	3.2895	2.0774	4.0136	2.5348

CO₂ precision data (units are mmHg)						
QC823	Mean CO₂ reading	N	Within run SD	Within run % CV	Total imprecision SD	Total imprecision %CV
Level 1	49.6472	36	0.5570	1.1219	2.7341	5.5071
Level 2	30.3194	36	0.2021	0.6666	1.5351	5.0631
Level 3	15.6722	36	0.1291	0.8238	1.0558	6.7368

Glucose precision data (units are mg/dL)						
QC823	Mean Glucose reading	N	Within run SD	Within run % CV	Total imprecision SD	Total imprecision %CV
Level 1	76.000	36	3.818	5.0237	5.088	6.6947
Level 2	170.350	36	3.946	2.3164	5.754	3.3778
Level 3	228.000	36	6.420	2.8158	9.888	4.3368

An additional within-run precision study was performed using whole blood samples collected into a heparinized tube. Different levels of analyte were tested in replicates of 10. Results are summarized below.

Whole blood within-run precision study results for pH:

	Level 1	Level 2	Level 3
Mean (pH units)	7.355	7.242	6.850
SD	0.018	0.014	0.009
%CV	0.242	0.200	0.137

Whole blood within-run precision study results for pCO₂:

	Level 1	Level 2	Level 3
Mean (mmHg)	39.3	68.3	96.55
SD	2.60	1.66	1.85
%CV	6.61	2.42	1.92

Whole blood within-run precision study results for pO₂:

	Level 1	Level 2	Level 3
Mean (mmHg)	30.4	91.3	478.57
SD	0.8	2.3	12.56
%CV	2.7	2.5	2.62

Whole blood within-run precision study results for K:

	Level 1	Level 2	Level 3
Mean (mmol/L)	4.10	6.65	2.42
SD	0.08	0.21	0.14
%CV	1.99	3.17	5.78

Whole blood within-run precision study results for Glucose:

	Level 1	Level 2	Level 3	Level 4
Mean (mg/dL)	88.4	215.0	47.56	365.72
SD	3.44	4.75	2.58	10.57
%CV	3.9	2.2	5.42	2.89

b. *Linearity/assay reportable range:*

Linearity study was designed based on CLSI EP6-A guideline. Human whole blood samples were drawn into heparinized tubes. Samples were spiked to the target analyte levels. 7 levels of each of the analyte measured were prepared and tested in duplicate on 3 IVD-GE02 instruments and on one Siemens Rapidlab 865 analyzer to generate the expected values. The observed values were plotted against the expected values and an appropriate line fitted by standard linear regression. All three instruments obtained similar linear regressions. One representative instrument results are summarized below.

pH tested ranged from 6.8-7.8 and the linear equation generated was $Y = 0.9973 X + 0.0229$, $r^2 = 0.9957$.

pCO₂ tested ranged from 5.8-101.9 mmHg and the linear equation generated was $Y = 1.073 X - 2.509$, $r^2 = 0.9957$.

pO₂ tested ranged from 28-500 mmHg and the linear equation generated was $Y = 0.9855 X + 0.4544$, $r^2 = 0.9987$.

K tested ranged from 2.06-9.71 mmol/L and the linear equation generated was $Y = 0.9203X + 0.4149$, $r^2 = 0.9917$.

Glucose tested ranged from 16.2-445.3 mg/dL and the linear equation generated was $Y = 0.9334 X + 3.092$, $r^2 = 0.9925$.

Results of the study support the sponsor claims for the following measuring/linearity ranges:

pH: 6.8 to 7.8

pCO₂: 15 to 100 mmHg

pO₂: 30 to 500 mmHg

K: 2.0 to 9.0 mmol/L

Glucose: 30.6-399.6 mg/dL

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

Traceability:

All the analytes in the calibration 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.

Analyte	Traceability
pH	*S1830 Calibrant I and II
pCO ₂	** Calibration Gas 1 and 2, EUR
pO ₂	** Calibration Gas 1 and 2, EUR
K	NIST KCL, SRM 918
glucose	NIST SRM 917

*Traceable to the IUPAC pH scale and the NIST pH scale.

**Primary, gravimetrically prepared standards, traceable to NIST traceable weights.

Value assignments of the calibration solutions were established by multiple determinations of the analytes. Calibration solutions have the following analyte target value:

Parameter	Units	Solution 1	Solution 2
pH	pH units	6.83	7.38
pCO ₂	Mm Hg	70	35
pO ₂	Mm Hg	80	200
K	mmol/L	9.0	4.0
Glucose	mg/dL	180.2	39.6

Stability of the calibration solutions: A real-time stability study was performed to demonstrate a maximum shelf life of 6 months at storage temperatures between 15 and 25 degrees C in unopened foil pouches. Protocols and acceptance criteria has been provided and found to be adequate. There is no open-vial stability because calibration solutions are opened and used immediately.

d. Detection limit:

The sponsor determined that the detection limit was defined by the linear range study. The minimum detection limit is defined as the lowest analyte concentrations over the range that the assay has been shown to be acceptably linear. Please see linearity study in section M.1.b. above.

In addition, the sponsor performed an intra-assay precision (N=12) of a whole blood sample with glucose concentration at 32 mg/dL and found that the intra-assay %CV was 3.95%.

The sponsor claimed the following as the detection limits:

pH: 6.8

pCO₂: 15 mmHg

pO₂: 30 mmHg

K: 2.0 mmol/L

Glucose: 30.6 mg/dL

e. Analytical specificity:

An interference study was designed according to CLSI EP7-A2 guideline. The study used human whole blood samples as the test materials and was conducted for the analytes pH, pCO₂, pO₂, K, and glucose at two analytes concentration. The whole blood samples were spiked with the potential interferents (test samples) and were measured against the samples that were not spiked (control samples). All samples were assayed in replicates of six (except pCO₂ use replicates of 8). The sponsor states that interferences are considered to be non-significant if the bias between the test and control samples are within ± 0.04 units for pH, and $\pm 10\%$ for pCO₂, pO₂, K, and glucose. The tables below summarize the results of the interference testing performed. “No” significant interference is defined using the criteria listed above,

Results of the interferences study are shown below:

Analyte	Interference substance	Highest Concentration tested	Significant interference seen
pH	Acetaminophen	1324 μ M	No
	Sodium pentothal	248 μ M	No
	Salicylic acid	4340 μ M	No
	Acetyl salicylic acid	2170 μ M	Yes*
pO ₂	Isoflurane	759 μ M	No
	Halothane	253 μ M	Yes*
	Nitrous oxide	84%	No
pCO ₂	Ibuprofen	2425 μ M	No
	Sodium pentothal	20.6 μ M	Yes*
K	Sodium pentothal	248 μ M	Yes*
Glucose	Acetaminophen	662 μ M	Yes*
	Heparin	3000 units/mL	No
	Salicylic acid	4340 μ M	No
	Ethanol	86800 μ M	No
	Dopamine	5.87 μ M	No
	Dobutamine	9.6 mg/L	No

	Acetyl salicylic acid	3620 μ M	No
	Sodium pentothal	248 μ M	No
	Oxygen	30 mmHg**	Yes*
	Hemoglobin	2 g/L	No
	Triglyceride	15 mmol/L (1327 mg/dL)	Yes*
	Bilirubin- conjugated	342 μ mol/L (28mg/dL)	No
	Bilirubin- unconjugated	342 μ mol/L (28mg/dL)	No
	L-Ascorbic acid	170 μ mol/L	No
	Uric acid	1.4 mmol/L (23.5mg/dL)	No
	Urea	42.9 mmol/L (257 mg/dL)	No

* The substances that were found to have significant interference ($\geq 10\%$) were listed in the Operator's manual.

In addition the following statement is included in the limitations section of the Operator's manual:

** Patients with an arterial blood oxygen level of 30 mmHg are in a critical condition and will urgently require treatment for this low oxygen level. Patients who have blood oxygen level of 30 mmHg should not be tested with the device because it will affect the glucose measurement.

A hematocrit study was performed to evaluate the effect of hematocrit on the glucose measurements on the IVD-GE02 system. Five different levels of glucose concentrations (40, 80, 120, 200, and 400 mg/dL) at two hematocrit levels (30% and 50%) were tested and compare with the normal hematocrit level (45%). All samples were prepared and tested on both the candidate device and the predicate device. All comparisons to the predicate device and to a normal hematocrit showed a bias of less than 15%. The results demonstrated that hematocrit within 30% to 50% has no significant effect on the glucose levels. In addition, in the method comparison study where native patient samples were used, sponsor also measured the hematocrit levels of these clinical samples. These samples covered a wide range of hematocrit levels (between 19% to 51%). Based on these data, there was no significant hematocrit effect on the glucose measurements.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. *Method comparison with predicate device:*

A method comparison study was performed using heparinized whole blood samples based on the CLSI EP9-A2 guideline. The study was performed in a hospital with patients' left-over arterial blood samples over a minimum of 5 days. All samples were assayed once on the IVD-GE02 system (candidate method) and on the Siemens Rapidlab 865 analyzer (predicate method). In order to cover the hard-to-find sample range and span the entire measuring range, some samples were altered or tonometered with different gases before measurements. Results of the study are summarized below.

Analyte	N	Slope	Intercept	R ²	Sample range tested
pH (units)	104	1.04	-0.26	0.9954	6.815-7.797
pCO ₂ (mmHg)	102	1.03	-1.00	0.9501	20.8-100
pO ₂ (mmHg)	105	0.97	3.66	0.9917	38.7-496.9
K (mmol/L)	111	1.00	0.29	0.9523	2.5-8.9
Glucose (mg/dL)	98	0.96	8.69	0.9559	48.6-397.8

b. *Matrix comparison:*

Not applicable. Only heparinized whole blood samples are the recommended sample type.

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 sponsor recommends in the labeling that each clinical laboratory should establish its own reference range for diagnostic evaluation of patient results. The reference range for each parameter has been established in the literature. The following table shows typical reference ranges cited from the literature^{1,2,3}.

Parameter	Units
pH	7.38-7.44 pH units
pCO2	80-100 mm Hg
pO2	35-45 mm Hg
K	3.5-5.0 mmol/L
Glucose	75-115 mg/dL

¹Katz A, Ferraro M, Sluss P M, and Lewandrowski K B. *Laboratory Reference Values – Case Records of the Massachusetts General Hospital* , New Engl J Med 2004;351: 1548-63

²Crapo R, Jensen R L, Hegewald and Tashkin P. *Arterial Blood Gas Reference Values for sea level and an Altitude of 1,400 meters*. Am J Respir. Crit. Care Med. Vol. 160 pp 1525 – 1531, 1999.

³Statland B. E. *Clinical Decision Levels for Lab Tests*. Oradell, NJ: Medical Economic Books 1987.

N. Instrument Name:

IVD-GE02 system

O. System Descriptions:

1. Modes of Operation:

Single sample

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:

Manual sample identification

4. Specimen Sampling and Handling:

Manual-syringe mode

5. Calibration:

The IVD-GE02 will automatically calibrate its sensor when the calibration sequence is run. Operator must initiate a calibration sequence with manual injections of the calibration solutions (2 levels).

6. Quality Control:

Operator must initiate an external quality control procedure with manual injections of the quality control materials. Recommendations for frequency of testing are including in the labeling. As a minimum, users are to follow regulatory guidelines for testing quality control materials.

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.