

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

A. 510(k) Number:

k111960

B. Purpose for Submission:

New Device

C. Measurand:

Carbon dioxide (CO₂)

D. Type of Test:

Quantitative

E. Applicant:

ELITech Vital Scientific

F. Proprietary and Established Names:

ELITech Clinical Systems ISE Total CO₂ Electrode
ELITech Clinical Systems ISE Calibrators

G. Regulatory Information:

Name	<u>Regulation section:</u>	<u>Classification:</u>	<u>Product code:</u>	<u>Panel:</u>
ELITech Clinical Systems ISE Total CO ₂ Electrode	21 CFR 862.1160	Class II	KHS	Chemistry 75
ELITech Clinical Systems ISE Calibrators	21 CFR 862.1150	Class II	JIX	Chemistry 75

H. Intended Use:

1. Intended use(s):

See Indications for Use

2. Indication(s) for use:

ISE CO₂ electrode:

The carbon dioxide electrode for the ELITech Clinical Systems Selectra ProM is intended for use for the quantitative in vitro diagnostic determination of Total CO₂ in human serum and plasma. Bicarbonate/carbon dioxide measurements are used in the diagnosis and treatment of numerous potentially serious disorders associated with changes in body acid-base balance

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ELITech Clinical Systems ISE CALIBRATORS:

ELITech Clinical Systems ISE Calibrators are used for the calibration of sodium (Na⁺), potassium (K⁺), chloride (Cl⁻) and carbon dioxide (Total CO₂) on ELITech Clinical Systems Selectra ProM analyzer equipped with ISE module.

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

ELITech Clinical Systems Selectra Pro M analyzer

I. Device Description:

The ELITech Clinical Systems ISE Total CO₂ is a dry electrode system that employs the principle of indirect potentiometry measurement using a Total CO₂ Ion-Selective Electrode installed in the ISE module of equipped Selectra analyzers along with liquid reagents. Total CO₂ reagent system is composed of two (2) different reagent kits:

ISE Diluent: Diluent is supplied in liquid ready-to-use form and consists in a buffered solution with surfactant.

ISE Reference Solution: Solution is supplied in liquid ready-to-use form and consists in a buffered solution with surfactant containing sodium, potassium, chloride and carbon dioxide.

The ELITech Clinical Systems ISE Calibrators consists of 2 levels, CAL L and CAL H. Calibrators are supplied in liquid ready-to-use form and are aqueous solutions containing sodium, potassium, chloride and Total CO₂. ELITech Clinical Systems ISE Calibrators were previously cleared for sodium, potassium and chloride in k102647.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Roche Diagnostics CO2-L, Bicarbonate liquid.
Roche Diagnostics Ammonia/Ethanol/CO2 calibrator.

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

k031879

3. Comparison with predicate:

	<u>ELITech Clinical Systems Device</u> (Candidate device)	<u>Predicate device</u> (ROCHE Diagnostics CO2-L, Bicarbonate liquid and Roche Diagnostics calibrators,Ammonia/Ethanol/ CO2
Intended use/Indication for Use	Same	It is intended for the quantitative determination of carbon dioxide in serum and plasma Bicarbonate/Carbon dioxide measurements are used in the diagnosis and treatment of numerous potentially serious disorders associated with changes in body acid-base balance.
Assay protocol	Indirect,potentiometry measurement with Ion-Selective Electrode	Enzymatic colorimetric test
Sample type	Serum and lithium heparin plasma	Same
Expected values	23-29 mEq/L	22-29 mmol/L
Measuring range	10.8 – 43.0 mEq/L	0.5-50 mmol/L
Traceability	According to the following reference material : Total CO2 : NIST SRM 924a	This method has been standardized against primary standard traceable to NIST or NERL.

<p>ISE Calibrators</p>	<p>Composition: Aqueous solutions containing sodium, potassium, chloride and total CO₂ with 2 different levels of concentrations. Concentrations are lot-specific. The values are given in the vial labels.</p> <p>Storage: Store at 2-30 °C.</p> <p>Stability: - After opening, calibrators is stable 30 days when stored at 2-30 °C capped to prevent contamination and evaporation.</p>	<p>Calibrator kit</p> <p>Composition: Aqueous buffer solution containing ammonia, ethanol and sodium bicarbonate with preservative. Liquid ready-to-use calibrators The concentrations of the calibrators components have been adjusted to ensure optimal calibration of the appropriate Roche methods on clinical chemistry analyzers.</p> <p>Storage Store at 2-8°C.</p> <p>Stability : - After opening, calibrators are stable 8 weeks when stored at 2-8 °C provided that dispensing of the calibrator takes place without microbial contamination, e.g. by pouring out .</p>
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K. Standard/Guidance Document Referenced (if applicable):

Number	Title
EP05-A2	CLSI Evaluation of precision performance of quantitative measurement methods; Approved guideline – Second Edition
EP06-A	CLSI Evaluation of the linearity of the measurement of quantitative procedures: a statistical approach
EP07-A2	CLSI Interference Testing in Clinical Chemistry; Approved Guideline, Second Edition
EP09-A2	CLSI Method comparison and Bias estimation using patient samples; Approved guideline, Second Edition

13640:2002	FDA Guidance Document "Stability Testing of in vitro Diagnostic Reagents"
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L. Test Principle:

Indirect potentiometric measurement with Ion-Selective Electrode i.e., ISE measurements are based on the potentiometric and Nernst Equation principle. The sample is diluted with a diluent and aspirated into ion-selective electrodes. The measured potential difference between the reference electrode and the ion specific electrodes is proportional to the Logarithm of the concentration of the measured ions.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Precision studies were performed with three pooled human serum samples at three different concentrations of CO₂, on two separate Selectra ProM analyzers, over twenty operating days. Samples were tested in duplicate twice a day (N=80). The results are summarized in the tables below:

Within-run

	n	Mean (mEq/L)	Within-run SD	Within-run CV%
Low level	80	12.1	0.5	3.9
Medium level	80	19.9	0.5	2.3
High level	80	27.5	0.6	2.3

Total precision

	n	Mean (mEq/L)	Total SD	Total CV%
Low level	80	12.1	0.8	6.8
Medium level	80	19.9	1.1	5.4
High level	80	27.5	1.4	5.2

b. Linearity/assay reportable range:

The linearity of CO₂ System was studied by mixing a sample with high value (43.0 mEq/L) and a sample with low value (10.8 mEq/L) to obtain 11 levels with equidistant concentrations of CO₂. All samples were tested in triplicate on the Selectra ProM analyzer. The expected values were plotted against the observed values and a linear regression line was fitted with the following regression:

$$Y = 1.0387 - 0.9 \text{ mEq /L}$$

$$r = 0.9998$$

The Standard error of the estimate, $S_{y.x}$ is equal to 0.2 mEq/L.

The results of the linearity study support the CO₂ assay measuring range from 10.8 to 43.0 mEq/L

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

Traceability

CO₂ value is traceable to the Standard Reference Material SRM 924a (of the National Institute of Standards and Technology).

Stability:

Calibrator material is purchased from a commercial vendor (previously cleared under k033501). The sponsor claimed the following for stability: ELITech Clinical Systems ISE Calibrators is stable until the expiration date printed on the label when stored at 2-8°C prior to reconstitution. After reconstitution the stability is 8 hours when stored at 15-25°C, 2 days at 2-8°C or 4 weeks (when frozen once) at -25° and -15°C. The labeling stated that the Calibrators should be stored tightly capped and protected from light when not in use.

Value Assignment

ELITech Clinical Systems ISE Calibrators are value assigned using multiple Vital Scientific Selectra ProM analyzers. Each sample is tested in triplicate over several days. The target value of Level I and II are the median of the observed values range. After validation of the target value, a confidence range (high and low values) is then calculated.

It is recommended to recalibrate after setting-up of a new vial of ISE Reference Solution or of ISE Diluent then every 4 hours when quality control results fall outside the established range, after replacing electrode, and after ISE cleaning and maintenance

d. Detection limit:

Detection limit is based on linearity study performed above. In addition, method comparison study also supports the low end measuring claims of 10.8 mEq/L.

The sponsor's claimed measuring range of the device is 10.8 – 43.0 mEq/L

e. Analytical specificity:

An endogenous interfering substances study was performed according to the CLSI EP7-A guideline. Serum samples containing the analyte at two levels (low and high) of the test were spiked with the potentially interfering substance unconjugated bilirubin, conjugated bilirubin, turbidity, ascorbic acid, hemoglobin and acetylsalicylate to several concentrations. Samples were then run in triplicate using the ProM analyzer. The recovery of the test at each concentration of interferents was calculated by comparing the mean result of testing with no interferents to the mean result at each level tested. The sponsor defines non-significant interference as bias <10% between the spiked and unspiked samples. The highest level tested with no significant interference is listed in the table below.

Interferents	Highest level tested with no interference
Turbidity	614 mg/dL
Unconjugated bilirubin	30.0 mg/dL, (513 µmol/L)
Conjugated bilirubin	29.5 mg/dL, (504 µmol/L)
Ascorbic acid	16.0 mg/dL Concentrations above the therapeutic levels will interfere and cause erroneous results
Acetylsalicylic acid	40 mg/dL. Concentrations above the therapeutic levels will interfere and cause erroneous results
Hemoglobin	300 mg/dL

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison study was performed between the predicate device (ROCHE CO2-L reagent) on a cobas c111 analyzer and the candidate device (Elitech Clinical Systems CO₂) on a Selectra ProM according to the CLSI guideline EP9-A2. This study was performed using 99 serum patient samples (including 5 spiked and 3 diluted samples) and over a span of 5 days.

Regression analysis of the results yielded the following:

$$y = 0.908 x + 2.2 \text{ mEq/L}$$

$$r = 0.985$$

$$r^2 = 0.970$$

Standard error of the estimate $S_{y.x} = 1.3$ mEq/L.

Sample range tested from 11.1 to 42.9 mEq/L

b. Matrix comparison:

40 paired serum and plasma (lithium heparin) samples, ranging from 11.7 to 39.7 mEq/L(including 2 spiked and 2 diluted), were tested on Selectra ProM according to the CLSI guideline EP9-A2.

Regression analysis of the results yielded the following:

$$y = 0.973 x - 0.1 \text{ mEq/L}$$

$$r = 0.995$$

$$r^2 = 0.991$$

Standard error of the estimate $S_{y.x} = 0.9$ mEq/L.

The sponsor claimed that lithium heparin is an acceptable anticoagulant to be used with the CO2 assay.

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:

Total CO2: 22-29 mEq/L for both serum and plasma

It is recommended each laboratory establishes and maintains its own reference values. The data given here are only for information.

Wu, A.H.B., Tietz Clinical guide to laboratory test, 4th Ed., (W.B. Saunders Company), (2006), 214, 234, 880, 992.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

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