



Food and Drug Administration
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RANDOX LABORATORIES LTD
PAULINE ARMSTRONG
QA/RA MANAGER
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February 24, 2016

Re: K152085

Trade/Device Name: LIQUID CO2-2 (LCO2-2)
Regulation Number: 21 CFR 862.1160
Regulation Name: Bicarbonate/carbon dioxide test system
Regulatory Class: II
Product Code: KHS
Dated: January 20, 2015
Received: January 27, 2015

Dear Pauline Armstrong:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>. Also, please note the regulation entitled, “Misbranding by reference to premarket notification” (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to <http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm> for the CDRH’s Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>.

Sincerely yours,


Katherine Serrano -S

FOR: Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known)
K152085

Device Name
LIQUID CO2-2 (LCO2-2)

Indications for Use (Describe)

For the quantitative in vitro determination of Carbon Dioxide in serum and plasma. Carbon Dioxide measurements are used in the diagnosis and treatment of numerous potentially serious disorders associated with changes in body acid-base balance.

This in vitro diagnostic device is intended for Rx Only.

Type of Use (Select one or both, as applicable)

Prescription Use (Part 21 CFR 801 Subpart D) Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(K) SUMMARY, LIQUID CO₂-2 (LCO₂-2)**1. SAFETY AND EFFECTIVENESS AS REQUIRED BY 21 CFR 807.92 STATEMENT**

This summary of the 510(k) safety and effectiveness information is being submitted in accordance with the requirement 21 CFR 807.92.

2. SUBMITTER NAME AND ADDRESS

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Date of Summary Preparation: February 9, 2016

3. 510k NUMBER, DEVICE PROPRIETARY NAME, COMMON NAME, PURPOSE FOR SUBMISSION, REGULATORY CLASSIFICATION, PANEL, PRODUCT CODE AND 21 CFR NUMBER

510k No: K152085

Device Proprietary Name: Liquid CO₂-2 (LCO₂-2)

Common Name: Liquid CO₂-2 (LCO₂-2)

Purpose for Submission: New Device

Product Code	Regulation Name	Classification	Regulation Section	Panel
KHS	Bicarbonate/ Carbon Dioxide test system	Class II	21 CFR 862.1160	Clinical Chemistry (75)

4. PREDICATE DEVICE PROPRIETARY NAMES AND 510 (k) NUMBERS

Predicate Device Proprietary Name:

Siemens ADVIA Chemistry Carbon Dioxide Liquid (CO2_L)

510 (k) Number: K100289

5. INTENDED USE

For the quantitative in vitro determination of Carbon Dioxide in serum and plasma. Carbon Dioxide measurements are used in the diagnosis and treatment of numerous potentially serious disorders associated with changes in body acid-base balance.

This in vitro diagnostic device is intended for Rx only.

6. DEVICE DESCRIPTION

The Liquid CO₂-2 (LCO₂-2) kit assay consists of ready to use reagent solutions.

CATALOGUE NUMBER: CD8357

R1. Liquid CO₂-2 Reagent 4 x 18 ml
CAL. Liquid CO₂-2 Calibrator 1 x 10 ml

REAGENT COMPOSITION

Contents	Concentration in the test
R1. Liquid CO₂-2 Reagent	
Phosphoenolpyruvate (PEP)	12.5 mmol/l
NADH analogue	0.6 mmol/l
Microbial Phosphoenolpyruvate Carboxylase (PEPC)	>400 U/l
Mammalian Malate Dehydrogenase (MDH)	>4100 U/l
Buffer	pH 7.6
Sodium Azide	0.08%
CAL. Liquid CO₂-2 Calibrator	See Lot Specific Insert

MATERIALS REQUIRED BUT NOT PROVIDED

Randox Assayed Multisera Level 2 (Cat. No. HN 1530) and Level 3 (Cat. No. HE 1532); 510(k) # k942458
0.9% NaCl solution for sample dilutions (if required)

7. PREDICATE DEVICE COMPARISON TABLE

Table 1 **Comparison of Liquid CO₂-2 test system for the RX Daytona plus to predicate device**

CHARACTERISTICS	Liquid CO ₂ -2 (LCO ₂ -2) Assay for RX daytona plus (New Device)	Siemens ADVIA Chemistry Carbon Dioxide Liquid (CO ₂ _L) ADVIA SYSTEMS K100289 (Predicate Device)
Similarities		
INTENDED USE	For the quantitative in vitro determination of Carbon Dioxide in serum and plasma. Carbon Dioxide measurements are used in the diagnosis and treatment of numerous potentially serious disorders associated with changes in body acid-base balance	Same
ASSAY PROTOCOL	Enzymatic Method	Same
INSTRUMENT MODE	Automatic Instrument	Same
STORAGE (UNOPENED)	Reagents are stable up to the expiry date when stored unopened at +2 to +8°C	Same
CALIBRATION FREQUENCY	Everyday, with a change of reagent lot or as indicated by quality control procedures.	Same
SAMPLE TYPE	Serum, heparinized plasma samples are suitable.	Same
TEST RANGE	10 – 40 mEq/L	Same

Differences		
REAGENT COMPOSITION	<p>Liquid CO₂-2 Reagent</p> <p>Phosphoenolpyruvate (PEP) 12.5 mmol/l NADH analogue 0.6 mmol/l Microbial Phosphoenolpyruvate Carboxylase (PEPC) >400 U/l Mammalian Malate Dehydrogenase (MDH) >4100 U/l Buffer pH 7.6 Sodium Azide 0.08%</p> <p>CAL. Liquid CO₂-2 Calibrator See Lot Specific Insert</p>	<p>1.Buffer</p> <p>Buffer pH 6.5 Phosphoenolpyruvate (PEP) 63 mmol/l NADH analogue 3.0 mmol/l Microbial Phosphoenolpyruvate Carboxylase (PEPC) ≥2000 U/l Mammalian Malate Dehydrogenase (MDH) ≥20000 U/l Sodium Azide 0.08%</p>
CONTROL FREQUENCY	Two levels of control should be assayed at least once a day	Follow laboratory accreditation requirements.

8. TEST PRINCIPLE ^(1,2)



The reduction in absorbance at 415 nm caused by the oxidation of NADH analogue is proportional to the bicarbonate concentration in the sample.

1. Jacobs, N., et al "Laboratory Test Handbook" 2nd. ed., Williams and Wilkins 1990.
2. Forrester, R.L., Wataji, L.J., Silverman, D.A., Pierre K.J., Clin, Chem. 1976; **22/2**: 243-245.

9. PERFORMANCE CHARACTERISTICS

Analytical performance:

a. Precision/Reproducibility:

Precision was evaluated consistent with C.L.S.I documents EP5-A2
Precision studies were performed by one operator on two RX Daytona plus systems using serum based control material and unaltered human serum samples that were spiked with carbon dioxide concentrations or diluted to achieve concentrations based on normal ranges 20 – 31 mEq/L. Testing was conducted for two reagent lots of liquid CO₂-2(LCO₂-2), one lot on each RX Daytona plus system, twice per day for 20 non-consecutive days. Two replicates per run were performed for each sample. The assay was calibrated daily. The results of Lot 1 which is representative of both lots of Liquid CO₂-2 (LCO₂-2) reagent is summarized in the following table

Table 2 **Precision Summary**

Lot 1	Method	Product	N	MEAN (mEq/L)	Within Run		Among Run		Among Day		Total	
					SD	CV	SD	CV	SD	CV	SD	CV
	LCO2	QC Level 3	80	17.7	0.41	2.3	0.68	3.8	0.05	0.3	0.79	4.5
	LCO2	QC Level 2	80	11.4	0.32	2.8	0.53	4.6	0.12	1.1	0.63	5.5
	LCO2	SP Level 1	80	11.1	0.22	2.0	0.67	6.0	0.25	2.2	0.75	6.7
	LCO2	SP Level 2	80	18.8	0.42	2.2	0.83	4.4	0.00	0.0	0.93	5.0
	LCO2	SP Level 3	80	35.4	0.59	1.7	1.00	2.8	0.66	1.9	1.33	3.8

b. Linearity/assay reportable range:

Linearity studies have been carried out in accordance with C.L.S.I. standard EP6-A. Linearity studies were performed at 11 levels to determine the analytical range of an assay - that is the range where the reported result is a linear function to the analyte concentration (or where deviation from linearity is less than 5%).

The linearity samples were prepared at 11 levels. Randox used a low serum pool sample around 4.0 mEq/l analyte concentration and a serum pool with a high concentration approximately 55 mEq/l using low and high serum pools. The low and high pools were mixed to make nine intermediate levels. Each level was run in replicates of five on two lots of Liquid CO₂-2 (LCO₂-2) reagent on one RX Daytona plus system. The observed values were compared to the expected values; the linear regression correlation between the expected values and the observed values are summarized in the following table:

Table 3 **Linearity Summary including Regression equation and correlation coefficient.**

Analyte Tested	CO ₂ (mEq/L)
Linear Regression	Y = 0.99 + 0.75
r	0.999

The reportable range of the assay is 10 to 40 mEq/L

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

Refer to K942458 Controls for Carbon Dioxide

The Liquid CO₂-2 Calibrator is traceable to an internal master reference material that in turn is traceable to Sodium Carbonate NIST reference material 351. Calibrators are value assigned using one instrument and multiple repetitions. The mean, standard deviation and %CV are calculated and evaluated against acceptance criteria.

Open vial stability

Open vial stability of the Liquid CO₂-2 Calibrator was assessed by preparing the material according to the package insert. Samples were stored at +2 to +8°C for 28 days and tested for Carbon Dioxide.

The acceptance criteria state the percentage deviation of stable to fresh should be ≤5%.

Current open vial studies support a reconstituted claim of 28 days when stored at +2°C to +8°C.

Real Time Testing

This study was designed to verify and validate the predicted or desirable shelf life of the Liquid CO₂-2 (LCO₂-2) reagent and calibrator. Kits were stored at the routinely stored temperature of +2 to +8°C and tested at various time points. The acceptance criteria states that the all controls should be within range.

Current Real Time studies support a 2 year shelf life.

d. Detection limit:

Sensitivity studies have been carried out in accordance with C.L.S.I. guideline EP17-A2 'Evaluation of detection capability for clinical laboratory measurement procedures; Approved Guideline Second Edition'. A Limit of Blank (L.o.B.), a Limit of Detection (L.o.D.) and a Limit of Quantification were performed on two lots of reagents tested by two operators on one RX Daytona Plus system.

The Limit of Detection (LoD) for Carbon Dioxide on the RX Daytona Plus is 1.98 mEq/L based on 240 determinations, with 4 low level samples.

The Limit of Blank (LoB) is 0.97 mEq/L.

The Limit of Quantitation (LoQ) is 4.5 mEq/L as determined by the lowest concentration at which precision is still met.

e. Analytical Specificity:

Interference studies have been carried out in accordance with C.L.S.I. guideline EP7-A2 'Interference testing in clinical chemistry; Approved Guideline Second Edition' The effects of potential interferents were determined by calculating the mean value of the spiked interferent with the corresponding control solution. The spiked sample results were compared to control samples prepared without the potential interferents.

Acceptance Criteria:

The criteria for no significant interference is recovery within ±10% of the initial value of Carbon Dioxide concentration of 20 mEq/L and 35 mEq/L

Haemoglobin	No significant interference up to 1000mg/dL
Total Bilirubin	No significant interference up to 60mg/dL
Conjugate Bilirubin	No significant interference up to 30mg/dL

Triglycerides	No significant interference up to 2000mg/dL
Intralipid®	No significant interference up to 2000mg/dL
Ascorbic Acid	No significant interference up to 6.0mg/dL

f. Method comparison with predicate device:

Correlation studies were carried out in accordance with C.L.S.I. guideline EP9-A2 'Method Comparison and Bias Estimation Using Patient Samples: Approved Guideline – Second Edition'.

97 serum patient samples spanning the range 12.5 to 39.4 mEq/L were tested by one operator on two lots of Liquid CO₂-2 (LCO₂-2) reagent on one RX Daytona plus analyzer and the predicate device tested on one ADVIA 1650 system across 3 working days with each sample tested in singlicate. The test method was compared to the predicate device and the following linear regression equation was obtained:

$$Y = 0.97x - 0.11$$

Correlation coefficient of $r = 0.994$

g. Matrix comparison:

Matrix method comparisons for Liquid CO₂-2 (LCO₂-2) assay was tested by one operator on one RX Daytona plus system and was assessed for two lots of reagents. Both serum and lithium heparin plasma were tested to determine whether method accuracy with plasma specimens are equivalent to serum results and that lithium heparin plasma does not interfere with either the method or the system.

Liquid CO₂-2 (LCO₂-2) matrix comparison on the RX Daytona plus (Lithium Heparin)

Patient samples were drawn in matched pairs – one sample serum (x) and the second sample lithium heparin plasma (y). 50 matched patient sample pairs were analyzed spanning the 13.9 to 38.1 mEq/L and the following linear regression equation was obtained:

$$Y = 0.97x + 0.94$$

Correlation coefficient of $r = 0.984$

Expected values/Reference range:

Referenced from literature

A reference interval for Carbon Dioxide was verified using NCCLS C28-A3 guidelines. In a study, human serum from 30 normal donors were tested in singlicate on the RX daytona plus. The results obtained were ordered from lowest to highest before being examined for outliers using the Dixon test.

Upon confirmation there were no outliers; the values were compared to the quoted ranges for Carbon Dioxide. Results of the study indicate that all values reported in the range for Healthy Individuals.

Table 4 **Reference Ranges**

<u>Analyte</u>	<u>Expected Values</u>
Carbon Dioxide ⁽³⁾	20 – 31 mEq/L

3. Tietz NW. *Clinical Guide to Laboratory Tests*. 3rd ed. Philadelphia, PA: WB Saunders Company; 1995:110-111.

10. CONCLUSION

Testing results indicate that the proposed device is substantially equivalent to the predicate device.