DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

April 21, 2017

RANDOX LABORATORIES LIMITED
PAULINE ARMSTRONG, QA/RA MANAGER
55 DIAMOND ROAD
CRUMLIN, COUNTY ANTRIM, BT29 4QY
GREAT BRITAIN

Re: K162275
Trade/Device Name: Randox RX Daytona Plus Alkaline Phosphatase (ALP)
Regulation Number: 21 CFR 862.1050
Regulation Name: Alkaline phosphatase or isoenzymes test system
Regulatory Class: II
Product Code: CJE
Dated: March 21, 2017
Received: March 23, 2017

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,

Kellie B. Kelm -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

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K162275

Device Name
Randox RX Daytona Plus Alkaline Phosphatase (ALP)

Indications for Use *(Describe)*
The Randox RX Daytona Plus Alkaline Phosphatase (ALP) test system is intended for the quantitative in vitro determination of Alkaline Phosphatase (ALP) activity in serum and lithium heparinized plasma. Measurements of alkaline phosphatase are used in the diagnosis, treatment and investigation of hepatobiliary disease and in bone disease.

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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K162275

510(K) SUMMARY

RANDOX RX DAYTONA PLUS ALKALINE PHOSPHATASE (ALP)

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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E-mail: Pauline.Armstrong@randox.com

Date of Summary Preparation: 20 April 2017

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

510(k) No: K162275

Device Proprietary Name: Randox RX Daytona Plus Alkaline Phosphatase (ALP)

Common Name: RX Daytona Plus Alkaline Phosphatase (ALP)

Purpose for Submission: New Device

Product Code	Regulation Name	Classification	Regulation Section	Panel
CJE	Alkaline Phosphatase or isoenzymes test system.	II	21 CFR 862.1050	Clinical Chemistry (75)

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

Predicate Device Proprietary Name: Siemens Alkaline Phosphatase (ALPAMP)

510(k) Number: K991576

5. INTENDED USE

The Randox RX Daytona Plus Alkaline Phosphatase (ALP) test system is intended for the quantitative *in vitro* determination of Alkaline Phosphatase (ALP) activity in serum and lithium heparinized plasma. Measurements of alkaline phosphatase are used in the diagnosis, treatment and investigation of hepatobiliary disease and in bone disease.

6. DEVICE DESCRIPTION

The Randox RX Daytona Plus Alkaline Phosphatase (ALP) assay consists of ready to use reagent solutions.

CATALOGUE NUMBER: AP8302

R1. Buffer 4 x 20 ml
R2. Substrate 4 x 7 ml

REAGENT COMPOSITION

Contents	Concentrations in the Test
R1. Buffer	
2-amino-2-methyl-I-propanol	0.35 mol/l, pH 10.4
Mg^{2+}	2.0 mmol/l
R2. Substrate	
p-nitrophenylphosphate	10 mmol/l

7. PREDICATE DEVICE COMPARISON TABLE

Table 1 - Comparison of Randox RX Daytona Plus Alkaline Phosphatase (ALP) to Predicate Device (Siemens Alkaline Phosphatase (ALPAMP)

CHARACTERISTICS	Candidate Device Randox RX Daytona Plus Alkaline Phosphatase (ALP) Assay (K162275)	Predicate Device Siemens Alkaline Phosphatase (ALPAMP) Assay (K991576)
	Similarities	
INTENDED USE	For the quantitative *in vitro* determination of Alkaline Phosphatase (ALP) activity in serum and plasma. Measurements of alkaline phosphatase are used in the diagnosis, treatment and investigation of hepatobilary disease and in bone disease.	For the quantitative *in vitro* determination of Alkaline Phosphatase (ALP) activity in serum and plasma. Such measurements are used in the diagnosis and treatment of hepatobiliary and bone disease.
ASSAY PROTOCOL	Colorimetric Method IFCC	Same
STORAGE (UNOPENED)	Reagents are stable up to the expiry date when stored unopened at +2 to +8°C	Same
SAMPLE TYPE	Serum Plasma (Li Heparin)	Same
REAGENT COMPOSITION	R1. Buffer 2-amino-2-methyl-I-propanol 0.35 mol/l, (pH 10.4) Mg^{2+} 2.0 mmol/l R2. Substrate p-nitrophenylphosphate 10 mmol/l	R1. AMP 0.438 mol/l Sodium azide 0.09% R2. p-nitrophenylphosphate 60 mmol/l Sodium azide 0.09%
REAGENT PREPARATION	Liquid, ready to use	Same
CONTROL FREQUENCY	Randox Assayed Multisera Levels 2 & 3 Two levels of control should be assayed at least once a day	Commercially available controls are recommended Analyse at least two levels of controls daily
MEASURING RANGE	8 – 918 U/l	0 – 1100 U/l

Table 1: Comparison of Randox RX Daytona Plus Alkaline Phosphatase (ALP) to Predicate Device (Siemens Alkaline Phosphatase (ALPAMP)

CHARACTERISTICS	Candidate Device Randox RX Daytona Plus Alkaline Phosphatase (ALP) Assay (K162275)	Predicate Device Siemens Alkaline Phosphatase (ALPAMP) Assay (K991576)
	Differences	
CALIBRATOR	Randox Calibration Serum Level 3	Fixed System Factor Value
CALIBRATION FREQUENCY	A 2 point calibration is recommended every 7 days or with a change of reagent lot	Not Required

8. TEST PRINCIPLE [(1)]

The substrate p-nitrophenyl phosphate is hydrolyzed by Alkaline Phosphatase from the sample, in the presence of Magnesium ions, to form p-nitrophenol which is yellow in colour and can be read at 405 nm.

The intensity of colour produced is proportional to the Alkaline Phosphatase activity in the sample.

p-nitrophenyl phosphate + H_2O $\xrightarrow{AP}$ phosphate + p-nitrophenol

1. Bowers, G.N., and R.B. Mc Comb., Clin Chem. 1975; 21: 1988.

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 two operators on two RX daytona plus systems using control material altered human serum samples and unaltered human serum samples that were spiked with ALP concentrations or diluted to achieve concentrations based on established ranges of 30 to 120 U/L for adults. Testing was conducted for two reagent lots of ALP, 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. Both lots yielded similar results. The results of one representative lot are summarized in the following table:

Table 2 - Precision Summary

Lot 1

			Within-Run		Total	
Sample	N	ALP Mean (IU/L)	SD	%CV	SD	%CV
QC1	80	127.83	0.5	0.4	2.87	2.2
QC2	80	328.94	1.19	0.4	6.53	2.0
QC3	80	353.25	1.26	0.4	7.61	2.2
Serum 1	80	81.44	1.56	1.9	1.89	2.3
Serum 2	80	212.76	3.35	1.6	3.44	1.6
Serum 3	80	244.36	3.63	1.5	3.77	1.5
Serum 4	80	349.39	4.41	1.3	5.31	1.5
Serum 5	80	24.86	0.80	3.2	1.31	5.3
Serum 6	80	480.71	3.65	0.8	15.26	3.2
Serum 7	80	706.24	4.87	0.7	24.48	3.5
Serum 8	80	895.00	4.49	0.5	30.79	3.4

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.

Acceptance Criteria:
LoQ / L1 pool $\leq$ 20% deviation to target
L2 to L11 $\leq$ 5% deviation to target
Slope 0.90 – 1.10
Intercept $\leq$ established LoQ
r $\geq$ 0.95

The linearity samples were prepared at 11 levels. The range was from 7.50 Ul/l analyte concentration up to a high concentration of approximately 922 U/l. The low and high level pools were mixed to create 9 intermediate levels. Each level was run in replicates of five on two lots of ALP reagent on one RX Daytona Plus system. The results are summarized in the following table:

Table 3 - Linearity Summary Serum

Analyte	ALP (U/l)
Linear Regression	y = 1.00x + 6.49
r	1.000

The claimed range of the assay is 8 – 918 U/l.

c. Calibration

The use of Saline and Randox Calibration Serum Level 3 is recommended for calibration of the Randox RX Daytona Plus Alkaline Phosphatase (ALP) assay.

d. Detection limit:

Sensitivity studies have been carried out in accordance with C.L.S.I. guideline EP17-A2 'Protocols for Determination of Limits of Detection and Limits of Quantification; Approved Guideline'. A Limit of Blank (LoB), a Limit of Detection (LoD) and a Limit of Quantification (LoQ) were performed on two lots of reagents tested by two operators on one RX Daytona Plus system.

The Limit of Detection (LoD) for ALP on the RX Daytona Plus is 1.0 U/L based on 240 determinations, with 4 low level samples.

The Limit of Blank (LoB) is 0.14 U/L.

The Limit of Quantitation (LoQ) is 7.5 U/L as determined as the lowest concentration which meets an imprecision of <10% bias.

e. Analytical Specificity:

The following analytes were tested up to the levels indicated at ALP concentrations of 80 U/l and 240 U/l and found not to interfere with the ALP assay.

Table 4 - ALP Interference Summary

Interferent	Highest concentration of substance tested which did not demonstrate significant interference
Haemoglobin	375 mg/dl
Total Bilirubin	60 mg/dl
Conjugate Bilirubin	60 mg/dl
Triglycerides	2000 mg/dl
Intralipid	750 mg/dl
Ascorbic Acid	6 mg/dl

Acceptance Criteria:
The control pool must be within 10% of the decision level target and the control and test pools must recover within 10% of each other, for the analyte to be deemed not to interfere.

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'.

106 serum patient samples spanning the range 8 to 883 U/L were tested by one operator on two lots of Randox ALP reagent on one RX daytona plus analyzer and one lot of Siemens ALPAMP reagent on one Advia 1800 system, across 3 working days with each sample tested in duplicate. The test method was compared to the predicate device and the following linear regression equation was obtained:

$y = 1.005x – 3.95$

Correlation coefficient of $r = 0.999$

g. Matrix comparison:

Matrix method comparisons for the Randox RX Daytona Plus Alkaline Phosphatase (ALP) assay was tested by one operator on one RX Daytona Plus system and was assessed for two lots of ALP reagents. Both serum and lithium heparin plasma were tested to determine whether method accuracy with lithium heparin specimens is equivalent to serum results and that lithium heparin plasma does not interfere with either the method or the system.

Patient samples were drawn in matched pairs – one sample serum (x) and the second sample lithium heparin plasma (y). A total of 46 matched patient sample pairs were analyzed spanning the 15.3 to 773.1 U/L and the following linear regression equation was obtained:

y = 1.00x - 0.13

Correlation coefficient of r = 1.00

Expected values/Reference range:

Referenced from literature

Reference intervals for ALP 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 ALP. Results of the study indicate that all values reported in the range for Healthy Individuals.

Table 5 - Reference Ranges

Analyte	**Serum**
ALP [2]	Adults: 30 – 120U/L

2. Mosby's Manual of Diagnostic and Laboratory Tests. 3rd Edition. Pagana and Pagana, 2006, page 49.

It is recommended that each laboratory establish its own reference range to reflect the age, sex, diet and geographical location of the population.

10. CONCLUSION

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