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

A. 510(k) Number:

k131554

B. Purpose for Submission:

Adding previously cleared assays on a new instrument platform

C. Measurand:

Aspartate Aminotransferase, Sodium, Potassium, and Chloride

D. Type of Test:

Quantitative, enzymatic and potentiometric measurement with Ion-Selective Electrodes

E. Applicant:

Randox Laboratories Limited

F. Proprietary and Established Names:

RX Daytona Plus Chemistry analyzer

RX Daytona Plus Aspartate amino transferase (AST) reagent

G. Regulatory Information:

Product Code	Regulation Name	Classification	Regulation Section	Panel
CIT	Aspartate amino transferase (AST/SGOT) Test system	II	21 CFR 862.1100	Chemistry (75)
JGS	Sodium Test System	II	21 CFR 862.1665	Chemistry (75)
CEM	Potassium Test System	II	21 CFR 862.1600	Chemistry (75)
CGZ	Chloride Test System	II	21 CFR 862.1170	Chemistry (75)
JJE	Discrete photometric chemistry analyzer for clinical use	I	21 CFR 862.2160	Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See indication(s) for use below

2. Indication(s) for use:
   The RX Daytona Plus Chemistry analyzer is a bench top fully automated random access clinical chemistry analyzer intended for use in clinical laboratories. It is intended to be used for a variety of assay methods. The RX Daytona Plus includes an optional Ion Selective Electrode (ISE) module for the measurement of sodium, potassium and chloride in serum and urine. The RX Daytona Plus is not for Point-Of-Care testing.

   Sodium measurements are used in the diagnosis and treatment of diseases involving electrolyte imbalance.

   Potassium measurements monitor electrolyte balance in the diagnosis and treatment of disease conditions characterized by low or high blood potassium levels.

   Chloride measurements are used in the diagnosis and treatment of electrolyte and metabolic disorders.

   The RX Daytona Plus AST reagent is for the quantitative in vitro diagnostic determination of the activity of the enzyme Aspartate aminotransferase (AST) in human serum. Aspartate amino transferase measurements are used in the diagnosis and treatment of certain types of liver and heart diseases.

3. Special conditions for use statement(s):

   For Prescription Use Only

4. Special instrument requirements:

   RX Daytona Plus chemistry analyzer with ISE module

I. Device Description:

The RX Daytona Plus analyzer with optional ISE is an automated, in-vitro analyzer capable of performing clinical chemistry and electrolyte tests. The analyzer is offered in two formats (with ISE module for measuring sodium, potassium and chloride electrometrically and without ISE module). The RX Daytona Plus is a bench-top fully automated random access clinical analyzer. The RX Daytona Plus has the capacity to perform up to 270 photometric tests or 450 tests per hour with ISE's and offers primary tube sampling, on-board sample dilution and a cooled reagent compartment.

- Cuvette wash system
- STAT facility
- Direct interface with host computer
- Automatic re-run and pre-dilution functions

The RX Daytona Plus uses dedicated software for access to all system facilities and functions. A color, graphic user interface guides through the operating functions and provides a data management system.

The ISE module is comprised of the ISE (sodium, potassium, and chloride) electrodes, plus ISE cleaning solution, ISE reference solution, ISE etching solution and ISE calibrators (L and H solution). The ISE calibrators consist of 2 levels: Lo solution and High. Calibrators are supplied in liquid ready-to-use form and are aqueous solutions containing sodium, potassium and chloride. The ISE module has been previously cleared in k052914.

The Randox AST reagent consists of 2 reagents: Reagent 1 contains Tris buffer, L-Aspartic Acid, Malate Dehydrogenase (MDH), and Lactate Dehydrogenase (LD). The R2 reagent contains α-oxoglutarate and NADH. This reagent has been previously cleared in k923505.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Randox AST assay
   Randox RX Imola Analyzer

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

   k923505 and k052914 respectively.

3. Comparison with predicate:

AST

Similarities and Differences		
Item	Randox Daytona Plus AST Reagent (Candidate device)	Randox AST Reagent k923505 (Predicate device)
Intended Use	For the quantitative in vitro diagnostic determination of the activity of the enzyme Aspartate aminotransferase (AST) in human serum.	Same
Sample Type	Serum	Serum or Plasma

Similarities and Differences		
Item	Randox Daytona Plus AST Reagent (Candidate device)	Randox AST Reagent k923505 (Predicate device)
Assay method	UV method	Same
Reagent format	Liquid, ready to use	Same
Calibration frequency	Every 28 days or as needed	Same

RX Daytona plus analyzer

Similarities and Differences		
Item	RX Daytona Plus Analyzer (Candidate device)	RX Imola Automated Analyzer (Predicate device) k052914
Intended use	Automated clinical chemistry system intended for use in clinical laboratories. It is intended to be used for a variety of assay methods.	Same
Technology	Spectrophotometric and electrochemical tests	Same
Assay Methods	Monochromatic, bi-chromatic, endpoint, kinetic, sample and reagent blanking and ISE (via optional integrated ISE)	Endpoint, Kinetic, Bichromatic, turbidimetric, sample blanking, reagent blanking and ISE.
Calibration Principle	Factor, Linear, Point to point, Log- logit, Exponential, Spline, Spline 2 and ISE	Factor, Linear, 2 point, point to point, spline, log-logit, exponential and ISE
Cuvettes	72 resin cuvettes (semi-disposable) (volume, 100ul min, 350ul max)	90 reusable pyrex cuvettes (volume, 150ul min, 450ul max)
Cycle Time	13 seconds	9 seconds
Detection Principle	12 wavelengths generated via diffraction grating:340, 380,415, 450,510,546,570,600,660,700,750	Same
ISE module:		
Technology	Indirect potentiometry measurement with Ion-Selective Electrode	Same
Sample Type	Serum and Urine	Same

Similarities and Differences		
Item	RX Daytona Plus Analyzer (Candidate device)	RX Imola Automated Analyzer (Predicate device) k052914
Calibration frequency	Calibration is recommended for every 8 hours or as needed	Every 24 hours or as needed.

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

CLSI-EP-17A- Protocols for Determination of Limits of Detection and Limits of Quantitation

CLSI-EP-09-A2- Method Comparison and Bias estimation using patient samples

CLSI-EP-05-A2-Evaluation or Precision of Quantitative Measurement Methods

CLSI-EP-07-A2- Interference Testing in Clinical Chemistry

CLSI-EP-06-A- Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach

CLSI-C28-A3- Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory

L. Test Principle:

AST measurements are based on A-oxoglutarate reacts with L-aspartine in the presence of AST to form L-glutamate plus oxaloacetate. The indicator reaction utilizes the oxaloacetate for a kinetic determination of NADH consumption.

The RX Daytona Plus analyzer with optional ISE is based on the potentiometric Nernst Equation principle. Sample is diluted with a diluent and aspirated into ion-selective electrodes. The measured potential difference between the reference electrode and the ion specific electrode is proportional to the logarithm of the concentration of the measured ions.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

AST Reagent

Precision was evaluated using 3 unaltered human serum samples at low, medium and high levels and 1 human serum sample spiked with AST to a concentration of 850

U/L. Three additional samples (1 calibrator and 2 control samples) were also tested. All samples were tested in duplicate twice a day for 20 days on the Randox RX Daytona Plus analyzer following CLSI-EP5-A2 guideline. Results are summarized in the table below:

AST

Material	n	Mean (U/L)	Within-run		Total	
			SD	CV (%)	SD	CV (%)
Control 1	40	161.74	2.23	1.4	2.69	1.7
Control 2	40	37.83	1.14	3.0	1.29	3.4
Control 3 (CAL)	40	142.95	1.82	1.3	2.20	1.5
Serum sample 1	40	391.33	2.26	0.6	9.47	2.4
Serum sample 2	40	18.83	0.43	2.3	1.08	5.8
Serum sample 3	40	850.27	4.57	0.5	11.62	1.4

Sodium

Precision was evaluated using 3 unaltered human serum samples (pools 1, 2 and 3) and two levels of quality control for serum. Urine precision was evaluated using 2 unaltered human urine samples (pools 1 and 2) and two urine based quality control samples. All samples were tested in duplicate twice a day for 20 days on the Randox RX Daytona Plus analyzer following CLSI-EP-5-A2 guideline. Results are summarized in the table below:

Sodium-Serum

Material	n	Mean (mmol/L)	Within-run		Total	
			SD	CV (%)	SD	CV (%)
Control 1	40	154.46	2.14	1.4	2.19	1.4
Control 2	40	138.28	1.62	1.2	3.39	2.4
Patient Pool 1	40	108.73	1.52	1.4	1.65	1.5
Patient Pool 2	40	134.70	1.40	1.0	1.46	1.1
Patient Pool 3	40	174.60	2.08	1.2	2.90	1.7

Sodium-Urine

Material	n	Mean (mmol/L)	Within-run		Total	
			SD	CV (%)	SD	CV (%)
Control 1	40	61.84	2.59	4.2	3.44	5.6
Control 2	40	192.25	6.2	3.2	9.34	4.9
Patient Pool 1	40	135.65	4.05	3.0	7.51	5.5
Patient Pool 2	40	281.59	5.37	1.9	12.02	4.3

Potassium

Precision was evaluated using 3 unaltered human serum samples (pools 1, 2 and 3) and two levels of quality control for serum. Urine precision was evaluated using 2

unaltered human urine samples (pools 1 and 2) and two urine based quality control samples. All samples were tested in duplicate twice a day for 20 days on the Randox RX Daytona Plus analyzer following CLSI-EP-5-A2 guideline. Results are summarized below:

Potassium-Serum

Material	n	Mean (mmol/L)	Within-run		Total	
			SD	CV (%)	SD	CV (%)
Control 1	40	6.0	0.06	1.1	0.08	1.3
Control 2	40	4.0	0.06	1.4	0.07	1.7
Patient Pool 1	40	3.3	0.05	1.6	0.06	1.9
Patient Pool 2	40	4.6	0.09	1.9	0.09	2.0
Patient Pool 3	40	6.7	0.08	1.2	0.11	1.7

Potassium –Urine

Material	n	Mean (mmol/L)	Within-run		Total	
			SD	CV (%)	SD	CV (%)
Control 1	40	32.7	0.55	1.7	0.97	3.0
Control 2	40	103.2	2.08	2.0	4.52	4.4
Patient Pool 1	40	31.9	0.57	1.8	0.87	2.7
Patient Pool 2	40	84.3	2.04	2.4	2.98	3.5

Chloride

Precision was evaluated using 3 unaltered human serum samples (pools 1, 2 and 3) and two levels of quality control for serum. Urine precision was evaluated using 2 unaltered human urine samples (pools 1 and 2) and two urine based quality control samples. All samples were tested in duplicate twice a day for 20 days on the Randox RX Daytona Plus analyzer following CLSI-EP-5-A2 guideline. Results are summarized below:

Chloride-Serum

Material	n	Mean (mmol/L)	Within-run		Total	
			SD	CV (%)	SD	CV (%)
Control 1	40	114.86	1.29	1.1	1.95	1.7
Control 2	40	100.35	1.40	1.4	1.58	1.6
Patient Pool 1	40	88.84	1.87	2.1	1.94	2.2
Patient Pool 2	40	105.73	1.07	1.0	1.49	1.4
Patient Pool 3	40	134.13	1.75	1.3	2.49	1.9

Chloride-Urine

Material	n	Mean (mmol/L)	Within-run		Total	
			SD	CV (%)	SD	CV (%)
Control 1	40	86.44	3.15	3.6	4.66	5.4
Control 2	40	240.25	5.23	2.2	15.04	6.3

Patient Pool 1	40	171.06	4.98	2.9	7.30	4.3
Patient Pool 2	40	260.24	3.74	1.4	7.75	3.0

b. Linearity/assay reportable range:

A linearity study was conducted for AST, sodium, potassium and chloride using low and high sample pools to create 11 sample levels across the measuring range of the device for both serum and urine samples types. All samples were measured in triplicate on the Randox RX Daytona Plus Analyzer. The observed results (obtained on the RX Daytona Plus Analyzer) for AST, sodium, potassium and chloride were plotted against the expected values and an appropriate line fitted by standard linear regression resulted in the following:

Serum

Analyte	Serum reportable range	Linear regression
AST	5-1116 U/L	y=1.00x+0.65; R^2=1.000
Sodium	90-226 mmol/l	y=1.05x-5.45; R^2=0.999
Potassium	0.5-11 mmol/l	y=1.02x-0.13; R^2=0.999
Chloride	72-210 mmol/l	y=0.99x+1.14; R^2=0.998

Urine

Analyte	Urine reportable range	Linear regression
Sodium	45-318 mmol/l	y=0.95x+7.26; R^2=0.998
Potassium	1.5-168 mmol/l	y=1.03x-1.20; R^2=1.000
Chloride	61-319 mmol/l	y=0.96x+3.41;R^2=0.999

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

Device	Traceability
AST	Standardized against primary calibrators traceable to AST reference material JSCC TS01
ISE: Sodium, Potassium and Chloride	Standardized against primary calibrators prepared gravimetrically from purified salts

<u>Stability</u>

On board stability for the AST reagent and ISE reagents was established by real time studies on the Randox Daytona Plus system. The on-board stability of the reagent is 45 days. The AST reagent is stable until the expiration date printed on the label when stored at 2-8°C. Acceptance criteria and study protocol have been provided and found to be adequated.

According to the sponsor, the on-board and open stability claims for the ISE reagents are as follows when stored at 15-25°C:

Component	Open Stability
ISE cleaning solution	6 months
ISE ref solution	1 month
ISE etching solution	12 months
L solution (ISE Calibrator)	1 month
H solution (ISE Calibrator)	1 month

Calibrators for AST assay: The Randox clinical chemistry calibration serum level 2 & 3 (previously cleared under k053153) are the recommended calibrators for use with this device. The Randox clinical chemistry calibrators, when reconstituted, are stable for 8 hours at 15-25°C or 7 days at 2-8°C, and 1 month when frozen once at -20°C.

Controls for both AST assay and ISE module: The Randox assayed human multi-sera level 2 & 3 (previously cleared under k942458) are the recommended controls for use with this device. The controls, when reconstituted, are stable for 8 hours at 15-25°C or 7 days at 2-8°C, and 1 month when frozen once at -20°C.

d. Detection limit:

A detection limit study was evaluated according to CLSI EP-17A. The Limit of Blank (LoB) was determined by assaying a blank sample 120 times on the Randox Daytona Plus analyzer. The LoB was determined by using the 95% value.

The limit of detection (LoD) was determined by assaying 120 replicates of two low level AST samples which were prepared by spiking AST into stripped human serum. The stock solution containing pure AST was added volumetrically to produce the 2 samples with desired concentrations of 0.5 and 1.0 U/L of AST. The LoD was determined using the median minus the 5^{th} percentile plus the LoB value.

The Limit of Quantitation (LoQ) was determined by assaying 120 replicates of 7 low AST sample pools. The LoQ was determined as the lowest concentration sample that had a %CV of ≤20%.

Analyte	LoB	LoD	LoQ
AST	0.50 U/L	1.37 U/L	5.0 U/L

The claimed measuring range is 5-1116 U/L for the AST assay.

The claimed measuring ranges of the ISE electrolytes were based on the linearity study and are summarized in the table below.

Analyte	Serum reportable range	Urine reportable range
Sodium	90-226 mmol/l	45-318 mmol/l
Potassium	0.5-11 mmol/l	1.5-168 mmol/l
Chloride	72-210 mmol/l	61-319 mmol/l

e. Analytical specificity:

Testing for interfering substances was based on CLSI EP-7A2. Testing for each analyte was performed at two concentration levels (low and high) using interfering substances at five difference concentration levels. Samples with increasing amounts of Hemoglobin, Bilirubin (total and conjugated), Intralipid and Triglycerides for AST plus Bromide, Ascorbic Acid, Thyiocyanate, Lithium, and salicylic acid were tested for sodium, potassium and chloride and compared to samples that did not contain the interfering substance.

The sponsor defined non-significant interference as the highest level tested that does not cause >10% change between the tested samples and the control samples.

AST

	Highest concentration tested that showed no significant interference
Hemoglobin	interferes
Total Bilirubin	60 mg/dl
Bilirubin (conjugated)	60 mg/dl
Intralipid	500 mg/dl
Triglycerides	500 mg/dl

The labeling states that serum samples free from hemolysis should be used with this AST assay.

Sodium, Potassium and Chloride Serum Interference summary showing highest concentration that does not interfere

Interferent	**Sodium**	**Potassium**	**Chloride**
Hemoglobin	500 mg/dl	62.5 mg/dl	750 mg/dl
Total Bilirubin	60 mg/dl	60 mg/dl	30 mg/dl
Bilirubin (conjugated)	60 mg/dl	60 mg/dl	60 mg/dl
Intralipid	2000 mg/dl	1500 mg/dl	2000 mg/dl
Triglycerides	2000 mg/dl	2000 mg/dl	2000 mg/dl
Bromide	37.5 mmol/L	Interferes causes false ↑	Interferes causes false ↑
Ascorbic Acid	342 mmol/l	342 mmol/l	342 mmol/l
Thyiocyanate	6.88 mmol/l	6.88 mmol/l	Interferes causes false ↑

Lithium	3.2 mmol/l	3.2 mmol/l	3.2 mmol/l
Salicylic Acid	4.34 mmol/l	4.34 mmol/l	interferes

The labeling states non-hemolyzed samples should be used as hemolyzed samples will elevate potassium.

Labeling also states Thyiocyanate and Salicylic acid will cause falsely elevated Chloride concentrations and Bromide will cause falsely elevated Chloride and Potassium concentrations.

Sodium, Potassium and Chloride Urine Interference summary showing highest concentration that does not interfere

Interferent	**Sodium**	**Potassium**	**Chloride**
Hemoglobin	500 mg/dl	500 mg/dl	750 mg/dl
Total Bilirubin	60 mg/dl	60 mg/dl	30 mg/dl
Bilirubin (conjugated)	30 mg/dl	60 mg/dl	45 mg/dl
Intralipid	2000 mg/dl	2000 mg/dl	1500 mg/dl
Triglycerides	2000 mg/dl	2000 mg/dl	2000 mg/dl

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

All method comparison studies were performed at the manufacturer's site.

AST

A method comparison study was performed using the Randox Rx Imola analyzer (predicate device) versus the Randox RX Daytona Plus Analyzer (candidate device). A total of 92 patient serum samples were analyzed in singlicate. The samples spanned the range of 5.0 – 817.0 U/L. Of these 92 samples, 0 were diluted and 6 were spiked. The results are presented in the table below.

ISE (NA^+, K^+, Cl^-)

A method comparison study was performed using the Randox Rx Imola analyzer (predicate device) versus the Randox RX Daytona Plus Analyzer with ISE module. A total of 50 samples were analyzed for Sodium (all native patient samples), 56 samples for Potassium (5 diluted, 0 spiked) and 61 samples for Chloride (3 diluted and 3 spiked).The results are presented in the table below.

Analyte	Units	Range	Total	Slope	Intercept	R^2
AST	U/L	5.0-817	92	1.03	2.33	0.999
Na^+	mmol/l	105-194	50	1.04	-9.57	0.990
K^+	mmol/l	0.75-9.58	56	1.02	-0.13	0.997
Cl^-	mmol/l	81.3-189.3	61	1.03	-1.16	0.970

Urine

ISE (NA^+, K^+, Cl^-)

A method comparison study was performed using the Randox Rx Imola analyzer (predicate device) versus the Randox RX Daytona Plus Analyzer with ISE module. A total of 42 samples were analyzed for Sodium, 43 samples for Potassium and 49 samples were analyzed for Chloride. No more than 20% of the samples were altered. The results are presented in the table below.

Analyte	Units	Range	Total	Slope	Intercept	R^2
Na^+	mmol/l	54.9-288.5	42	1.01	-7.99	0.996
K^+	mmol/l	10.6-145.1	43	1.04	-1.48	0.999
Cl^-	mmol/l	74.1-287.2	44	0.97	5.08	0.997

b. Matrix comparison:

AST

Serum only

ISE (NA^+, K^+, Cl^-)

Serum and urine only

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:

   Reference Values are provided in the labeling according to literature as follows:

Analyte	Serum	Urine
AST[1]	Men-Up to 35 U/L; Women up to 31 U/L	N/A
Sodium (Na^+)[2]	136-145 mmol/l	40-220 mmol/24h
Potassium (K^+)[2]	3.5-5.1 mmol/l	25-125 mmol/24h
Chloride (Cl^-)[2]	98-107 mmol/l	110-250 mmol/24h

   [1]Schumann G, Klauke R. New IFCC reference procedures for the determination of catalytic activity concentrations of five enzymes in serum; preliminary upper reference limits obtained in hospitalized subjects. Clin Chem Acta 2003; 327 (1-2) 69-79.

   [2]Tietz NW, Pruden EL, Siggaard-Andersen O. Electrolytes. In: Burtis CA, Ashwood ER, eds. Tietz Textbook of Clinical Chemistry. 2nd ed. Philadelphia: WB Saunders 1994:1354-1374.

   In the labeling, the sponsor recommends that each laboratory should establish and maintain its own reference values.

N. Instrument Name:

Randox RX Daytona Plus Chemistry analyzer

O. System Descriptions:

1. Modes of Operation:

   Automated continuous random access analyzer.

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:

   Barcoding or Manual Entry

4. Specimen Sampling and Handling:

   Samples in sample tubes or sample cups with a tube adaptor are places into sample tray and automatically measured by the analyzer.

5. Calibration:

   Sponsor recommends that user perform a calibration and a quality control measurement after installing a new lamp, new lot of reagent or a fresh bottle of reagent. ISE calibration is recommended every 8 hours or when quality control results fall outside the established ranges. It is recommended that AST be calibrated every 28 days or as needed.

6. Quality Control:

   The software contains a quality control program that evaluated control results and determined if they are within specified acceptable limits.

   In the labeling the sponsor recommends that control measurements be assayed daily and the frequency depends on the test method. Quality control materials should be used in accordance with local, state and/or federal guidelines.

P. Proposed Labeling:

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

Q. Conclusion:

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