

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k113751

B. Purpose for Submission:

New device

C. Measurand:

Cocaine metabolite

D. Type of Test:

Qualitative and semi-quantitative enzyme immunoassay

E. Applicant:

Randox Laboratories Ltd.

F. Proprietary and Established Names:

Randox Cocaine Metabolite Assay
Randox Multidrug Calibrator Set
Randox Multidrug Controls, Level 1&2

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
DIO – Cocaine and cocaine metabolite test system	II	862.3250	91-Toxicology
DLJ -Clinical toxicology calibrator	II	862.3200	91- Toxicology
LAS -Clinical toxicology control material	I, reserved	862.3280	91- Toxicology

H. Intended Use:

1. Intended use(s):

See Indications for use below.

2. Indication(s) for use:

Randox Cocaine Metabolite Assay

The Randox Laboratories Ltd. Cocaine Metabolite Assay is an in vitro diagnostic test for the qualitative and semi-quantitative detection of Cocaine in human urine. The cut off for both the qualitative and semi-quantitative modes of the assay is 300 ng/ml for benzoylecgonine. Qualitative and semi-quantitative results can be utilized in the diagnosis and treatment of Cocaine use or overdose. The Randox Cocaine Metabolite assay has been developed for use on the RX series analyzers, which includes the RX Daytona and RX imola.

This in vitro diagnostic device is intended for prescription use only.

The semi-quantitative modes is for purpose of

- (1) enabling laboratories to determine an appropriate dilution of the specimen for confirmation by a confirmatory method such as GCMS or
- (2) permitting laboratories to establish quality control procedures.

This assay provides only a preliminary result. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. Gas Chromatography/ Mass Spectrometry (GC/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be exercised with any drug of abuse test result, particularly when the preliminary result is positive.

Randox Multidrug Calibrator Set

The Randox Multidrug Calibrator Set consists of liquid calibrators containing Methamphetamine, Secobarbital, Oxazepam, Benzoylecgonine and Methadone. There are 5 levels of calibrator. They have been developed for use in the calibration of Amphetamine, Barbiturates, Cocaine, and Methadone assays on the on the RX series analyzers, which includes the RX daytona and RX imola. This in vitro diagnostic device is intended for prescription use only.

Randox Multidrug Controls, Level 1&2

The Randox Multidrug Controls, Level 1&2 are liquid controls containing Methamphetamine, Secobarbital, Oxazepam, Benzoylecgonine and Methadone. There are 2 levels of controls. They have been developed for use in the quality control of Amphetamine, Barbiturates, Cocaine, and Methadone assays on the RX

series analyzers, which includes the RX daytona and RX imola. This in vitro diagnostic device is intended for prescription use only.

3. Special conditions for use statement(s):

For prescription use only.

4. Special instrument requirements:

RX series analyzers, which includes the RX daytona and RX imola.

I. Device Description:

The assay consists of ready-to-use liquid reagents. Reagent 1 contains a mouse monoclonal anti-benzoyllecgonine antibody, glucose-6-phosphate (G6P), nicotinamide adenine dinucleotide (NAD), stabilizers and sodium azide (<0.1%) as a preservative. Reagent 2 contains glucose-6-phosphate dehydrogenase (G6PDH) labeled with benzoyllecgonine in buffer with sodium azide (<0.1%) as a preservative.

The calibrators and controls are sold separately. The calibrator has 5 levels and the control has 2 levels. They consist of human urine samples containing benzoyllecgonine with sodium azide (<0.1%) as a preservative.

J. Substantial Equivalence Information:

1. Predicate device name (s):

Thermo Scientific DRI Cocaine Metabolite Assay

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

k960187

3. Comparison with predicate:

Items	CEDIA Opiate OFT Assay (Candidate Device)	Thermo DRI Cocaine Metabolite Assay (Predicate Device)
Similarity		
Intended use /Indication for use	Same	Qualitative and semi-quantitative determination of Benzoyllecgonine (cocaine metabolite) in human urine.
Sample type	Same	Urine
Calibrated against	Same	Benzoyllecgonine
Test Principle	Same	Competitive enzyme immunoassay
Cutoff	Same	300 ng/mL

Reagent	Same	Liquid ready to use, two reagent assay
Calibrator Levels	Same	0, 150, 300, 500, 1000 ng/mL
Control Levels	Same	225, 375 ng/mL

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

CLSI EP07-A2, Interference Testing in Clinical Chemistry

CLSI EP17-A, Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline.

L. Test Principle:

The assay is based on competition between drug in the sample and drug labeled with the enzyme glucose-6-phosphate dehydrogenase (G6PDH) for a fixed amount of antibody in the reagent. Enzyme activity decreases upon binding to the antibody, and the drug concentration in the sample is measured in terms of enzyme activity. In the absence of drug in the sample, benzoylecgonine-labelled G6PDH conjugate is bound to antibody, and the enzyme activity is inhibited. On the other hand, when free drug is present in the sample, antibody would bind to free drug; the unbound benzoylecgonine-labelled G6PDH then exhibits its maximal enzyme activity. Active enzyme converts nicotinamide adenine dinucleotide (NAD) to NADH, resulting in an absorbance change that can be measured spectrophotometrically at 340 nm.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Benzoylecgonine (BZG) solution (1 mg/ml) was added to a human urine pool to create samples with BZG concentrations ranging from 0 to 611 ng/mL. These samples were tested for precision in qualitative and semi-quantitative modes on RX daytona and RX imola. Each sample was assayed two times per run, 2 runs per day, for 20 days. The results are summarized in the below tables.

RX daytona Semi-Quantitative

GC/MS Confirmed Conc. (ng/ml)	Conc. relative to cutoff (approximate)	No. of Determinations	Results #Neg/#Pos
0	-100%	80	80 Neg
57	-75%	80	80 Neg
137	-50%	80	80 Neg
231	-25%	80	80 Neg
374	+25%	80	80 Pos

398	+50%	80	80 Pos
543	+75%	80	80 Pos
611	+100%	80	80 Pos

RX daytona Qualitative

GC/MS Confirmed Conc. (ng/ml)	Conc. relative to cutoff (approximate)	No. of Determinations	Results #Neg/#Pos
0	-100%	80	80 Neg
57	-75%	80	80 Neg
137	-50%	80	80 Neg
231	-25%	80	80 Neg
374	+25%	80	80 Pos
398	+50%	80	80 Pos
543	+75%	80	80 Pos
611	+100%	80	80 Pos

RX imola Semi-Quantitative

GC/MS Confirmed Conc. (ng/ml)	Conc. relative to cutoff (approximate)	No. of Determinations	Results #Neg/#Pos
0	-100%	80	80 Neg
57	-75%	80	80 Neg
137	-50%	80	80 Neg
231	-25%	80	80 Neg
374	+25%	80	80 Pos
398	+50%	80	80 Pos
543	+75%	80	80 Pos
611	+100%	80	80 Pos

RX imola Qualitative

GC/MS Confirmed Conc. (ng/ml)	Conc. relative to cutoff (approximate)	No. of Determinations	Results #Neg/#Pos
0	-100%	80	80 Neg
57	-75%	80	80 Neg
137	-50%	80	80 Neg
231	-25%	80	80 Neg
374	+25%	80	80 Pos
398	+50%	80	80 Pos
543	+75%	80	80 Pos
611	+100%	80	80 Pos

Conclusion:

All samples spiked at levels below the cutoff detected as negative and all samples spiked at levels above the cutoff detected as positive.

b. Linearity/assay reportable range:

Recovery across the range was tested by serially diluting a spiked urine pool containing 1000 ng/mL of benzoylecgonine into concentration levels listed in

the table below. Each sample was assayed in the semi-quantitative mode. The results were averaged and compared to the expected result and the percent recovery was calculated.

RX imola Semi-Quantitative

Level (% of 1000 ng/mL)	Expected Conc. (ng/mL)	RX imola Result (ng/mL)	% Recovery
0	0	14.74	N/A
1	10	15.88	158.77%
2	20	17.28	86.38%
3	30	19.44	64.81%
4	40	28.35	70.88%
5	50	42.44	84.89%
6	60	44.04	73.39%
7	70	41.21	58.88%
8	80	60.18	75.23%
9	90	72.01	80.01%
10	100	104.89	104.89%
20	200	190.34	95.17%
30	300	299.44	99.81%
40	400	375.34	93.83%
50	500	474.03	94.81%
60	600	576.05	96.01%
70	700	719.66	102.81%
80	800	818.96	102.37%
90	900	901.95	100.22%
100	1000	981.64	98.16%

RX daytona Semi-Quantitative

Linearity Level (% of 1000 ng/mL)	Expected Conc. (ng/mL)	RX imola Result (ng/mL)	% Recovery
0	0	0.00	N/A
1	10	22.11	221.13%
2	20	27.93	139.63%
3	30	41.91	139.71%
4	40	56.36	140.90%
5	50	38.46	76.92%
6	60	66.38	110.64%
7	70	66.94	95.62%
8	80	67.23	84.04%
9	90	68.45	76.06%
10	100	104.05	104.05%
20	200	199.29	99.65%
30	300	308.95	102.98%

40	400	428.05	107.01%
50	500	542.06	108.41%
60	600	621.06	103.51%
70	700	736.18	105.17%
80	800	820.35	102.54%
90	900	885.70	98.41%
100	1000	956.28	95.63%

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

Traceability

The controls and calibrators are prepared using commercially available benzoylecgonine standard the accuracy of which is ensured by purity determinations and gravimetric preparation using balances calibrated with NIST traceable weight. Concentration of drug in the master lots are GC/MS quantified.

Value assignments

Value assigned to each test lot is the mean of 10 measurements, adjusted by the %CV the master lot (10 measurements) is from its assigned target. The %CV of the master and the test lot measurements should be <5% with the exception of calibrator level 1, where a <10% CV is allowed. The % deviation to the target value should be <5% with the exception of calibrator level 1, where a <10% deviation is allowed.

Shelf-life stability

Real time and accelerated studies have been conducted. Protocols and acceptance criteria were described and found to be acceptable. The manufacturer's claims and the supporting studies are summarized below:

Calibrators: Real time and accelerated studies support 18 months of shelf life at 2-8°C.

Controls: Accelerated studies support 18 months of shelf life at 2-8°C. Real time testing is on going.

Reagents: Real time studies support 18 months of shelf life at 2-8°C.

Open-vial stability:

Real time testing supports open-vial stability of 28 days for the Calibrators, Controls and the Reagents.

d. *Detection limit:*

Not applicable

e. Analytical specificity:

Cross-reactivity:

The parent drug, metabolites, and drugs commonly found in samples were tested for cross-reactivity with the assay. Test compounds were spiked into GC/MS verified negative urine and each sample was evaluated against the cut-off calibrator (300ng/mL). The percent cross-reactivity of those compounds are presented below:

Structurally Related Compounds RX daytona -Qualitative

Compound	Tested Conc. (mg/dl)	Response equivalent to 300 ng/ml cut-off	Cross-reactivity %
Benzoyllecgonine	300	POS	100.00%
Cocaethylene	40,298	POS	0.74%
Cocaine	24,391	POS	1.23%
Ecgonine methyl ester	100,000	NEG	0.00%
Ecgonine	68,565	POS	0.44%

Structurally Related Compounds RX imola-Qualitative

Compound	Conc. Of compound (mg/dl)	Response equivalent to 300 ng/ml cut-off	Cross-reactivity %
Benzoyllecgonine	300	POS	100.00%
Cocaethylene	37,485	POS	0.80%
Cocaine	21,753	POS	1.38%
Ecgonine methyl ester	100,000	NEG	0.00%
Ecgonine	21,753	POS	1.38%

Structurally Related Compounds RX Daytona-Semi Quantitative

Compound	Tested Conc. (mg/dl)	Response equivalent to 300 ng/ml cut-off	Cross-reactivity %
Benzoyllecgonine	300	POS	100.00%
Cocaethylene	21,423	POS	1.40%
Cocaine	17,933	POS	1.67%
Ecgonine methyl ester	100,000	NEG	0.00%
Ecgonine	59,045	POS	0.51%

Structurally Related Compounds RX imola-Semi Quantitative

Compound	Conc. Of compound (mg/dl)	Response equivalent to 300 ng/ml cut-off	Cross-reactivity %
Benzoyllecgonine	300	POS	100.00%
Cocaethylene	44,579	POS	0.67%
Cocaine	28,172	POS	1.06%
Ecgonine methyl ester	100,000	NEG	0.00%
Ecgonine	28,172	POS	1.06%

Structural unrelated

RX daytona (same result were obtained on RX imola)

Compound	Conc. tested (ng/mL)	-25% of the cutoff		+25% of the cutoff e	
		Qualitative	Semi-quant	Qualitative	Semi-quant
11-hydroxy-delta9-THC	100,000	Neg	Neg	Pos	Pos
11-nor9-carboxy-delta9-THC	100,000	Neg	Neg	Pos	Pos
6 Acetyl-morphine	100,000	Neg	Neg	Pos	Pos
Amitriptyline	100,000	Neg	Neg	Pos	Pos
Amobarbital	100,000	Neg	Neg	Pos	Pos
(+/-)-amphetamine	100,000	Neg	Neg	Pos	Pos
Ascorbic acid	100,000	Neg	Neg	Pos	Pos
Aspirin	100,000	Neg	Neg	Pos	Pos
β-phenylethylamine	100,000	Neg	Neg	Pos	Pos
Caffeine	100,000	Neg	Neg	Pos	Pos
Cannabidiol	100,000	Neg	Neg	Pos	Pos
Chlorpheniramine	100,000	Neg	Neg	Pos	Pos
Codeine	100,000	Neg	Neg	Pos	Pos
Cotinine	100,000	Neg	Neg	Pos	Pos
delta9-THC	100,000	Neg	Neg	Pos	Pos
Diazepam	100,000	Neg	Neg	Pos	Pos
Dihydrocodeine	100,000	Neg	Neg	Pos	Pos
EDDP	100,000	Neg	Neg	Pos	Pos
EMDP	100,000	Neg	Neg	Pos	Pos
d,l-Ephedrine	100,000	Neg	Neg	Pos	Pos
l-Ephedrine	100,000	Neg	Neg	Pos	Pos
d-Ephedrine	100,000	Neg	Neg	Pos	Pos
R,R(-) Pseudoephedrine	100,000	Neg	Neg	Pos	Pos
S,S(+) Pseudoephedrine	100,000	Neg	Neg	Pos	Pos
Heroin	100,000	Neg	Neg	Pos	Pos
LAAM	100,000	Neg	Neg	Pos	Pos
MBDB	100,000	Neg	Neg	Pos	Pos
MDA	100,000	Neg	Neg	Pos	Pos
MDEA	100,000	Neg	Neg	Pos	Pos
MDMA	100,000	Neg	Neg	Pos	Pos
Methadone	100,000	Neg	Neg	Pos	Pos
d,l-Methamphetamine	100,000	Neg	Neg	Pos	Pos

Morphine	100,000	Neg	Neg	Pos	Pos
Oxycodone	100,000	Neg	Neg	Pos	Pos
Paracetamol	100,000	Neg	Neg	Pos	Pos
Temazepam	100,000	Neg	Neg	Pos	Pos
Ibuprofen	100,000	Neg	Neg	Pos	Pos
d-amphetamine	100,000	Neg	Neg	Pos	Pos

Interference

The potential effect of endogenous compounds and pH on the recovery of BZG using the Randox Cocaine metabolite assay was assessed by spiking known amounts of potentially interfering substances into GC/MS verified negative urine and urine samples with cocaine metabolite concentrations +/- 25% of the assay cut-off. Substances were determined not to interfere with the assay if the recovery of the negative sample was below the assay cut-off and if the +/-25% samples recovered within 10% of a sample containing no interferent.

Endogenous compounds in negative urine-RX daytona

Compound	Tested Conc. (mg/dl)	Response to equivalent to 300 ng/ml cutoff		Cross-reactivity %	
		Qualitative	Semi-quant.	Qualitative	Semi-quant.
Total Bilirubin	15	NEG	NEG	0%	0%
Direct Bilirubin	5	NEG	NEG	0%	0%
Haemoglobin	115	NEG	NEG	0%	0%
Creatinine	30	NEG	NEG	0%	0%
Urea	258	NEG	NEG	0%	0%
Glucose	2000	NEG	NEG	0%	0%
H.S.A.	500	NEG	NEG	0%	0%
Ethanol	1000	NEG	NEG	0%	0%
Acetone	1000	NEG	NEG	0%	0%
Gamma globulin	500	NEG	NEG	0%	0%
Oxalic acid	100	NEG	NEG	0%	0%
Riboflavin	7.5	NEG	NEG	0%	0%
Sodium chloride	6000	NEG	NEG	0%	0%
Boric acid	1000	NEG	NEG	0%	0%
Sodium azide	1000	NEG	NEG	0%	0%
Sodium fluoride	1000	NEG	NEG	0%	0%

Endogenous compounds in +/-25% cutoff urine -RX daytona

Compound	Tested Conc. (mg/dl)	-25% of 300 ng/ml BZG cutoff		+25% of 300 ng/ml BZG cutoff	
		Qualitative	Semi-quant.	Qualitative	Semi-quant.
Total Bilirubin	15	NEG	NEG	POS	POS
Direct Bilirubin	5	NEG	NEG	POS	POS
Haemoglobin	115	NEG	NEG	POS	POS
Creatinine	30	NEG	NEG	POS	POS
Urea	258	NEG	NEG	POS	POS
Glucose	2000	NEG	NEG	POS	POS
H.S.A.	500	NEG	NEG	POS	POS
Ethanol	1000	NEG	NEG	POS	POS
Acetone	1000	NEG	NEG	POS	POS
Gamma globulin	500	NEG	NEG	POS	POS
Oxalic acid	100	NEG	NEG	POS	POS
Riboflavin	7.5	NEG	NEG	POS	POS
Sodium chloride	1500	NEG	NEG	POS	POS
Boric acid	125	NEG	NEG	POS	POS
Sodium azide	1000	NEG	NEG	POS	POS
Sodium fluoride	1000	NEG	NEG	POS	POS
Specific gravity range	1.00 - 1.03	NEG	NEG	POS	POS
pH range	3 - 9	NEG	NEG	POS	POS

Endogenous compounds in negative urine-RX imola

Compound	Tested Conc. (mg/dl)	Response to equivalent to 300 ng/ml cutoff		Cross-reactivity %	
		Qualitative	Semi-quant.	Qualitative	Semi-quant.
Total Bilirubin	15	NEG	NEG	0%	0%
Direct Bilirubin	5	NEG	NEG	0%	0%
Haemoglobin	115	NEG	NEG	0%	0%
Creatinine	30	NEG	NEG	0%	0%
Urea	258	NEG	NEG	0%	0%
Glucose	2000	NEG	NEG	0%	0%
H.S.A.	500	NEG	NEG	0%	0%
Ethanol	1000	NEG	NEG	0%	0%
Acetone	1000	NEG	NEG	0%	0%
Gamma globulin	500	NEG	NEG	0%	0%
Oxalic acid	100	NEG	NEG	0%	0%
Riboflavin	7.5	NEG	NEG	0%	0%

Sodium chloride	6000	NEG	NEG	0%	0%
Boric acid	1000	NEG	NEG	0%	0%
Sodium azide	1000	NEG	NEG	0%	0%
Sodium fluoride	1000	NEG	NEG	0%	0%

Endogenous compounds in +/-25% cutoff urine-RX imola

Compound	Conc. Of compound (mg/dl)	-25% of 300 ng/ml BZG cutoff		+25% of 300 ng/ml BZG cutoff	
		Qualitative	Semi-quant.	Qualitative	Semi-quant.
Total Bilirubin	15	NEG	NEG	POS	POS
Direct Bilirubin	5	NEG	NEG	POS	POS
Haemoglobin	115	NEG	NEG	POS	POS
Creatinine	30	NEG	NEG	POS	POS
Urea	258	NEG	NEG	POS	POS
Glucose	2000	NEG	NEG	POS	POS
H.S.A.	500	NEG	NEG	POS	POS
Ethanol	1000	NEG	NEG	POS	POS
Acetone	1000	NEG	NEG	POS	POS
Gamma globulin	500	NEG	NEG	POS	POS
Oxalic acid	100	NEG	NEG	POS	POS
Riboflavin	7.5	NEG	NEG	POS	POS
Sodium chloride	6000	NEG	NEG	POS	POS
Boric acid	125	NEG	NEG	POS	POS
Sodium azide	1000	NEG	NEG	POS	POS
Sodium fluoride	1000	NEG	NEG	POS	POS
Specific gravity range	1.00 - 1.03	NEG	NEG	POS	POS
pH range	3 - 9	NEG	NEG	POS	POS

f. Assay cut-off:

300 ng/mL

2. Comparison studies:

a. *Method comparison with predicate device:*

137 urine samples were obtained from a clinical laboratory where they had

been tested by GC/MS for the presence or absence of Cocaine Metabolites. Among the 137 samples, 70 were positive and 67 were negative for Cocaine Metabolites based on GC/MS test results. These samples were tested with Randox Cocaine Metabolite assay on the Rx Daytona and Rx Imola instruments. Concordance of the results (Randox vs GC/MS) were provided in the below tables.

RX daytona Semi-Quantitative

Device Results	Negative by GC/MS	Near Cutoff Negative (between 50% below the cutoff and the cutoff conc.)	Near Cutoff Positive (between the cutoff and 50% above the cutoff conc.)	High Positive (greater than 50% above the cutoff conc.)	% Agreement with GC/MS
Pos	0	0	17	53	100.0%
Neg	50	15	1*	1**	97.2%

RX daytona Qualitative

Device Results	Negative by GC/MS	Near Cutoff Negative (between 50% below the cutoff and the cutoff conc.)	Near Cutoff Positive (between the cutoff and 50% above the cutoff conc.)	High Positive (greater than 50% above the cutoff conc.)	% Agreement with GC/MS
Pos	0	0	17	53	100.0%
Neg	50	15	1*	1**	97.2%

RX imola Semi-Quantitative

Device Results	Negative by GC/MS	Near Cutoff Negative (between 50% below the cutoff and the cutoff conc.)	Near Cutoff Positive (between the cutoff and 50% above the cutoff conc.)	High Positive (greater than 50% above the cutoff conc.)	% Agreement with GC/MS
Pos	0	0	18	53	100.0%
Neg	50	15	0	1**	98.6%

RX imola Qualitative

Device Results	Negative by GC/MS	Near Cutoff Negative (between 50% below the cutoff and the cutoff conc.)	Near Cutoff Positive (between the cutoff and 50% above the cutoff conc.)	High Positive (greater than 50% above the cutoff conc.)	% Agreement with GC/MS
Pos	0	0	18	53	100.0%
Neg	50	15	0	1**	98.6%

* Discrepant results.

** A root cause analysis has revealed that the labeled GC/MS value on the original sample is incorrect, due to mislabeling of the sample. Repeated

GC/MS result for the original sample show that the sample is negative for the drug.

GC/MS SUMMARY OF DISCREPANT RESULT

RX daytona Semi-Quantitative

Cut-off Value (ng/mL)	Randox BZG assay (POS/ NEG)	Drug/Metabolite GC/MS value (ng/mL)
300	NEG	310 (BZG)

RX daytona Qualitative

Cut-off Value (ng/mL)	Randox BZG assay (POS/ NEG)	Drug/Metabolite GC/MS value (ng/mL)
300	NEG	310 (BZG)

b. Matrix comparison:

Not applicable. The assay is intended for urine samples only.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable. Clinical studies are not typically submitted for this device type.

b. Clinical specificity:

Not applicable. Clinical studies are not typically submitted for this device type.

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:

Not applicable

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.