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

A. 510(k) Number:

k092275

B. Purpose for Submission:

New Device

C. Measurand:

Methylenedioxymethamphetamine (MDMA)

D. Type of Test:

Competitive enzyme immunoassay; qualitative and semi-quantitative

E. Applicant:

Randox Laboratories, Ltd.

F. Proprietary and Established Names:

Randox Ecstasy Assay
Randox Ecstasy Calibrator Set
Randox Ecstasy Controls, Level 1 & 2

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
DKZ	Class II	21 CFR 862.3650-Amphetamine Test System	Toxicology (91)
DLJ	Class II	21 CFR 862.3200 Clinical Toxicology Calibrators	Toxicology (91)
LAS	Class I, reserved	21 CFR 862.3280 Clinical Toxicology control material	Toxicology (91)

H. Intended Use:

1. Intended use(s):
   See Indications for use, below.

2. Indication(s) for use:

   The Randox Laboratories Ltd. Ecstasy Assay is an in vitro diagnostic test for the detection of MDMA in human urine with a cut off concentration of 500 ng/mL, for use on the Rx Daytona and Rx Imola analyzers in qualitative and semi-quantitative mode. The assay is calibrated against MDMA. This in vitro diagnostic device is intended for prescription use only.

   The semi-quantitative mode is for purposes 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 analytical result. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. Gas chromatograph/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.

   The Randox Ecstasy Calibrator Set
   The Randox Ecstasy Calibrator Set consists of liquid calibrators containing MDMA. There are 5 levels of calibrator. They have been developed for use in the calibration of Ecstasy assays on the Rx Daytona and the Rx Imola analyzers. This in vitro diagnostic device is intended for prescription use only.

   The Randox Ecstasy Controls, Level 1 & 2
   The Randox Ecstasy Controls, level 1 and 2 are liquid controls containing MDMA. There are 2 levels of controls. They have been developed for use in the quality control of the Ecstasy assay on the Rx Daytona and the Rx Imola analyzers. This in vitro diagnostic device is intended for prescription use only.

3. Special conditions for use statement(s):

   The assay is for prescription use.

4. Special instrument requirements:

The Rx Daytona and the Rx Imola analyzers

I. Device Description:

The assay consists of two ready-to-use liquid reagents, R1 (2 x 16.9 mL) and R2 (2 x 8 mL). R1, the Antibody/Substrate Reagent, contains mouse monoclonal anti-MDMA antibodies, glucose-6-phosphate (G6P), nicotinamide adenine dinucleotide (NAD), stabilizers, and sodium azide (<0.1%). R2, the Enzyme-Drug Conjugate Reagent, contains MDMA-labeled glucose-6-phosphate dehydrogenase (G6PDH) in buffer, with sodium azide (<0.1%).

The calibrator set includes 5 ready to use levels (0, 100, 500, 750, 1000 ng/mL MDMA) derived from human urine.

The control set contains 2 ready to use levels (375 ng/mL and 695 ng/mL MDMA) derived from human urine.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Microgenics DRI Ecstasy Assay (k012110)
   Microgenics DRI Ecstasy Urine Calibrators (k012109)
   Microgenics MGC DAU Control Set (k040758)

2. Predicate 510(k) number(s):
   k012110
   k012109
   k040758

3. Comparison with predicate:

Similarities and Differences		
Item	Candidate device (Ecstasy assay)	Predicate device (k012110)
Intended Use	For the qualitative and semi-quantitative detection of MDMA in human urine	Same
Sample Types	Human urine	Same
Test Principle	Competitive enzyme immunoassay	Same
Cutoff	500 ng/mL	500 and 1000 ng/mL
Item	Candidate device (Randox Ecstasy Calibrator Set)	Predicate device (k012109)

Similarities and Differences		
Intended Use	For use in the calibration of Ecstasy Assays	Same
Calibrator Matrix	Human Urine	Same
Type of Reagent	Liquid Ready to Use 0, 100, 500, 750, 1000 ng/mL	Liquid Ready to Use 250, 500, 750, 1000 ng/mL
Item	Candidate device (Randox Ecstasy Controls)	Predicate device (k040758)
Intended Use	For use in the quality control of MDMA assays	Same
Control Matirx	Human Urine	Same
Type of Reagent	Liquid Ready to Use 375 and 625 ng/mL	Liquid Ready to Use 375 and 625 ng/mL

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

- CLSI Protocol EP7-A2: Interference Testing in Clinical Chemistry

L. Test Principle:

The Ecstasy assay is a competitive enzyme immunoassay 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. In the absence of drug in the samples the MDMA labeled G6PDH conjugate is bound to antibody and enzyme activity is inhibited. When free drug is present in the sample, antibody binds to the free drug and the unbound MDMA labeled G6PDH exhibits its maximum enzyme activity. Active enzyme converts NAD to NADH resulting in an absorbance change measured spectrophotometrically at 340 nm.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

Performance was evaluated on the Rx Daytona and Rx Imola.

a. Precision/Reproducibility:

Samples prepared by spiking drug-free urine samples with MDMA were evaluated at the concentrations of ±25%, ±50%, ±75%, and ±100% relative to the 500 ng/mL cut-off. Concentrations were confirmed by GC/MS. Samples were measured on 2 Rx Daytona and 2 Rx Imola systems, in replicated, twice per day, for 20 days (N=80). The qualitative and semi-quantitative results are

presented below.

Rx Daytona: Total Precision for semi-quantitative and qualitative modes:

Sample concentration % of cut-off	Number of Observations	Results in semi-quantitative mode	Results in Qualitative Mode
-100%	80	80 Negative	80 Negative
-75%	80	80 Negative	80 Negative
-50%	80	80 Negative	80 Negative
-25%	80	80 Negative	80 Negative
+25%	80	80 Positive	80 Positive
+50%	80	80 Positive	80 Positive
+75%	80	80 Positive	80 Positive
+100%	80	80 Positive	80 Positive

Rx Imola: Total Precision for semi-quantitative and qualitative modes:

Sample concentration % of cut-off	Number of Observations	Results in semi-quantitative mode	Results in Qualitative Mode
-100%	80	80 Negative	80 Negative
-75%	80	80 Negative	80 Negative
-50%	80	80 Negative	80 Negative
-25%	80	80 Negative	80 Negative
+25%	80	80 Positive	80 Positive
+50%	80	80 Positive	80 Positive
+75%	80	80 Positive	80 Positive
+100%	80	80 Positive	80 Positive

b. Linearity/assay reportable range:

To demonstrate linearity in the semi-quantitative mode, which is used for purposes of sample dilution and quality control procedures, a drug-free urine pool spiked with pure MDMA to 1000 ng/mL was serially diluted in increments of 10% with drug-free urine. For each sample the average of 3 replicates in the semi-quantitative mode was obtained and compared to the expected value and the percent recovery was calculated. Results are presented in the tables below for the Rx Daytona and Rx Imola:

	Rx Daytona			**Rx Imola**	
Target Concentration (ng/mL)	Result (ng/mL)	% Recovery		Result (ng/mL)	% Recovery
0	0.00	Not		0.00	Not

		applicable			applicable
10	45.80	458.03		5.54	55.40
20	56.99	284.97		11.23	56.15
30	91.69	305.62		23.11	77.03
40	69.43	173.57		40.20	100.50
50	126.71	253.43		45.32	90.46
60	92.65	154.42		39.50	65.83
70	125.94	179.92		84.87	121.24
80	145.53	181.92		88.23	110.29
90	97.72	108.58		68.76	76.40
100	99.46	99.46		102.92	102.92
200	192.05	96.03		181.08	90.54
300	267.47	89.16		281.52	93.84
400	384.43	96.11		438.03	109.51
500	496.04	99.21		564.26	112.85
600	628.07	104.68		665.29	110.88
700	718.03	102.58		777.07	111.01
800	815.16	101.90		848.04	106.00
900	882.46	98.05		969.66	107.74
1000	935.89	93.59		1019.80	101.98

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

Traceability and Value Assignment: Randox Ecstasy Calibrator set and Randox Ecstasy Control Level 1 and Level 2 are specified in the assay labeling as required but are not provided. The Randox Ecstasy Calibrator Set includes 5 five levels of liquid ready to use calibrators that contain 0, 100, 500, 750, 1000 ng/mL of MDMA. The Randox Ecstasy control material is available in 2 levels of liquid ready to use controls that contain either 375 or 675 ng/mL of MDMA.

The Randox Ecstasy Calibrator Set and the Ecstasy Controls (Level 1 and Level 2) are derived from human urine and are traceable to master lots that are GC/MS quantified. The master lots are made by spiking MDMA into a human urine matrix. MDMA is supplied by Cerilliant Corporation, the accuracy of which is ensured by purity determination (GC/FID, HPLC and NMR) and gravimetric preparation using balances calibrated with NIST traceable standards. Each of the Randox calibrator and control level is value assigned using Rx Daytona and Rx Imola analyzers. The target value for each level is the median of the observed values.

Stability:
Shelf-life and open-vial stability studies were performed for the calibrators and controls using both accelerated and on-going real-time studies. The protocols were found to be adequate. The Randox Ecstasy controls and

calibrators are stable for 18 months when stored unopened at +2 to 8°C and for 28 days once opened and stored at +2 to 8°C.

d. Detection limit:

Performance at low drug concentrations in the semi-quantitative mode was characterized by determination of recovery (see section M.1.b above).

e. Analytical specificity:

The Randox Laboratory Ltd. Ecstasy Assay was evaluated for interference according to the CLSI Guideline EP7-A2 recommendations. These studies were performed by spiking structurally related and structurally unrelated compounds into drug-free and drug-containing urine samples. Drug-containing urine samples were tested at two different concentrations, +25% and -25% of the cut-off concentration of 500 ng/mL. Drug-free urine samples were used as controls. Percent cross-reactivity was calculated using the cross-reactant concentration that gives a reaction absorbance which matches the reaction absorbance obtained by the cut-off calibrator. The cut-off calibrator concentration divided by the cross-reactant concentration that achieved the matching reactant absorbance x 100% gives the % cross-reactivity. These studies were performed on both, the Rx Daytona and Rx Imola analyzers. Similar results were obtained with both analyzers and in both qualitative and semi-quantitative modes. The percent cross-reactivity of the tested compounds are presented below:

Structurally related compounds tested -- Rx Daytona:

	Semi-Quantitative			**Qualitative**	
Compound	**Tested Conc. (ng/mL)**	**Cross-reactivity (%)**		**Tested Conc. (ng/mL)**	**Cross-reactivity (%)**
d-Amphetamine	692,874	0.07		669,230	0.07
(+/-)-Amphetamine	108,316	0.46		112,959	0.44
BDB	829	60.33		888	56.32
d-Methamphetamines	692,874	0.07		657,360	0.08
d,l-Methamphetamines	53713	0.93		75422	0.66
HMMA	100,000	0.00		100,000	0.00
MBDB	1409	35.49		1389	36.00
MDMA	500	100.00		500	100.00
MDA	528	94.64		700	71.46
MDEA	438	114.22		467	107.12
PMA	2254	22.18		2221	22.51
PMMA	1083	46.18		1055	47.38

Structurally related compounds tested -- Rx Imola:

	Semi-Quantitative			Qualitative	
Compound	**Tested Conc. (ng/mL)**	**Cross-reactivity (%)**		**Tested Conc. (ng/mL)**	**Cross-reactivity (%)**
d-Amphetamine	761,775	0.07		782,790	0.06
(+/-)-Amphetamine	166,261	0.30		174,512	0.29
BDB	956	52.30		938	53.30
d-Methamphetamines	827,530	0.06		811,297	0.06
d,l-Methamphetamines	65180	0.77		67381	0.74
HMMA	100,000	0.00		100,000	0.00
MBDB	1466	34.11		1511	33.10
MDMA	500	100.00		500	100.00
MDA	738	67.77		733	68.25
MDEA	427	117.08		436	114.64
PMA	2426	20.61		2711	18.45
PMMA	1059	47.20		1059	45.66

The following structurally unrelated compounds were all tested at 100,000 ng/mL on the Rx Dayton and Rx Imola in the qualitative and semi-quantitative modes.

Structurally Unrelated compounds tested:

Substance Tested	**Cross-reactivity (%) Rx Daytona**		**Cross-reactivity (%) Rx Imola**	
	Qualitative	**Semi-Quant**	**Qualitative**	**Semi-Quant**
11-Hydroxy-Δ9-THC	0.00	0.00	0.00	0.00
11-Nor9-carboxy-Δ9-THC	0.00	0.03	0.00	0.00
6 Acety-morphine	0.00	0.03	0.00	0.00
Amitriptyline	0.00	0.00	0.00	0.00
Amobarbital	0.00	0.00	0.00	0.00
Ascorbic acid	0.00	0.00	0.00	0.00
Aspirin	0.00	0.00	0.00	0.02
Benzoylecgonine	0.00	0.00	0.00	0.03
β-phenylethylamine	0.08	0.18	0.08	0.16
Caffine	0.00	0.01	0.00	0.01
Cannabidiol	0.00	0.00	0.00	0.00
Chlorpheniramine	0.00	0.00	0.00	0.04
Cocaethylene	0.00	0.04	0.00	0.03
Cocaine	0.00	0.01	0.00	0.00
Cotinine	0.00	0.00	0.00	0.00
Δ9-THC	0.00	0.02	0.00	0.00

Diazepam	0.00	0.00	0.00	0.00
dihydrocodeine	0.00	0.00	0.00	0.00
Ecgonine Methyl Ester	0.00	0.04	0.00	0.00
EDDP	0.00	0.00	0.00	0.00
EMDP	0.00	0.00	0.00	0.00
d,l-ephedrine	0.00	0.04	0.00	0.00
d-ephedrine	0.00	0.02	0.00	0.00
l-ephedrine	0.01	0.08	0.01	0.00
R,R (-) Pseudoephedirne	0.06	0.16	0.06	0.12
S,S (+) Pseudoephedrine	0.00	0.05	0.00	0.00
Heroin	0.00	0.00	0.00	0.00
LAAM	0.00	0.00	0.00	0.00
Methadone	0.00	0.00	0.00	0.00
Morphine	0.00	0.00	0.00	0.03
Oxycodone	0.00	0.00	0.00	0.03
Paracetamol	0.00	0.00	0.00	0.05
Temazepam	0.00	0.07	0.00	0.00
Ibuprofen	0.00	0.04	0.00	0.00

Endogenous compounds tested:
The following endogenous compounds were added into drug-free urine and urine containing MDMA at the concentrations corresponding to +/- 25% of the assay cutoff. These samples were tested using both, the Rx Daytona and Rx Imola analyzers. The substances listed in the table below were determined not to interfere at the concentration shown:

Compound	**Tested Concentration (mg/dL)**
Total bilirubin	15
Direct bilirubin	5
Hemoglobin	115
Creatinine	30
Urea	258
Glucose	2000
HSA	500
Ethanol	1000
Acetone	1000
Gamma globulin	500
Oxalic acid	100
Riboflavin	7.5
Sodium chloride	6000
Boric acid	1000
Sodium azide	1000
Sodium fluoride	1000

The package insert includes the complete list of all structurally related and unrelated compounds and metabolites tested.

In addition, the performance of the assay was evaluated under varying pH levels of: 3, 5, 7, 9 and 11, which also had no effect on results. Further, variations in specific gravity between 1.00 and 1.03 had no effect on results on either the Rx Daytona or Rx Imola.

f. Assay cut-off:

Analytical performance of the device around the claimed cutoff is described in precision section (M.1.a.) above.

2. Comparison studies:

a. Method comparison with predicate device:
Eighty unaltered clinical urine samples were evaluated by the Randox MDMA assay and compared to results obtained by GC/MS. Eight of the samples contained 300 to 496 ng/mL MDMA and 12 samples contained 508 to 745 mg/dL of MDMA according to GC/MS. Results are presented below for the 500 ng/mL cut-off in the semi-quantitative and qualitative modes:

Rx Daytona Semi-quantitative

GCMS for Ecstasy (based on cross reactivity profile) → **500 ng/mL cutoff Ecstasy Assay ↓**	**Negative**	**Low Negative by GC/MS (concentration < 50% below the cutoff concentration for Ecstasy)**	**Near Cutoff Negative (concentration between 50% below the cutoff and the cutoff concentration for Ecstasy)**	**Near Cutoff Positive (concentration between 50% above the cutoff and the cutoff concentration for Ecstasy)**	**High Positive (concentration > 50% above the cutoff concentration for Ecstasy)**	**Percent Agreement with GCMS for Ecstasy (based on cross reactivity profile)**
Positive	0	0	4	12	28	100
Negative	33	0	4	0	0	90.24

Rx Daytona Qualitative

GCMS for Ecstasy (based on cross reactivity profile) →	**Negative**	**Low Negative by GC/MS (concentration < 50% below the cutoff**	**Near Cutoff Negative (concentration between 50% below the cutoff and**	**Near Cutoff Positive (concentration between 50% above the cutoff and the**	**High Positive (concentration > 50% above the cutoff concentration**	**Percent Agreement with GCMS for Ecstasy (based on**

500 ng/mL cutoff Ecstasy Assay ↓		concentration for Ecstasy)	the cutoff concentration for Ecstasy)	cutoff concentration for Ecstasy)	for Ecstasy)	cross reactivity profile)
Positive	0	0	4	12	28	100
Negative	33	0	4	0	0	90.24

Rx Imola Semi-quantitative

GCMS for Ecstasy (based on cross reactivity profile) → / 500 ng/mL cutoff MDMA Assay ↓	Negative	Low Negative by GC/MS (concentration < 50% below the cutoff concentration for MDMA)	Near Cutoff Negative (concentration between 50% below the cutoff and the cutoff concentration for MDMA)	Near Cutoff Positive (concentration between 50% above the cutoff and the cutoff concentration for MDMA)	High Positive (concentration > 50% above the cutoff concentration for MDMA)	Percent Agreement with GCMS for MDMA (based on cross reactivity profile)
Positive	0	0	4	11	28	97.50
Negative	33	0	4	1	0	90.24

Rx Imola Qualitative

GCMS for Ecstasy (based on cross reactivity profile) → / 500 ng/mL cutoff MDMA Assay ↓	Negative	Low Negative by GC/MS (concentration < 50% below the cutoff concentration for MDMA)	Near Cutoff Negative (concentration between 50% below the cutoff and the cutoff concentration for MDMA)	Near Cutoff Positive (concentration between 50% above the cutoff and the cutoff concentration for MDMA)	High Positive (concentration > 50% above the cutoff concentration for MDMA)	Percent Agreement with GCMS for MDMA (based on cross reactivity profile)
Positive	0	0	4	11	28	97.50
Negative	33	0	4	1	0	90.24

GC/MS Summary of Discrepant Results:

Rx Daytona – Semi-quantitative

Cut-off value (ng/mL) for MDMA	Randox MDMA Assay (POS/NEG)	Drug/Metabolite GC/MS value (ng/mL) based on cross reactivity profile
500	POS	476
	POS	482
	POS	490

	POS	495

Rx Daytona – Qualitative

Cut-off value (ng/mL) for MDMA	Randox MDMA Assay (POS/NEG)	Drug/Metabolite GC/MS value (ng/mL) based on cross reactivity profile
500	POS	476
	POS	482
	POS	490
	POS	495

Rx Imola – Semi-quantitative

Cut-off value (ng/mL) for MDMA	Randox MDMA Assay (POS/NEG)	Drug/Metabolite GC/MS value (ng/mL) based on cross reactivity profile
500	POS	476
	POS	482
	POS	490
	POS	495
	NEG	508

Rx Imola – Qualitative

Cut-off value (ng/mL) for MDMA	Randox MDMA Assay (POS/NEG)	Drug/Metabolite GC/MS value (ng/mL) based on cross reactivity profile
500	POS	476
	POS	482
	POS	490
	POS	495
	NEG	508

The tables above show that in this study qualitatively discrepant results were observed only for near-cutoff samples (+/- 50% of the cutoff concentration.)

b. Matrix comparison:

Not Applicable, urine is the only indicated matrix.

3. Clinical studies:

a. Clinical Sensitivity: Not reviewed for this device type.

*b. Clinical specificity**:*** Not reviewed for this device type.

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off**:**

   Not applicable; the device is for determining a presumptive positive or negative based on the analytical cutoffs of 500 ng/mL for both qualitative and semi-quantitative analysis.

5. Expected values/Reference range:

   Not applicable. The test is not intended for quantifying MDMA, it is intended to be used to (1) enable laboratories to determine an appropriate dilution of the specimen for confirmation by a confirmatory method such as GCMS and (2) to permit laboratories to establish quality control procedures.

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.