

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

**A. 510(k) Number:**

k092269

**B. Purpose for Submission:**

New assay

**C. Measurand:**

Tetrahydrocannabinol

**D. Type of Test:**

Homogeneous enzyme immunoassay – qualitative and semi- quantitative

**E. Applicant:**

Randox Laboratories Ltd.

**F. Proprietary and Established Names:**

Cannabinoid Assay

**G. Regulatory Information:**

1. Regulation section:

21 CFR 862.3870, Cannabinoid Test System, 21CFR 862.1150, Calibrator, 21 CFR 862.1660, Quality Control Material

2. Classification:

Class II, II and I, respectively

3. Product code:

LDJ, JIT, JJX

4. Panel:

Toxicology (91)

## H. Intended Use:

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

The Randox Laboratories Ltd. Cannabinoid Assay is an in vitro diagnostic test for the detection of 11-nor- $\Delta^9$ -THC-9-COOH (THC) in human urine with a cut off concentration of 50ng/ml, for use on the Rx Imola and Rx Daytona analyzers in qualitative or semi-quantitative mode. 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 Cannabinoid Calibrator Set consists of liquid calibrators containing 11-nor- $\Delta^9$ -THC-9-COOH (THC). There are 5 levels of calibrator. They have been developed for use in the calibration of THC assays on the Rx Imola and Rx Daytona analyzers. This in vitro diagnostic device is intended for prescription use only.

The Randox Cannabinoid Controls, level 1 and 2 are liquid controls containing 11-nor- $\Delta^9$ -THC-9-COOH (THC). There are 2 levels of controls. They have been developed for use in the quality control of the THC assay on the Rx Imola and Rx Daytona analyzers. 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:

The assay has been developed for use on the Rx Daytona™, and Rx Imola™.

**I. Device Description:**

The assay consists of two reagent bottles supplied ready for use. R-1 contains monoclonal 11-nor- $\Delta^9$ -THC-9-COOH antibodies, glucose-6-phosphate (G6P), nicotinamide adenine dinucleotide NAD, stabilizers, and sodium azide <0.1% w/v. R-2 is an enzyme-drug conjugate reagent containing buffer,  $\Delta^9$ -THC-9-COOH-labelled G6PDH, and sodium azide, <0.1% w/v.

Calibrators and control materials are liquid ready to use containing 11-nor- $\Delta^9$ -THC-9-COOH at levels of (0, 20, 50, 100, 200 ng/mL) for the calibrator and 37.5 and 62.5 ng/ml for the control material.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):  
Microgenics DRI Cannabinoid Assay, Calibrators and Controls.
2. Predicate 510(k) number(s):  
k943998
3. Comparison with predicate:  
See the table below. The intended use and test principle are the same for both assays.

ITEM	Randox Cannabinoid Assay k092269	Microgenics DRI Cannabinoid Assay k943998
Intended Use	Qualitative and semi-quantitative analysis Cannabinoids in human urine	Same
Cutoff	50 ng/mL	20, 50 or 100 ng/mL
Test Principle	A homogeneous enzyme immunoassay based on competition between drug in the sample and drug labelled with the enzyme glucose-6-phosphate dehydrogenase (G6PDH).	Same
Sample type	Human urine	Same
Type of reagent	Liquid Ready to use Two reagent assay	Same
Calibrators – intended use	For THC assay calibration	Same

Calibrators – format	Liquid ready to use (0, 20, 50, 100, 200 ng/mL)	Liquid ready to use (20, 50, 100, 200 ng/mL)
Controls – intended use	For THC assay quality control	Same
Controls –format	Liquid ready to use 37.5, 62.5 ng/ml	Liquid ready to use 40, 60, 75, 125 ng/mL

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

None were referenced.

**L. Test Principle:**

The assay is a homogeneous enzyme immunoassay with ready-to-use liquid reagent. 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. In the absence of drug in the sample, the antibody binds the conjugated G6PDH-THC  $\Delta^9$  thus the enzyme activity is inhibited. When free drug is present on the sample, the antibody will bind to the free drug and the unbound G6PDH-conjugated drug exhibits its maximal enzyme activity. The G6PDH activity is measured spectrophotometrically at 340 nm due to conversion of NAD to NADH by the active enzyme.

**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:

Performance was evaluated on the Rx Daytona™, and Rx Imola™.

a. *Precision/Reproducibility:*

Negative urine samples spiked with 11-nor-9-carboxy- $\Delta^9$ -THC were evaluated. Samples contained the following concentrations relative to the 200ng/mL cut-off: +/- 25%, +/-50%, +/-75% and +/-100%. Samples were tested in random order on two Rx Daytona systems and two Rx Imola systems twice per day for 20 non-consecutive days. Calibrations were carried out twice throughout the duration. Results are shown below.

Rx Daytona Semi-Quantitative

THC concentration (% cutoff)	No. of determinations	Results #Neg/#Pos
-100	80	80 Neg
-75	80	80 Neg
-50	80	80 Neg
-25	80	80 Neg

+25	80	80 Pos
+50	80	80 Pos
+75	80	80 Pos
+100	80	80 Pos

Identical results were obtained for semi-quantitative and qualitative results on both the Imola and the Daytona Instruments.

*b. Linearity/assay reportable range:*

A drug free urine pool was spiked with pure secobarbital. A 100ng/mL sample was further diluted in increments of 10% to a concentration of 10ng/mL. Samples were tested in semi-quantitative mode in a random order in triplicate. Results are shown below.

Expected Concentration (ng/mL)	Imola Result (ng/mL)	Percent recovery Rx Imola	Daytona result (ng/mL)	Percent recovery Rx Daytona
0	15.3	N/A	6.5	N/A
2	12.8	641	5.2	259
4	15.0	374	8.2	205
6	10.1	168	13.3	221
8	19.4	242	10.4	129
10	16.3	163	11.3	113
12	14.8	124	17.2	143
14	12.9	92	15.9	114
16	16.7	104	23.1	144
18	20.0	111	26.3	146
20	22.5	113	18.8	94
40	39.2	98	42.5	106
60	58.4	97	63.0	105
80	73.9	92	83.9	105
100	94.8	95	100.6	101
140	148.5	106	151.2	108
200	193.7	97	210.6	105

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

**Traceability:**

THC calibrators and THC controls are both traceable to GC/MS quantified master lots. The master lots are prepared by spiking 11-nor- $\Delta^9$ -THC-9-COOH at the appropriate levels into a buffered human urine matrix that also contains 0.05% sodium azide by gravimetric preparation using balances calibrated with NIST traceable weights. Purity of material used for spiking is determined using GC/FID, HPLC and NMR. Value assignment for control materials and

calibrator materials is determined against the current master lot by performing nested testing of the new control materials and the new calibrator materials. The new lots are analyzed in replicates of 10. Results need to meet the sponsor's pre-determined acceptance criteria %CV and % recovery against the current master lot.

The estimated un-certainty in the calibrator value assignments is shown below.

Calibrator Level	Target Value (ng/mL)	Total Uncertainty (ng/mL)
1	20	+/- 8.51
2	50	+/- 5.65
3	100	+/- 5.99
4	200	+/- 7.93

#### Stability

To determine a shelf-life claim for the THC calibrators and THC controls, materials stored at +2-8°C are tested at multiple time points up to 18 months. The assay is calibrated at each time point with known stable calibrators, and controls are tested. The recoveries achieved at each time-point are compared to those achieved at Day 0 and must fall within the sponsor's predetermined acceptance criteria. Open vials of control materials and calibrator materials are stable for 28 days at 2-8° C.

Real time stability studies up to nine months were included in the 510(k). No decrease in stability was observed over nine months.

*d. Detection limit:*

Performance at low drug concentration in the semi-quantitative assay was characterized by determination of the lowest concentration of drug that is capable of producing a positive result. This concentration was sufficiently below the claimed cutoff.

*e. Analytical specificity:*

Interference and cross-reactivity studies were carried out in the qualitative and semi-quantitative modes to evaluate potential cross-reactive compounds, potential interfering compounds including structurally related compounds and potentially interfering endogenous compounds. Test compounds were spiked into GC/MS verified negative urine and into GC/MS verified urine spiked at cannabinoid concentrations +/-25% of the assay cut-off. Replicates of each

sample were measured, and evaluated against the cut-off calibrator (50ng/mL).

Results of cross-reactivity studies are shown in the table below:

Compound	Range of percents cross-reactivity observed.
11-nor $\Delta$ 9-THC-9-COOH	100%
11-OH- $\Delta$ 9-THC	18-36%
Cannabidiol	<1%
$\Delta$ 9-THC	10-24%

#### Endogenous compounds

No interference was observed (in either semi-quantitative or qualitative mode on either instrument) from the substances below at the concentrations shown.

Compound	Tested Conc. (mg/dL)
Total Bilirubin	15
Direct Bilirubin	5
Hemoglobin	115
Creatinine	30
Urea	258
Glucose	2000
H.S.A.	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

Studies examining the effects on performance of variations in pH and specific gravity were also carried out. Specific gravity was tested across the range of 1.000 – 1.030 and pH across the range of 3 – 11 and no interference was observed.

Commonly co-administered prescription and OTC compounds:

The potential effect of other compounds on the recovery of cannabinoid using the Randox Cannabinoid assay was assessed. The complete list of compounds tested is shown in the package insert. No interference was observed.

*f. Assay cut-off:*

See Detection Limit Section, above. The claimed assay cutoff is 50 ng/mL.

2. Comparison studies:

*a. Method comparison with predicate device:*

Urine samples obtained from a clinical laboratory where they had been tested by GC/MS for the presence or absence of THC were assayed on the Daytona and Imola instruments in qualitative and semi-quantitative mode. Results are shown in the tables below:

		<b>Less than half the cut-off conc. by GC/MS</b>	<b>Between 50% below the cutoff and the cutoff conc.</b>	<b>Between the cutoff and 50% above the cutoff conc.</b>	<b>Greater than 50% above the cutoff conc.</b>	<b>% Agreement with GC/MS</b>
<b>Daytona Semi-quantitative</b>	<b>Neg by GCMS</b>					
<b>Positive</b>	0	2	17	35	69	83.3%
<b>Negative</b>	75	3	17	2	0	98.1%

The list of discrepant results is shown in the table below.

<b>Daytona Semi-Quantitative</b>	<b>Drug GC/MS value (ng/mL)</b>
POS	18
POS	21
POS	25
POS	31
POS	32
POS	34
POS	35
POS	38
POS	38

POS	41
POS	41
POS	41
POS	42
POS	43
POS	44
POS	44
POS	47
POS	48
POS	48
NEG	50
NEG	52

			<b>Between 50% below the cutoff and the cutoff conc.</b>	<b>Between the cutoff and 50% above the cutoff conc.</b>	<b>Greater than 50% above the cutoff conc.</b>	<b>% Agree- ment with GC/MS</b>
<b>Daytona qualitative</b>	<b>Neg</b>	<b>Less than half the cut- off conc. by GC/MS</b>				
<b>Positive</b>	0	2	17	33	69	83.3%
<b>Negative</b>	75	3	17	4	0	96.2%

The list of discrepant results is shown in the table below.

<b>Daytona Qualitative</b>	<b>Drug/ Metabolite GC/MS value (ng/mL)</b>
POS	18
POS	21
POS	25
POS	31
POS	32
POS	34
POS	35
POS	38
POS	38
POS	41
POS	41
POS	42
POS	43

POS	44
POS	44
POS	47
POS	48
POS	48
NEG	50
NEG	52
NEG	52
NEG	53

<b>Imola Semi-quantitative</b>	<b>Neg</b>	<b>Less than half the cutoff conc. by GC/MS</b>	<b>Between 50% below the cutoff and the cutoff conc.</b>	<b>Between the cutoff and 50% above the cutoff conc.</b>	<b>Greater than 50% above the cutoff conc.</b>	<b>% Agreement with GC/MS</b>
<b>Positive</b>	0	2	16	33	69	86.0%
<b>Negative</b>	75	3	18	4	0	96.2%

The list of discrepant results is shown in the table below.

<b>IMOLA Semi-Quantitative</b>	<b>Drug GC/MS value (ng/mL)</b>
POS	18
POS	21
POS	25
POS	31
POS	32
POS	34
POS	35
POS	38
POS	38
POS	41
POS	41
POS	42
POS	43
POS	44
POS	44
POS	47

POS	48
POS	48
NEG	50
NEG	52
NEG	52
NEG	64

<b>Imola qualitative</b>	<b>Neg</b>	<b>Less than half the cutoff conc. by GC/MS</b>	<b>Between 50% below the cutoff and the cutoff conc.</b>	<b>Between the cutoff and 50% above the cutoff conc.</b>	<b>Greater than 50% above the cutoff conc.</b>	<b>% Agreement with GC/MS</b>
<b>Positive</b>	0	2	16	33	69	86.0%
<b>Negative</b>	75	3	18	4	0	96.2%

The list of discrepant results is shown in the table below.

<b>Imola qualitative</b>	<b>Drug/ Metabolite GC/MS value (ng/mL)</b>
POS	18
POS	21
POS	25
POS	31
POS	32
POS	34
POS	35
POS	38
POS	38
POS	41
POS	41
POS	42
POS	43
POS	44
POS	44
POS	47
POS	48
POS	48
NEG	50

NEG	52
NEG	52
NEG	64

Additional information was submitted by the sponsor to support that positive readings for samples with GCMS values below 25 ng/mL were due to metabolites.

- b. Matrix comparison:* Not applicable. The test is only for urine specimens.
3. Clinical studies:
- a. Clinical Sensitivity:* Not typically reviewed for this device type.
  - b. Clinical specificity:* Not typically reviewed for this device type.
  - c. Other clinical supportive data (when a. and b. are not applicable):*
4. Clinical cut-off: Not typically reviewed for this type of test. The analytical cutoff is 50 ng/mL
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.