

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

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

k092268

**B. Purpose for Submission:**

New assay

**C. Measurand:**

Barbiturates

**D. Type of Test:**

Homogeneous enzyme immunoassay – qualitative and semi- quantitative

**E. Applicant:**

Randox Laboratories Ltd.

**F. Proprietary and Established Names:**

Randox Barbiturates assay

Randox Multidrug Calibrator Set

Randox Multidrug Controls, Levels 1 and 2

**G. Regulatory Information:**

1. Regulation section:

<b>Product Code</b>	<b>Classification</b>	<b>Regulation Section</b>	<b>Panel</b>
DIS	Class II	21 CFR § 862.3200, Barbiturate test system	91-Toxicology
DLJ	Class II	21 CFR § 862.3200, Calibrators, Drug specific	91-Toxicology
LAS	Class I, reserved	21 CFR 862.3280 Clinical Toxicology control material	91-Toxicology

## H. Intended Use:

1. Intended use(s):

See Indications for use below.

2. Indication(s) for use:

Randox Barbiturates Assay:

The Randox Laboratories Ltd. Barbiturates Assay is an in vitro diagnostic test for the detection of Barbiturates, in human urine on the Rx Imola and Rx Daytona.

The cutoff for secobarbital is 200 ng/mL. This in vitro diagnostic device is intended for prescription use only.

The semi-quantitative mode 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 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.**

Randox Multidrug Calibrator Set:

Randox Multidrug Calibrator Set consists of liquid calibrators containing Secobarbital, Oxazepam and Methadone. There are 5 levels of calibrator. They have been developed for use in the calibration of Barbiturates, Benzodiazepines and Methadone assays for use on the Rx analysers, which includes the Rx Daytona™ and the Rx Imola. This in vitro diagnostic device is intended for prescription use only.

Randox Multidrug Controls, Level 1 and 2:

Randox Multidrug Controls, Level 1 & 2 are liquid controls containing Secobarbital, Oxazepam and Methadone. There are 2 levels of controls. They have been developed for use in the quality control of Barbiturates, Benzodiazepines and Methadone assays for use on the Rx analysers, which includes the Rx-Daytona™ and the Rx-Imola. This in vitro diagnostic device is intended for prescription use only.

3. Special conditions for use statement(s):

The assay is for prescription use

The sponsor includes the following limitations in their labeling:

The test is not intended for quantifying barbiturates in patient samples and is not intended for therapeutic drug management.

A positive result does not indicate drug abuse.

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 mouse monoclonal anti- secobarbital antibodies, glucose-6-phosphate (G6P), nicotinamide adenine dinucleotide (NAD), stabilizers, and sodium azide <0.1% w/v. R2 contains enzyme-drug conjugate reagent, buffer, secobarbital-labelled G6PDH, and sodium azide <0.1% w/v. The calibrators and controls are ready to use human urine-based liquid (concentrations are listed in the comparison table, below).

**J. Substantial Equivalence Information:**

1. Predicate device name(s):

DRI Barbiturates Assay; DRI Multi-Drug Calibrators and controls

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

k955928 (assay); k983159 (calibrators and controls)

3. Comparison with predicate:

The intended use and test principle are the same for both assays. See the table below for further comparison.

ITEM	Randox Barbiturate Assay k092268	DRI Barbiturates Assay, k955928
Cutoff	200 ng/mL	Same
Intended Use	Qualitative and semi-quantitative analysis of Barbiturates in human urine	Same

Test Principle	A competitive enzyme immunoassay based on competition between drug in the sample and drug labelled with the enzyme glucose-6-phosphate dehydrogenase (G6PDH) for a fixed amount of antibody in the reagent.	Same
Sample type	Human urine	Same
Type of reagent	Liquid Ready to use Two reagent assay	Same

	<b>Randox Multidrug Calibrator Set</b>	<b>DRI Multi-Drug Calibrators K983159</b>
Indications	Randox Multidrug Calibrator Set consists of liquid calibrators containing Secobarbital, Oxazepam and Methadone. They have been developed for use in the calibration of Barbiturates, Benzodiazepines and Methadone assays for use on the Rx analysers, which includes the Rdaytona™ and the RxImola. This in vitro diagnostic device is intended for prescription use only.	The Multi-Drug Urine Calibrators and Controls are intended to be used for calibration and validation of DRI's drugs of abuse enzyme immunoassays to detect amphetamines, barbiturates, benzodiazepines, cocaine metabolites, methadone, methaqualone, opiates, phencyclidine and propoxyphene in human urine.
Form and concentrations	Liquid ready to use (0, 100, 200, 1000 ng/mL)	Liquid ready to use (100, 200, 500, 1000ng/mL)
	<b>Randox Multidrug Controls</b>	<b>DRI Multi-Drug controls K983159</b>
Indications	Randox Multidrug Controls have been developed for use in the quality control of Barbiturates, Benzodiazepines and Methadone assays This in vitro diagnostic device is intended for prescription use only.	Same
Form and concentrations	Liquid ready to use (150, 250ng/mL)	Liquid ready to use (150, 300ng/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-barbiturates 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):**

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

1. Analytical performance:

a. *Precision/Reproducibility:*

Secobarbital stock solution and a human urine pool were used to prepare samples. Concentrations were confirmed by GC/MS. These samples were tested for precision in qualitative and semi-quantitative modes. Each sample was assayed two times per run, 2 runs per day, for 20 days on both the Imola and Daytona instruments.

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

Secobarbital concentration (ng/mL) (cutoff=200 ng/mL)	No. of determinations	Results #Neg/#Pos
0	80	80 Neg
65	80	80 Neg
105	80	80 Neg
144	80	80 Neg
272	80	80 Pos
338	80	80 Pos
399	80	80 Pos
449	80	80 Pos

b. *Linearity/assay reportable range:*

Drug free urine pool was spiked with pure Secobarbital. A 1000 ng/mL sample was further diluted in increments of 10% to a concentration of

10ng/mL. These samples were tested in a random order in triplicate. Results are shown below.

Rx Imola and Daytona Semi-Quantitative Recovery

Expected Concentration	Imola Result (ng/mL)	Percent recovery Rx Imola	Daytona result (ng/mL)	Percent recovery Rx Daytona
0	2.2	N/A	0.0	N/A
10	10.7	107	16.8	168
20	28.2	141	24.6	123
30	47.9	160	40.3	134
40	46.8	117	28.7	72
50	69.2	138	43.7	87
60	79.4	132	48.3	80
70	88.9	127	71.5	102
80	87.1	109	72.5	91
90	100.6	112	104.2	116
100	104.2	104	107.9	108
200	187.2	94	189.6	95
300	291.7	97	334.5	111
400	390.7	98	410.4	103
500	437.2	87	453.0	91
700	691.6	99	635.9	91
1000	1110.5	111	991.2	99

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

Traceability and value assignment

The 4 levels of calibrator and 2 levels of control materials are traceable to master lots that have been GC/MS quantified. The master lots were made by spiking commercially available drug into a human urine matrix. The accuracy of the drug is ensured by spectrophotometric methods and gravimetric preparation using balances calibrated with NIST traceable standards. Each of the Randox calibrator/control level is value assigned using Rx Daytona and Rx Imola. The target value for each level is the median of the observed values.

Stability

Real time stability testing including shelf-life and on-board stability studies for the assay, controls and calibrators for both instruments. Controls and calibrators are stable for 12 months when stored unopened at 2 – 8° C and 28 days at 2 – 8° C.

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 for both instruments.

e. *Analytical specificity:*

Interference and cross-reactivity studies were evaluated in both qualitative and semi-quantitative modes to evaluate potential cross-reactive compounds, potential interfering compounds including structurally related compounds and potentially interfering endogenous compounds.

Cross-reactivity for barbiturates:

The drugs listed in the table below were tested for cross-reactivity with the assay. Drugs were spiked into urine and concentrations were verified by GC/MS. Each sample was evaluated against the cut-off calibrator (200 ng/mL secobarbital) to determine percent cross-reactivity. Results from both instruments are shown below. Some variations in cross-reactivity were observed depending on the assay mode and instrument. The ranges observed across modes and instruments are included in the table:

Compound	Percents cross-reactivity observed			
	Daytona qualitative	Daytona semi-quantitative	Imola qualitative	Imola semi-quantitative
Alphenal	66	73	66	63
Amobarbital	19	18	19	19
Butobarbital	24	33	29	29
Hexobarbital	2	3	1	3
Pentobarbital	32	32	43	43
Phenobarbital	52	73	52	83
Thiopental	<1	<1	1	1
Butalbital	52	51	52	53
Secobarbital	100	100	100	100

Endogenous compounds

Potential interference from endogenous compounds pH, and specific gravity was assessed by spiking known amounts of potentially interfering substances into urine containing secobarbital concentrations +/- 25% of the assay cut-off. 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

Commonly co-administered prescription and OTC compounds

The potential effect of other compounds on the recovery of barbiturates using the Randox Barbiturates assay was assessed by spiking known amounts of the compounds into urine containing secobarbital at concentrations +/- 25% of the assay cutoff. Compounds were identified by the manufacturer as non- cross-interfering with the assay if the recovery of the samples containing secobarbital at +/-25% of the cutoff recovered within 10% of a sample containing no cross-reactant. No compounds were shown to interfere.

The complete list of co-administered prescription and OTC compounds tested is shown in the package insert. No interference was observed with non-barbiturate compounds.

*f. Assay cut-off*

The assay is calibrated to a cutoff of 200 ng/mL with secobarbital. See also precision and detection limit sections, above.

2. Comparison studies:

*a. Method comparison with predicate device:*

Urine samples were obtained from a clinical laboratory where they had been tested by GC/MS for the presence or absence of various barbiturates including butabarbital, butalbital, phenobarbital, and secobarbital. Results are shown in the tables below. For purposes of comparison relative to the 200 ng/mL cutoff for secobarbital, the following adjustment was applied to samples containing other barbiturates, based on the cross-reactivity of each barbiturate:

$$\text{(GCMS-determined concentration) X (percent cross-reactivity)} \\ = \text{“adjusted concentration”}$$

The table below is based on these adjusted concentrations.

<b>Daytona Semi-quantitative</b>	<b>Neg</b>	<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>Positive</b>	0	10	17	24	76
<b>Negative</b>	85	8	7	2	0

The list of discrepant results is shown in the table below. Concentrations shown in tables are the actual measured GCMS concentration for each drug listed in parentheses.

<b>Daytona Semi-Quantitative</b>	<b>Drug/ Metabolite GC/MS value (ng/mL) based on cross-reactivity profile (ng/mL)</b>	<b>GCMS value of drug indicated (ng/mL)</b>
POS	65	200 (Butabarbital)
POS	69	210 (Butabarbital)
POS	72	220 (Butabarbital)
POS	75	230 (Butabarbital)
POS	76	150 (Butalbital)
POS	78	240 (Butabarbital)
POS	78	240 (Butabarbital)
POS	82	250 (Butabarbital)
POS	86	168 (Butalbital)
POS	93	182 (Butalbital)
POS	102	312 (Butabarbital)
POS	102	312 (Butabarbital)
POS	116	228 (Butalbital)
POS	130	177 (Phenobarbital)
POS	134	183 (Phenobarbital)
POS	143	439 (Butabarbital)
POS	147	449 (Butabarbital)
POS	150	150 (Secobarbital)
POS	150	150 (Secobarbital)
POS	150	150 (Secobarbital)
POS	150	460 (Butabarbital)
POS	160	160 (Secobarbital)
POS	164	502 (Butabarbital)
POS	179	245 (Phenobarbital)

POS	180	180 (Secobarbital)
POS	182	559 (Butabarbital)
POS	195	383 (Butalbital)
NEG	260	355 (Phenobarbital)
NEG	270	270 (Secobarbital)

Daytona Qualitative	Neg	Less than half the cut-off conc. by GC/MS	Between 50% below the cutoff and the cutoff conc.	Between the cutoff and 50% above the cutoff conc.	Greater than 50% above the cutoff conc.
Positive	0	12	13	23	72
Negative	85	10	9	5	0

Daytona Qualitative	Drug/ Metabolite GC/MS value (ng/mL) based on cross-reactivity profile	GCMS value of drug indicated (ng/mL)
POS	49	200 (Butabarbital)
POS	51	210 (Butabarbital)
POS	52	215 (Butabarbital)
POS	56	230 (Butabarbital)
POS	58	240 (Butabarbital)
POS	58	240 (Butabarbital)
POS	61	250 (Butabarbital)
POS	76	312 (Butabarbital)
POS	76	312 (Butabarbital)
POS	78	150 (Butalbital)
POS	88	168 (Butalbital)
POS	95	183 (Phenobarbital)
POS	107	439 (Butabarbital)
POS	109	449 (Butabarbital)
POS	112	460 (Butabarbital)
POS	119	228 (Butalbital)
POS	122	502 (Butabarbital)
POS	122	502 (Butabarbital)
POS	128	245 (Phenobarbital)
POS	136	559 (Butabarbital)
POS	150	150 (Secobarbital)
POS	160	160 (Secobarbital)

POS	169	695 (Butabarbital)
POS	180	180 (Secobarbital)
POS	192	369 (Phenobarbital)
Neg	200	383 (Butalbital)
Neg	220	220 (Secobarbital)
Neg	220	422 (Phenobarbital)
Neg	240	240 (Secobarbital)
Neg	270	270 (Secobarbital)

<b>Imola Semi-quantitative</b>	<b>Neg</b>	<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>Positive</b>	0	11	13	28	76
<b>Negative</b>	85	9	6	1	0

<b>Imola Semi-quantitative</b>	<b>Drug/ Metabolite GC/MS value (ng/mL) based on cross-reactivity profile</b>	<b>GCMS value of drug indicated (ng/mL)</b>
POS	59	200 (butabarbital)
POS	62	210 (butabarbital)
POS	68	230 (butabarbital)
POS	70	240 (butabarbital)
POS	70	240 (butabarbital)
POS	73	250 (butabarbital)
POS	80	150 (Butalbital)
POS	89	168 (Butalbital)
POS	92	312 (butabarbital)
POS	92	312 (butabarbital)
POS	97	182 (Butalbital)
POS	121	228 (Butalbital)
POS	129	439 (butabarbital)
POS	132	449 (butabarbital)
POS	135	460 (butabarbital)
POS	147	177 (Phenobarbital)
POS	147	502 (butabarbital)
POS	147	502 (butabarbital)
POS	150	150 (Secobarbital)

POS	150	150 (Secobarbital)
POS	152	183 (Phenobarbital)
POS	160	160 (Secobarbital)
POS	164	559 (butobarbital)
POS	190	190 (Secobarbital)
Neg	223	269 (Phenobarbital)

<b>Imola Qualitative</b>	<b>Neg</b>	<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>Positive</b>	0	15	13	23	73
<b>Negative</b>	85	8	8	4	0

<b>Imola Qualitative</b>	<b>Drug/ Metabolite GC/MS value (ng/mL) based on cross-reactivity profile</b>	<b>GCMS value of drug indicated (ng/mL)</b>
POS	58	200 (Butobarbital)
POS	61	210 (Butobarbital)
POS	63	220 (Butobarbital)
POS	66	230 (Butobarbital)
POS	69	240 (Butobarbital)
POS	69	240 (Butobarbital)
POS	72	250 (Butobarbital)
POS	77	150 (Butalbital)
POS	87	168 (Butalbital)
POS	90	312 (Butobarbital)
POS	90	312 (Butobarbital)
POS	91	177 (Phenobarbital)
POS	94	182 (Butalbital)
POS	94	183 (Phenobarbital)
POS	99	193 (Phenobarbital)
POS	118	228 (Butalbital)
POS	126	245 (Butalbital)
POS	126	439 (Butobarbital)
POS	129	449 (Butobarbital)
POS	132	460 (Butobarbital)

POS	145	502 (Butabarbital)
POS	145	502 (Butabarbital)
POS	150	150 (Secobarbital)
POS	160	160 (Secobarbital)
POS	161	559 (Butabarbital)
POS	180	180 (Secobarbital)
POS	190	369 (Butalbital)
POS	198	383 (Butalbital)
NEG	217	423 (Phenobarbital)
NEG	220	220 (Secobarbital)
NEG	240	240 (Secobarbital)
NEG	280	280 (Secobarbital)

Additional information was submitted by the sponsor to support that positive results for samples with GCMS values below 100 ng/mL were due to barbiturate 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 200 ng/mL for secobarbital.

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.