

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

A. 510(k) Number: k030360

B. Analyte: cocaine metabolite

C. Type of Test: automated qualitative immunoassay

D. Applicant: Randox Corporation

E. Proprietary and Established Names: Randox Cocaine Metabolite Assay (for use on the Randox Evidence[®] Analyzer)

F. Regulatory Information:

1. Regulation section:

21CFR862.3250, Cocaine and Cocaine Metabolites Test System.

21CFR862.2160, Discrete Photometric Chemistry Analyzer for Clinical Use,

21CFR862.1150, Calibrator

2. Classification: Class II

3. Product Code: DIO, JJE, DLJ

4. Panel: Toxicology (91), Chemistry (75)

G. Intended Use:

Cocaine Assay:

1. Indication(s) for use: The Randox Laboratories Limited Cocaine Metabolite Assay is an *in vitro* diagnostic test for the qualitative determination of the major metabolite of cocaine, benzylecgonine in human urine. This is a competitive immunoassay. A cutoff of 300 ng/mL benzylecgonine has been established in line with SAMHSA recommendations. The assay is for use only on the automated Evidence[®] Analyzer.

2. Special condition for use statement(s): The assay provides only a preliminary analytical test result. A more specific alternative chemical method must be used to obtain a confirmed analytical result. Gas chromatography/Mass spectrometry is the preferred confirmatory method. Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are used.

The Cocaine Metabolite Assay must only be used by suitably qualified laboratory personnel under appropriate laboratory conditions.
For prescription use.

3. Special instrument Requirements: The Randox Laboratories Limited Cocaine Metabolite Assay is designed for use on the Randox Evidence® Analyzer.

Calibrators

The Randox Laboratories Limited Drugs of Abuse Calibrators are liquid calibrators containing benzylecgonine. There are 9 levels of calibrator. They have been developed for use in calibration of the Evidence® System.

Evidence® Automated Immunoassay Analyzer

Evidence® is an automated immunoassay analyzer with dedicated software. It is for use with the Randox Cocaine Metabolite Assay.

H. Device Description: The Randox Cocaine Metabolite Assay includes biochips and reagents ready to use on the Randox Evidence® Analyzer System, including HRP-labeled cocaine and assay diluent. Also, provided separately are wash solution, displacement fluid, signal reagents and calibrators.

I. Substantial Equivalence Information:

1. Predicate device name(s): Microgenics CEDIA DAU Cocaine
2. Predicate K number(s): k945345
3. Comparison with predicate: Both devices detect cocaine metabolite in urine at a cutoff concentration of 300 ng/mL. The predicate device is indicated for semi-quantitative as well as qualitative use; this device is indicated for qualitative use only. Both devices use competitive immunoassay technology. Reactions of the predicate device occur in solution; reactions of this device occur on a biochip. The predicate device is for use on various automated chemistry analyzers; the new device is for use specifically with the Randox Evidence® Analyzer.

J. Standard/Guidance Document Referenced (if applicable): NCCLS EP5-T2; NCCLS EP7-A.

K. Test Principle

The Evidence® Analyzer measures cocaine on the surface of a biochip using competitive immunoassay technology. The biochip contains benzylecgonine-specific antibodies. Attachment of a benzylecgonine-enzyme (horseradish peroxidase) conjugate followed by addition of signal reagent (containing luminol) to the biochip results in generation of a chemiluminescent signal. In the absence of patient sample, the light output is proportional to the concentration of bound, labeled benzylecgonine-enzyme conjugate. When a patient sample containing benzylecgonine is added, the analyte competes with the enzyme-labeled benzylecgonine. This reduces the number of labeled analytes bound and as a result reduces the signal output. Analyte in the patient sample is inversely proportional to the light signal output.

The Evidence[®] System Analyzer uses a CCD camera for image capture. It performs image processing and stores data. The analyzer generates a calibration curve which is stored and used to determine results.

L. Performance Characteristics (if/when applicable):

Performance was evaluated on the Randox Evidence[®] Analyzer.

1. Analytical performance:

a. Precision/Reproducibility:

Precision was evaluated using calibrator material at four near-cutoff levels listed in the table below. Samples were evaluated for 20 days, 2 runs per day in replicates of 2 per run and calculated as total precision, per NCCLS EP5. The evaluation was conducted at two sites, with a single batch of reagents per site. A new calibration was performed for each run. Normalized values referred to in the table are defined as the RLU at the cutoff/ RLU of an individual sample.

concentrations (ng/ml)	168	222	281	383
Site #1 average reading (normalized values)	63.9	78.5	99.4	118.3
Site #1 SD (normalized values)	7.5	9.7	10.4	16.0
Site #1 %cv	11.8	12.4	10.5	13.6
Site #2 average reading (normalized value)	69.7	81.3	100.1	120.0
Site #2 SD (normalized value)	7.7	8.7	13.0	15.8
Site 2 %cv	11.1	10.7	13.0	13.2

b. Linearity/assay reportable range:

Not applicable. This test is for qualitative determinations.

c. Traceability (controls, calibrators, or method):

The values of nine levels of calibrators are assigned relative to a master lot which is verified based on replicate GCMS analysis. Calibrators are prepared in phosphate buffer with stabilizers, preservatives, and drug.

To evaluate stability, separate aliquots of calibrator were stored at -80°C and $2-8^{\circ}\text{C}$, the recommended storage temperature. The two sets of calibrators are compared in terms of relative light units (rlu), B/B_0 , (B is rlu for any individual calibrator and B_0 is rlu for the 0-level calibrator) and normalized values (RLU at cutoff/ RLU of an individual calibrator) at a time point of one year. Percent differences in either B/B_0 or normalized values were $<10\%$. (Stability of the assay components used in this testing was independently assessed.) Results support expiration dating in the labeling.

Another set of calibrators were opened daily and tested, similarly. Results of that testing supports the expiration dating for open calibrators, provided in the labeling.

d. *Detection limit:*

To evaluate the limit of the blank, 20 repeat measurements were performed for a negative urine sample. The mean value minus 2 standard deviations was calculated. The resultant normalized value was 14.1.

e. *Analytical specificity:*

Specificity and cross-reactivity of related compounds and metabolites were evaluated using a dose-response series. Each compound was diluted in GCMS verified negative urine to specific concentrations and tested in replicates. Concentrations of cross-reactants which would produce a response equal to that of the target compound were calculated. Results for parent compounds and metabolites are in the table below.

Compound	Concentration (ng/ml) which produce a response equivalent to cocaine metabolite at 300 ng/ml.	% cross-reactivity
Cocaine	4734	6.3
Cocaethylene	7356	4.1
Ecgonine	$>500,000$	<0.06
Ecgonine methyl ester	$>10,000$	<3.0
Norcocaine	$>500,000$	<0.06

More than 80 structurally unrelated drugs were evaluated for potential interference by spiking into negative urine. Results indicated that at an assay cutoff of 300 ng/ml benzyecgonine, a negative response was observed for all the drugs tested. Some of the specific drugs and concentrations at which they were tested are listed in the package insert.

A variety of over-the-counter and prescription drugs were tested for interference by spiking into negative urine and measuring the percent

difference between the control sample (no potential interferent) and the test sample (containing potential interferent). Results are tabulated below:

Compound	Concentration tested (mg/dL)	% difference	Compound	Concentration tested (mg/dL)	% difference
Acetone	1000	-5.0	Hemoglobin	300	1.4
Ascorbic acid	1500	0.8	Riboflavin	7.5	6.3
Creatinine	500	-3.2	Urea	3500	0.9
Ethanol	1000	-5.2	Sodium Chloride	6000	0.6
Galactose	10	-1.9	Acetaminophen	1 mg/mL	2.5
Gamma globulin	500	-2.9	Acetylsalicylic Acid	1 mg/mL	-3.3
Glucose	3000	-1.2	Caffeine	1 mg/mL	-2.2
Human serum albumin	500	-1.5	Ibuprofen	1 mg/mL	-1.0

To evaluate the effect of pH and specific gravity negative urine was adjusted to specific gravity between 1.00 -1.04 and pH was adjusted to 3-11. Acceptable ranges (defined as results within 10% of control samples) were determined to be pH of 3-9.0 and within the specific gravity range of 1.002-1.04.

f. Assay cut-off:

Precision around the 300 ng/mL cutoff was evaluated using urine-based commercial control material. Ten replicates each were measured for samples at the 300 ng/mL cutoff and 25% above and below the 300 ng/mL cutoff. Results are tabulated below. Values are listed as normalized results:

	75% cutoff	100% cutoff	125% cutoff
Mean	81.1	121.7	140.9
SD	8.8	13.7	16.4
%CV	10.9	11.2	11.6

2. Comparison studies:

a. Method comparison with predicate device:

Evaluation of samples using the Randox Cocaine Metabolite Assay was performed at an external laboratory. Results were compared to GCMS, as well as to the predicate device. A total of 1336 clinical urine samples

were selected randomly by the external site and tested using the Randox Cocaine Metabolite Assay, as well as the predicate device. Of these samples, 224 positive samples and 16 negative samples were also compared with GCMS. Based on GCMS determinations, samples spanned the range from 0 to greater than 300,000 ng/mL benzylicgonine and 24 of the samples were within 75% to 125% of the cutoff concentration. Results of the comparison with GCMS are tabulated below:

Randox cocaine metabolite assay	GCMS negative	GCMS near-cutoff negative (within -25%)	GCMS near-cutoff positive (within + 25%)	GCMS positive	Percent agreement with GCMS
Positive	1	11	10	186	94.2%
Negative	13	2	1	0	5.8%

The remainder of the negative samples was compared to the predicate device. Results of the comparison to the predicate device are tabulated below:

Randox		Predicate immunoassay	
		+	-
	+	243	4
	-	1	1088

b. Matrix comparison: Not applicable. The device is indicated only for urine specimens.

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):*

4. Clinical cut-off: Not applicable

5. Expected values/Reference range: Not applicable

M. Instrument Name:

Randox Evidence® Analyzer

N. System Descriptions:1. Modes of Operation:

The immunoassay is performed on the surface of a biochip, which is transported to various treatment stations within the 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. Sample Identification:

Barcoded samples can be used, or patient identification can be entered by the operator.

4. Specimen Sampling and Handling:

Specimen sampling is automated

5. Assay Types:

The Randox Cocaine Metabolite Assay is a qualitative assay.

6. Reaction Types:

The Randox Cocaine Metabolite Assay is a competitive immunoassay performed on a biochip.

7. Calibration:

A calibration curve is generated for each calibration run. Calibration curves are stored in the software and used in calculations. Calibrators are supplied with a calibration CD. The CD contains pre-defined calibration specifications which are loaded directly onto the analyzer software and used to analyze and validate calibration results. Recalibration is recommended with each run and under other manufacturer-specified conditions.

8. Quality Control: External quality control materials are commercially available.**O. Other Supportive Instrument Performance Characteristics Data Not Covered In The "L. Performance Characteristics" Section Of The SE Determination**

Decision Summary. The Evidence Analyzer is designed to comply with IVD Directive 98/79/EC, EN 61010-1, EN 61326, UL 3101-1, FCC Standards on emissions, ISO 9001, Low Voltage Directive 73/23/EEC, EMC Directive 89/336 EEC.

P. Conclusion: I recommend that the Randox Cocaine Metabolite Assay run on the Randox Evidence[®] Analyzer is substantially equivalent to the predicate device.