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

A. 510(k) Number:
K043071

B. Purpose for Submission:
New Device

C. Measurand:
Phencyclidine (PCP)

D. Type of Test:
Qualitative immunoassay

E. Applicant:
Randox Laboratories Limited

F. Proprietary and Established Names:
Randox evidence® Phencyclidine Assay
Randox evidence® Drugs of Abuse Calibrators

G. Regulatory Information:

1. Regulation section:
   21 CFR § 862.3100, Enzyme Immunoassay, Phencyclidine
   21 CFR § 862.3200, Calibrators, Drug Mixture
2. Classification:
   Both Class II
3. Product Code:
   LCM
   DKB
4. Panel:
   Toxicology (91)

H. Intended Use:

1. Intended use(s):
   Refer to Indications for use.

2. Indication(s) for use:
   The Randox evidence® Phencyclidine test has been designed for use only on the evidence® analyzer for qualitative detection of phencyclidine in human urine, using a cutoff concentration of 25 ng/ml. Qualitative results obtained can be utilized in the diagnosis and treatment of phencyclidine use or overdose.

This 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 (GC/MS) is the preferred method. Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are used.

The Phencyclidine Assay must be used only by suitably qualified laboratory personnel under appropriate laboratory conditions.

The evidence® Drugs of Abuse Calibrators are liquid calibrators containing benzoylecgonine, amphetamine, methamphetamine, methadone, opiates, and phencyclidine. There are nine levels of calibrator. They have been developed for use in calibration of the evidence® system.

The evidence® Drugs of Abuse Calibrators must be used only by suitably qualified laboratory personnel under appropriate laboratory conditions.

3. Special condition for use statement(s):

   The device is for in vitro diagnostic use.

   The device is for prescription use.

   The assay is not designated for use in point-of-care settings.

4. Special instrument Requirements:
   This assay is intended to be used on the Randox evidence® system only.

I. Device Description:

The evidence analyser is a fully automated Biochip Array System. It performs simultaneous detection of multiple analytes from a single patient sample. The core technology is the Randox Biochip, a solid-state device containing an array of discrete test regions containing immobilized antibodies specific for various analytes, including phencyclidine.

The evidence® Drugs of Abuse Calibrators are phosphate buffer based materials containing phencyclidine in addition to other analytes. There are nine levels of each analyte supplied in the calibrators. Phencyclidine concentrations range from 0 to 68.7 ng/mL. The sponsor recommends daily calibrations.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Microgenics CEDIA Dau Phencyclidine Assay
2. Predicate K number(s):
   K946059

3. Comparison with predicate:

Both devices are for the qualitative determination of the same analyte(s) in the same matrix, and utilize the same cutoff concentration. The predicate device can also produce semi-quantitative results.
The reagent formulations vary between the two devices.

Similarities		
Item	**Device**	**Predicate**
Matrix	Same	Human Urine
Assay Principle	Same	Competitive Immunoassay
Cutoff	Same	25 ng/mL

Differences		
Item	**Device**	**Predicate**
Type of Measurement	Qualitative Only	Qualitative and Semiquantitative
Analyzer(s)	Evidence Analyzer Only	Multiple Automated Clinical Chemistry Analyzers
Kit Contents	Drugs of Abuse Assay Diluent Drugs of Abuse Assay Conjugate Drugs of Abuse Assay Biochip	1 Enzyme acceptor reconstitution buffer 1a Enzyme acceptor reagent 2 Enzyme donor reconstitution buffer 2a Enzyme donor reagent
Antibody Type and Source	Polyclonal, Sheep	Monoclonal, Mouse
Sample Volume	7 µL	8 µL
Number of Calibrators	9	4

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

NCCLS EP5-T2, Evaluation of Precision Performance of Clinical Chemistry Devices
NCCLS EP7-A, Interference Testing in Clinical Chemistry; Approved Guideline

L. Test Principle:

The Randox Biochip contains polyclonal sheep antibody against phencyclidine (in addition to other drug-specific antibodies). After addition of sample to the biochip, phencyclidine present in the sample competes with phencyclidine labeled with horseradish peroxidase (HRP) for the antibody binding sites. The amount of drug in the sample is inversely proportional to the signal generated; i.e., higher levels of drug in the sample will cause reduced binding of HRP-labeled drug to the biochip and thus a reduction in the chemiluminescent signal.

The light signal generated from the test region on the biochip is detected using digital imaging technology and compared to that from a stored calibration curve. A normalized value is calculated as a percentage of the signal intensity emitted from the cutoff point on the calibration curve relative to the signal intensity emitted from the sample test region. Samples producing a response greater than or equal to the response value of the calibrator cutoff are considered positive (normalized result ≥ 100). Samples producing a response less than the response value of the calibrator cutoff are considered negative (normalized value < 100).

M. Performance Characteristics (if/when applicable):

Performance was demonstrated in this submission on the Randox evidence® analyzer

1. Analytical performance:
    a. Precision/Reproducibility:

    Specimen description: drug free urine spiked with PCP (calibrators)
    Number of days: twenty
    Replicates per day: four (duplicates run twice per day)
    Lots of product used: one
    Number of operators: one per site (see below)
    Operators: manufacturer staff and clinical staff
    Testing Facility: precision studies were conducted at the sponsor's laboratory facilities and at a clinical site

Results of the study are presented below:

PCP Total Precision Study Results

Testing facility	Concentration of sample, ng/mL	Number of determinations	Mean	SD	CV (%)
Sponsor's lab	15.6	80	79.6	5.5	6.9
Sponsor's lab	21.6	80	87.9	8.4	9.6
Sponsor's lab	23.4	80	98.4	8.8	8.9
Sponsor's lab	35.4	80	123.8	17.1	13.8
Clinical site	15.6	80	78.1	11.2	14.3
Clinical site	21.6	80	84.7	12.0	14.2
Clinical site	23.4	80	97.2	12.9	13.3
Clinical site	35.4	80	130.2	21.6	16.6

Results are expressed as normalized values. The sponsor defines a normalized value as the percentage of the Relative Light Units of the cutoff test region / Relative Light Units of the sample test region. Any normalized result ≥ 100 is classified as positive, while any result < 100 is classified as negative.

b. Linearity/assay reportable range:

Not applicable. The assay is intended for qualitative use.

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

The sponsor recommends that Biorad Urine Liquichek ™ Toxicology Controls Levels 1 and 2 be run as routine quality control to validate the calibration.

Nine levels of Calibrators are provided separately. Approximate concentrations of phencyclidine in the calibrators are 0, 5.3, 10.0, 13.7, 18.0, 22.7, 30.3, 47.0, and 68.7 ng/mL.

The sponsor recommends daily calibrations of the test system.

Value Assignment:
The sponsor states that a Master Lot of calibrators has been quantified for the component drugs of abuse in all 9 levels by assaying 4 replicates for each component by GC/MS. The values assigned to each lot are the mean of those measurements. The laboratory performing the analysis is certified by the College of American Pathologists. The Master Lot is stored at –80 ºC and is used to assign concentrations to subsequent calibrator lots.

A minimum of 20 replicates from each subsequent production lot are assayed and quantified by direct comparison to the mean values of a

minimum of 20 replicate standard curves from the Master Lot of calibrators. Results are assigned to the calibrators by applying mean readings read from the standard curves. The acceptable deviation from the Master Lot material is +/- 10%.

Stability:
Stability studies are summarized for the calibrators. Aliquots of the calibrators were stored at -80 ºC for reference purposes (the baseline) while the remainder were stored at 2-8 ºC. After one year, the two sets of calibrators were directly compared. The following acceptance criteria were applied:

The Relative Light Units (RLU), curve shape (B/Bo, where B is the RLU for an individual calibrator level and Bo is the RLU for the level 1 calibrator) and normalized values were examined. A stability of 1 year (at 2-8 ºC) was assigned if the % difference in either %B/Bo or normalized values between the -80 ºC and the 2-8 ºC is less than 10%

Open vial stability was assessed for 14 days, using an acceptance criterion of 10% when compared to the baseline.

d. Detection limit:

The sensitivity of the assay was established by analyzing 20 repeat determinations of a GC/MS verified negative urine sample. The mean normalized value for the 20 replicates was calculated and 2 standard deviations added.

The normalized value of 24 represents the lowest concentration of phencyclidine which can be distinguished from the zero calibrator with a confidence level of 95%.

e. Analytical specificity:
Cross-reactivity was established by spiking various concentrations of similarly structured drug compounds into GC-MS verified drug-free urine. By analyzing various concentration of each compound the sponsor determined the concentration of the drug that produced a response approximately equivalent to the cutoff concentration of the assay. Results of those studies appear in the table(s) below:

Phencyclidine

Compound	Conc Equiv to cutoff (ng/mL)	% Cross-reactivity
Phencyclidine	25	100
1-1-(2-Thienyl-cyclohexyl) piperidine	28	90

The following compounds were evaluated for potential positive interference with the assay. To evaluate for interference the sponsor spiked the following compounds into drug-free urine. The concentrations of those compounds listed below represent the highest concentration tested which produced a negative result with the Phencyclidine assay.

COMPOUND	**CONC (ng/mL)**
(-) PSEUDOEPHEDRINE	500,000
(+) EPHEDRINE	500,000
(+) PSEUDOEPHEDRINE	500,000
1,3-DIMETHYLBARBITURIC ACID	500,000
11-HYDROXY-Δ^9-THC	10,000
11-NOR-Δ^8-THC COOH	10,000
4-BROMO 2,5-DIMETHOXYPHENETHYLAMINE	100,000
4-HYDROXYNORDIAZEPAM	500,000
6-MAM	300,000
7-AMINONITRAZEPAM	500,000
ALPHENAL	100.000
AMOBARBITAL	500,000
APROBARBITAL	50,000
BARBITAL	500,000
BDB	100,000
BENZOYLECGONINE	100,000
BUPRENORPHINE	500,000
BUTABARBITAL	50,000
BUTALBITAL	10,000
CANNABIDIOL	10,000
CANNABINOL	10,000
CODEINE	100,000
CYCLOPENTOBARBITAL	100,000
d,l-AMPHETAMINE	500,000
d-AMPHETAMINE	500,000
DEXTROMETHORPHAN	10,000

COMPOUND	CONC (ng/mL)
DIHYDROCODEINE	100,000
EDDP	500,000
EMDP	500,000
FENCAMFAMINE	150,000
FENFLURAMINE	500,000
FLUNITRAZEPAM	500,000
HEROIN	45,000
HEXOBARBITAL	500,000
HMMA	100,000
HYDROCODONE	27,000
HYDROMORPHONE	15,000
LAAM	500,000
L-AMPHETAMINE	500,000
LORAZEPAM	500,000
LORAZEPAM GLUCURONIDE	10,000
MBDB	500,000
MDA	500,000
MDEA	500,000
MDMA	500,000
MDPA	100,000
MEPHENTERMINE	1,000,000
METHADONE	500,000
MEPHOBARBITAL	500,000
METHAMPHETAMINE	500,000
METHOHEXITAL	500,000
METHOXYPHENAMINE	500,000
MORPHINE	100,000
MORPHINE-3-GLUCURONIDE	46,000
N,N-DIMETHYL-3,4-MDA	500,000
NALORPHINE	50,000
N-ETHYLAMPHETAMINE	500,000
N-HYDROXY-MDA	150,000
NITRAZEPAM	500,000
NORCODEINE	500,000
NORDIAZEPAM	500,000
NORMEPERIDINE	500,000
NOROXYCODONE	500,000
N-PROPYLAMPHETAMINE	100,000
OXAZEPAM	500,000
OXAZEPAM GLUCURONIDE	10,000
OXYCODONE	500,000
OXYMORPHONE	100,000
PENTOBARBITAL	500,000

COMPOUND	CONC (ng/mL)
PHENDIMENTRAZINE	500,000
PHENMETRAZINE	500,000
PHENTERMINE	500,000
PHENYLPROPANOLAMINE	500,000
P-HYDROXY-MA	500,000
p-HYDROXYPHENOBARBITAL	100,000
PROPRANOLOL	500,000
QUINACRINE	500,000
RANITIDINE	500,000
SECOBARBITAL	500,000
TALBUTAL	500,000
TEMAZEPAM	500,000
TEMAZEPAM GLUCURONIDE	10,000
THEBAINE	50,000
THIOPENTAL	500,000

There is the possibility that other substances and/or factors not listed above may interfere with the test and cause false results, e.g., technical or procedural errors.

To test for potential positive/and or negative interference from endogenous conditions the sponsor prepared a study control sample. The control sample consisted of drug-free urine spiked with 25 ng/mL of the targeted drug. The effect of various endogenous compounds is listed below.

Compound	Conc (mg/dL)	% Bias
Acetaminophen	1 mg/mL	-1.0
Acetone	1000	-4.4
Acetylsalicylic Acid	1 mg/mL	-6.6
Ascorbic acid	1500	8.7
Caffeine	1 mg/mL	9.9
Creatinine	500	0.1
Ethanol	1000	-9.0
Galactose	10	-6.7
Gamma globulin	500	-1.7
Glucose	1.75 g/dL	10.0
Glucose	3 g/dL	21.3
Hemoglobin	300	9.1
Human Serum albumin	500	-1.9
Ibuprofen	1 mg/mL	7.5

Oxalic acid	100	1.2
Ranitidine	0.9 mg/mL	-5.7
Riboflavin	7.5	6.4
Sodium Chloride	6000	4.8
Urea	1100	-4.1

Aliquots of the control sample were then altered to span the following ranges of conditions, and analyzed: pH from 3-11 and specific gravity from 1.002 to 1.04. Results were as follows:

Sample pH	PCP (ng/mL)	% diff from pH 7
3	24.1	7.1
5	23.1	2.6
7	22.5	0.0
9	23.3	3.4
11	21.6	-4.2
Specific gravity	PCP (ng/mL)	% diff from sp. gr. of 1.002
1.002	21.0	0.0
1.012	22.4	6.5
1.021	21.4	1.6
1.031	23.1	9.7
1.04	28.6	36.2

f. Assay cut-off:

The identified cutoff concentration of the assay is recommended for use by the Substance Abuse and Mental Health Services Administration (SAMHSA).

In order to characterize how the device performs around the cutoff, the sponsor analyzed a commercial calibrator at a concentration of 25% below the cutoff and 25% above the cutoff. In addition, the two calibrators were combined to produce a concentration at the cutoff.

Results were as follows:

Sample replicate	Normalized Results		
	Cutoff - 25%	Cutoff	Cutoff + 25%
1	82.7	106.7	126.6
2	89.7	105.2	127.9
3	72.1	109.0	139.7
4	84.4	102.4	136.9
5	82.9	99.5	131.4
6	82.8	123.4	139.1
7	95.6	112.0	123.9
8	86.4	119.1	135.0
9	73.9	102.2	118.4
10	82.4	103.7	123.6
Mean	83.3	108.3	130.3
Standard Deviation	6.8	7.8	7.3
% Coefficient of Variation	8.2	7.2	5.6
n	10	10	10

2 Comparison studies:

g. Method comparison with predicate device:

A total of 1365 samples (1259 negative and 106 positive) were evaluated by the candidate device and the predicate device. Samples are designated as positive or negative according to the predicate device result.

A total of 144 samples were evaluated by the candidate device and by GC-MS. Samples are designated as positive or negative by comparing the GC-MS result to the sponsor's cutoff. The sponsor states that borderline, positive, or discrepant samples were analyzed by GC/MS. This included 41 samples that were below the cutoff concentration of the assay and 103 samples that were at or above the cutoff concentration of the assay, as measured by GC-MS.

Sample description: 1365 unaltered clinical urine samples were evaluated. Ten additional diluted samples were also included in the study. The samples were prepared by diluting clinical samples with high drug concentrations with drug-free urine. This was done in order to obtain samples near the cutoff concentration of the assay,

because the sponsor was not able to obtain unaltered samples near the cutoff.

Sample selection: Samples previously analyzed by the predicate device were selected to be analyzed by the candidate device.

The study included an adequate number of samples that contained drugs near to the cutoff concentration of the assay. Approximately 10% of the study samples are evenly distributed between plus and minus 50% of the claimed cutoff concentration.

Number of study sites: one
Type of study site(s): clinical setting

Operator description: clinical site staff

Candidate Device Results vs. Predicate Device Results

	Positive by Predicate Device	Negative by Predicate Device
Positive by Candidate Device	105	22
Negative by Candidate Device	1	1237

% Agreement among positives is 99%
% Agreement among negatives is 98%

Candidate Device Results vs. stratified GC/MS Values

Candidate Device Results	0 concentration by GC-MS	Less than 50% below the cutoff concentration but greater than 0 by GC/MS	Between 50% below the cutoff and 25% below the cutoff	Between the cutoff and 24% below the cutoff	Between the cutoff and 24% above the cutoff concentration	Between 25% above the cutoff and 50% above the cutoff	High Positive (greater than 50% above the cutoff concentration)
Positive	7	1	7	9	9	9	85
Negative	16	0	1	0	0	0	0

GC/MS values used to categorize samples in this table are based on the concentration of phencyclidine found in the sample.

% Agreement among positives is 100%
% Agreement among negatives is 41%

h. Matrix comparison:
Not applicable. The assay is intended for only one sample matrix.

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.

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.