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

A. 510(k) Number:

k111926

B. Purpose for Submission:

New device

C. Measurand:

Opiates

D. Type of Test:

Qualitative enzyme immunoassay (EIA)

E. Applicant:

Psychemedics Corp.

F. Proprietary and Established Names:

Psychemedics Microplate EIA for Opiates in Hair

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
DJG	Class II	862.3650 – Opiate test system	91-Toxicology

H. Intended Use:

1. Intended use(s):

   See indications for use below.

2. Indication(s) for use:

   The Psychemedics Microplate EIA for Opiates is an enzyme immunoassay (EIA) for the preliminary qualitative detection of opiates in human head and body hair using a morphine calibrator at 2 ng /10 mg hair cutoff for the purpose of

identifying opiate use. This is an *in vitro* diagnostic device intended exclusively for Psychemedics use only and is not intended for sale to anyone.

The Psychemedics Microplate EIA for Opiates assay provides only a preliminary analytical test result. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. Gas or Liquid Chromatography/Mass Spectrometry (GC/MS or LC/MS or LC/MS/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.

3. Special conditions for use statement(s):

   This assay is for over the counter use.

4. Special instrument requirements:

   The device is for use with a microplate reader capable of measuring at 450 and 650 nm. Plate washing also requires an instrument specifically designed to effectively and reproducibly wash all wells uniformly.

I. Device Description:

The test consists of two parts; a pre-analytical hair treatment procedure (to convert the solid matrix of hair to a measurable liquid matrix) and the screening assay, the Psychemedics Microplate EIA for Opiates. The drug is recovered from the hair using a patented method. The screening portion of the test system consists of (1) microplate wells coated with multiple drugs including morphine conjugated to bovine serum albumin (BSA), polyclonal sheep anti-morphine, rabbit anti-goat secondary antibody conjugated to HRP (horseradish peroxidase), substrate [3, 3', 5, 5' tetramethylbenzidine (TMB)], HCl to acidify the final reaction, and wash buffer for washing the plates. Absorbance in the wells is read with a microplate reader.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Psychemedics Morphine RIA Assay

2. Predicate K number(s):

   k000851

3. Comparison with predicate:

Item	Device	Predicate
Indications/ Intended Use	The Psychemedics Microplate EIA for Opiates is an enzyme immunoassay (EIA) for the preliminary qualitative detection of opiates in human head and body hair using a morphine calibrator at 2 ng /10 mg hair cutoff for the purpose of identifying opiate use.	Same
Sample matrix	Hair	Same
Method of measurement	Microplate reader	Gamma counter
Cutoff	2 ng morphine/10 mg hair	Same
Test Principle	EIA	RIA

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

None were referenced.

L. Test Principle:

Hair sample extracts and primary antibody are combined in the wells and incubated. After washing, secondary antibody-HRP is added and incubated. After washing, substrate is added, and, after a final incubation, the wells are acidified and read with the microplate reader. Results are normalized by expression as B/B0 x 100. If morphine or related opiates are present in the sample, less primary antibody will be bound to the solid-phase antigen, thereby resulting in less binding of HRP-labeled secondary antibody; the absorbance produced is inversely proportional to the amount of opiates in the sample (specimen, calibrator or control).

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Precision studies were performed by taking commercially available materials consisting of morphine in methanol, to prepare spiking solutions at the following concentrations; negative, ±75%, ±50%, ±25% and 100% of the cutoff. The concentration of each sample was confirmed by LC/MS/MS. The morphine solutions were then used to spike 15 replicates of negative hair samples. Intra-assay precision was performed in one run and inter-assay precision was performed over 5 non-consecutive days. The results are presented in the tables below:

Intra-assay

Opiate (ng/ 10mg hair)	Percent of Cut-off	Replicate Number	Pos/Neg
0	-100%	15	0/15
0.5	-75%	15	0/15
1.0	-50%	15	0/15
1.5	-25%	15	0/15
2.5	+25%	15	15/0
3.0	+50%	15	15/0
3.5	+75%	15	15/0
4.0	+100%	15	15/0

Inter-assay

Opiate (ng/10 mg hair)	Percent of Cut-off	Replicate Number	Pos/Neg
0	-100%	75	0/75
0.5	-75%	75	0/75
1.0	-50%	75	0/75
1.5	-25%	75	0/75
2.5	+25%	75	75/0
3.0	+50%	75	75/0
3.5	+75%	75	75/0
4.0	+100%	75	75/0

b. Linearity/assay reportable range:

Not applicable. This is a qualitative assay.

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

Psychemedics manufactures calibrators and control materials using drug stocks purchased from a commercial vendor. Each lot of drug is received with its specific certificate of analysis. The commercially obtained stock is made into the calibrators and controls to the desired concentrations. The concentrations are confirmed by GC/MS.

Stability studies for both controls and calibrators have been conducted. Protocols and acceptance criteria were described and found to be acceptable. The manufacturer claims the following expiration date for both controls and calibrators:

When stored at less than or equal to 10 ºC product is stable for 12 months.

d. Detection limit:

Not required since this is a qualitative test

e. Analytical specificity:

Cross-reactivity was established by spiking various concentrations of each substance into drug-free sample and evaluating the result against the cutoff control.

Results are expressed as the concentration of compound required to produce a response approximately equivalent to the cutoff concentration of the assay. The results are presented in the table below:

Compound	Approximate concentration of compound (pg/mg) Equivalent to 2 ng/10 mg hair Opiate Cutoff	% Cross reactivity
Codeine	1.8	111
Hydromorphone	38	5.2
Hydrocodone	4.8	41.7
Acetylcodeine	3.5	57.1
6-Acetylmorphine	4.6	43.5
Oxycodone	46	4.3
Oxymorphone	250	<1
Methadone	>5000	<1
Morphine Glucuronide	13.3	15
Naloxone	>1000	< 0.2%
Naltrexone	>1000	< 0.2%
Propoxyphene	>1000	< 0.2%
Meperidine	>1000	< 0.2%

Structurally unrelated:

Negative hair samples were spiked with morphine to -50%, and +50% of the cutoff. Structurally related and unrelated compounds were added to methanol to a concentration of 100 ng/10 mg hair then added to the negative hair

sample. The following compounds do not cause interference at +/- 50% of the cutoff; Anhydroecgonine methyl ester, Atropine, Bupropion, Cotinine, Cannabinol, Chlorpheniramine maleate, O-Desmethyvenlafaxine, Desipramine, Doxylamine succinate, 1S, 2R Ephedrine, Ethosuximide, Ibuprofen, LSD, Haloperidol, Meperidine, Methadone, Methaqualone, Methyl phenidate, Naloxone, Naltrexone, Nicotine, Naproxen, Nortriptyline, Propoxyphene, R,R Pseudoephedrine, Thioridazine, Cis-Tramadol, Venlafaxine hydrochloride, 8(-)-11-nor-9-Carboxy-delta-9 THC, 11-nor-9-Carboxy-delta-9-THC, Delta 8-THC, Streptomycin, Procaine, Benzocaine, Erythromycin, Penicillin G, Mepivacaine, Phendimetrazine bitartrate, Diazepam, Despropionyl fentanyl, Ethylmorphine, Nalorphine, Codeine, Morphine, Hydromorphone, Oxycodone, Glutethimide, Meprobamate, Methyprylon, Flurazepam, Lorazepam, Medazepam, Temazepam, Carbamazepine, Diazepam, Nordiazepam, Oxazepam, Acetaminophen, Caffeine, Dyphylline, Methaqualone, Theophylline, Amitriptyline, Dextromethorphan, Lidocaine, Methocarbamol, Nordoxepin, Pentazocine, Phenylephrine, Triamterene, Ethosuximide, a-methyl-a-propylsuccimide, metharbital, barbital, methsuximide, phensuximide, phensuximide, N-Normethsuximide, Mephenytoin, Ethotoin, Mephobarbital, PEMA, Phenobarbital, Methyl PEMA, 10,11-Dihydrocarbamazepine, Primidone, Carbamazepine, 5,5-Diphenylhydantoin, 4-Methylprimidone, Butabarbital, Amobarbital, Secobarbital, Hexobarbital, Phenobarbital, Medazepam, Oxazepam, Lorazepam, Diazepam, Temazepam, Bromazepam, Amitriptyline, Desipramine, Doxepin, Imipramine, Nordoxepin, Nortiptyline, Protriptyline, Trimipramine, Glutethimide, Chlorpromazine, Flurazepam, Amoxillin, Propanolol, Promethazine, Phenmetrazinbe, Phendimetrazine, Benzocaine, Ecgonine, Metanephrin, amphetamine, caffeine, Imipramine, Methamphetamine, Phencyclidine, Phenmetrazine, Phenylpropanolamine, Cocaine, Cocaethylene, amitripty;ine, Dextromethrophan, Lidocaine, Methocarbamol, Nordoxepin, Pentazocine, Phenylephrine, Triamterene, Pheniramine, Mephenytoin, Orphenadrine, Methylphenidate, Ibuprofen.

There is the possibility that other substances and/or factors not listed above may interfere with the test and cause false results.

Cosmetic Treatment

Tests were performed to determine the effects of various hair treatments (i.e. bleaching, dyeing, relaxer, shampoo, permanent) on samples tested using the Psychemedics Microplate EIA for Opiates. The ethnic origin, hair color and curvature were documented.

Effects on Positive Samples:

60 specimens determined to be positive for opiate were used in the study. The study was conducted with two different hair treatments.

Six different hair samples were used for each hair treatment. ELSIA absorbance readings before and after treatment were compared. Average changes in absorbance values after were -2.25% for bleach, -4.65% for dye, -4.5% for perm, -3.15% for relaxer and 1.1% for shampoo, where a negative sign indicates a sample becoming "more negative" due to treatment an a positive sign indicates a sample becoming "more positive." None of the positive samples became negative after treatment.

Effect on Negative Samples:

One hundred specimens previously determined to be negative were used in the study. The study was conducted with two different hair treatments. Ten different hair samples were used for each hair treatment. ELSIA absorbance readings before and after treatment were compared. All samples determined to be negative prior to treatment remained negative post treatment

Environmental Study:

Preliminary positive hair sample results by the screening method could be due to environmental contamination. All positive should be sent for confirmation testing on a reference method to distinguish between true positive and those samples that were positive due to external exposure.

f. Assay cut-off:

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

2. Comparison studies:

a. Method comparison with predicate device:

The study was performed by comparing ELSIA results against the LC/MS/MS results on the same head or body hair samples. A total of 243 donor hair samples were tested (97 negative and 146 positive). The results are presented in the table below:

Opiate Test Result	Negative by GC/MS	Less than half the cutoff concentration by GC/MS	Near Cutoff Negative (Between 50% below the cutoff and the cutoff concentration)	Near Cutoff Positive (Between the cutoff and 50% above the cutoff concentration)	High Positive (Greater than 50% above the cutoff concentration)
Positive	0	2	8	10	136
Negative	86	11	2	0	0

Screening Cutoff (ng/10 mg hair)	ELSIA Opiate Test Results (POS/NEG)	LC/MS/MS Drug Result (pg/ 10 mg hair)
2	POS	0.9 oxycodone
2	POS	0.9 hydrocodone
2	POS	1.2 hydrocodone
2	POS	1.4 hydrocodone
2	POS	1.4 hydrocodone
2	POS	1.4 hydrocodone
2	POS	1.5 hydrocodone
2	POS	1.5 6-MAM
2	POS	1.5 hydrocodone
2	POS	1.7 6-MAM and oxycodone

b. Matrix comparison:

Not applicable. The assay is intended for only one sample matrix.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

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

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Not applicable

N. Proposed Labeling:

They have not provided adequate 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.